REVIEW: WILDLIFE ECOLOGY

Emerging Infectious Diseases of Wildlife—Threats to Biodiversity and Human Health

Peter Daszak,[1, 2*] Andrew A. Cunningham,[3] Alex D. Hyatt[4]

Emerging infectious diseases (EIDs) of free-living wild animals can be classified into three major groups on the basis of key epizootiological criteria: (i) EIDs associated with "spill-over" from domestic animals to wildlife populations living in proximity; (ii) EIDs related directly to human intervention, via host or parasite translocations; and (iii) EIDs with no overt human or domestic animal involvement. These phenomena have two major biological implications: first, many wildlife species are reservoirs of pathogens that threaten domestic animal and human health; second, wildlife EIDs pose a substantial threat to the conservation of global biodiversity.

The past two decades have seen the emergence of pathogenic infectious diseases, such as acquired immunodeficiency syndrome, multidrug-resistant tuberculosis, and tick-borne diseases, which represent a substantial global threat to human health (*1*). Emergence is associated with a range of underlying causal factors (*1*, *2*). These include interactions with zoonotic pathogens within a host-parasite continuum between wildlife, domestic animal, and human populations (Fig. 1). In this review, we identify a number of EIDs that predominantly involve wildlife [(*3*, *4*), Table 1, and Web table 1 (*5*)]. We define wildlife EIDs by applying criteria similar to those used to define human EIDs (*1*, *2*) and categorize them according to their specific characteristics that are "emerging" or novel (Table 2) and to their epizootiology.

Wildlife EID, Past and Present

Parallels between human and wildlife EIDs extend to early human colonization of the globe and the dissemination of exotic pathogens. In the same way that Spanish conquistadors introduced smallpox and measles to the Americas, the movement of domestic and other animals during colonization introduced their own suite of pathogens. The African rinderpest panzootic of the late 1880s and 1890s is a paradigm for the introduction, spread, and impact of virulent exotic pathogens on wildlife populations (*4*, *6*). This highly pathogenic morbillivirus disease, enzootic to Asia, was introduced into Africa in 1889. The panzootic front traveled 5000 km in 10 years, reaching the Cape of Good Hope by 1897, extirpating more than 90% of Kenya's buffalo population and causing secondary effects on predator populations and local extinctions of the tsetse fly. Populations of some species remain depleted and the persistence of rinderpest in eastern Africa continues to threaten bovid populations.

Pandemics of cholera, influenza, and other diseases seriously impact human populations. Such clear-cut panzootic outbreaks of diseases in wildlife are probably rare events, but a lack of awareness and reporting, particularly during the earlier decades of European expansion, almost certainly belies their true extent. Historically, wildlife diseases have been considered important only when agriculture or human health have been threatened. However, because of outbreaks of disease in endangered species (*7*), increasing veterinary involvement (*8*, *9*), and advances in host-parasite population biology (*4*, *10*), the threat of wildlife diseases is now taken more seriously (*11–13*).

Common Causal Themes

The increasing number of wildlife EIDs may reflect increasing vigilance, but parallels between causal factors driving the emergence of human and wildlife EIDs suggest that this trend is valid (*14*) (Fig. 1). Disease emergence most frequently results from a change in ecology of host, pathogen, or both (*15*). Human population expansion has driven the emergence of EIDs via increasing population density, especially in urban areas (dengue, cholera), and encroachment into wildlife habitat (Ross River virus disease) (*2*, *16*). This encroachment may have been a key factor in Africa for the global emergence of Marburg and Ebola viruses and human immunodeficiency virus (HIV) (*2*, *17*). Pressures of human encroachment on shrinking wildlife habitat also cause increased wildlife population densities and the emergence of wildlife EIDs (*11–13*, *18*). The international movement of livestock and modern agricultural practices have led to EIDs such as rinderpest in Africa and bovine spongiform encephalitis (BSE) in Europe. Similar situations occur in wildlife populations managed either in situ or in captivity. The extent of in situ management may be substantially underestimated. Recent analysis (*19*) suggests that 15,000 tons of pea-

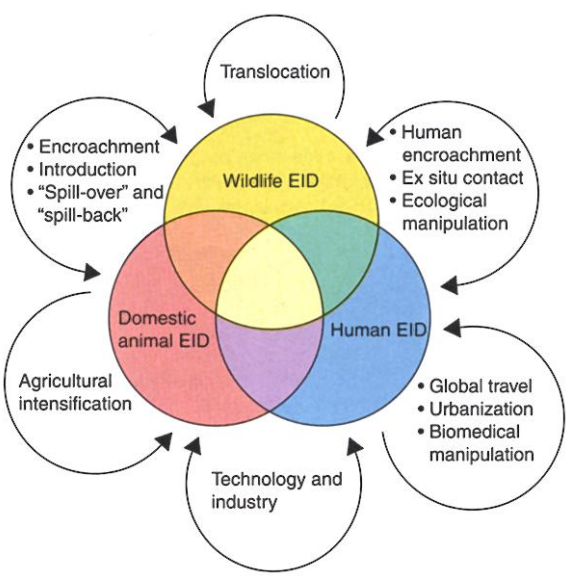

Fig. 1. The host-parasite ecological continuum (here parasites include viruses and parasitic prokaryotes). Most emerging diseases exist within a host and parasite continuum between wildlife, domestic animal, and human populations. Few diseases affect exclusively any one group, and the complex relations between host populations set the scene for disease emergence. Examples of EIDs that overlap these categories are canine distemper (domestic animals to wildlife), Lyme disease (wildlife to humans), cat scratch fever (domestic animals to humans) and rabies (all three categories). Arrows denote some of the key factors driving disease emergence.

[1]Institute of Ecology, University of Georgia, Athens, GA 30602, USA. [2]Infectious Disease and Pathology Activity, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. [3]Institute of Zoology, Zoological Society of London, Regent's Park, London NW1 4RY, UK. [4]Australian Animal Health Laboratory, CSIRO, Private Bag 24, Geelong, Victoria 3220, Australia.

*To whom correspondence should be addressed. E-mail: daszak@uga.edu

nuts are fed annually to United Kingdom garden birds. This form of provisioning has led to the emergence of infection by *Salmonella typhimurium* DT40 and *Escherichia coli* 086:K61 in Britain and *Mycoplasma gallisepticum* in the United States. because of a high density and diversity of birds at feeding stations (*19*). The maintenance of brucellosis in bison in the Grand Teton National Park (United States) is related to the presence of disease in managed sympatric elk (*20*). Even changes in arable farming may lead to disease emergence, such as the shift in agriculture from the eastern United States to the Midwest, which allowed reforestation of New England, providing the conditions for Lyme disease emergence (*21*).

Anthropogenic global climate change is likely to cause major changes to the geographic range and incidence of arthropod-borne infectious diseases. Expansion of mosquito vector geographical ranges has been proposed to explain the reemergence of malaria and dengue in South America, central Africa, and Asia during the 1980s and 1990s (*22*). Similarly, the biting midge vector for African horse sickness (AHS) and bluetongue has recently invaded Europe and North Africa (*23*).

Spill-Over and "Spill-Back"

The transmission of infectious agents from reservoir animal populations (often domesticated species) to sympatric wildlife, termed spill-over, underpins the emergence of a range of wildlife EIDs. Spill-over is a particular threat to endangered species, because the presence of infected reservoir hosts can lower the pathogen's threshold density and lead to local (population) extinction (*8*, *9*, *11*). Populations of the African wild dog (*Lycaon pictus*) have been declining since the 1960s. This species is now endangered and, with a fragmented population of less than 5000, is susceptible to stochastic events such as disease outbreaks. Wild dogs became extinct in the Serengeti in 1991, concurrent with epizootic canine distemper in sympatric domestic dogs (*18*, *24*). Rabies has also caused mortality of wild dogs, and a viral variant

Table 1. Selected emerging* infectious diseases (EIDs) of humans and terrestrial wildlife, classified to demonstrate degrees of involvement of humans, domesticated animals, and wildlife. Taken together with those mentioned in text, this list is representative, and examples are chosen purely to demonstrate the range of pathogens, hosts, and factors underlying emergence. The expanded table (Web table 1) is available as supplementary material (*5*). EIDs that involve only humans, both humans and domesticated animals, or domesticated animals only are not included. EIDs of marine environments are covered in a separate, related paper (*3*).

Disease and class of EID†	Pathogen	Hosts‡	Geography of emergence	Impact on wildlife populations	Factors associated with emergence	Refs.
		Humans–domestic animals–wildlife				
Hendra virus disease 1	Hendra virus (paramyxovirus)	Humans, horses, fruit bat reservoir	Australia, Papua New Guinea	Unknown	Unknown	(*16*)
Nipah virus disease 1	Nipah virus (paramyxovirus)	Humans, domestic pigs and dogs, fruit bats	Malaysia and Singapore	Unknown	Unknown	(*45*)
Cryptosporidiosis 4	*Cryptosporidium parvum* (protozoan parasite)	Humans, cattle, wild rodents and other mammals	Europe, USA	Unknown	Farming practices, emergence of HIV, cross-species transfer	(*36*)
		Humans–wildlife				
Hantavirus pulmonary syndrome 1	Sin Nombre and other strains of hantavirus (bunyaviruses)	Humans, *Peromyscus* spp., and other rodents	Americas, esp. SW USA	Probably little impact	ENSO event and human encroachment	(*37*)
Marburg virus and Ebola virus hemorrhagic fever 1	Marburg and Ebola virus (filoviruses)	Humans and nonhuman primates, insectivorous or fruit bat reservoir suspected	Sub-Saharan Africa, Indonesia, Philippines	High mortality in captive and wild nonhuman primates	Marburg: translocation of infected monkeys for lab research; Ebola: contact with infected human or nonhuman carcasses or patients	(*17*)
Human monocytotropic granulocytotropic ehrlichioses 1,4	*Ehrlichia chaffeensis, E. phagocytophila and E. equi* (tick-borne rickettsia)	Humans, cervids, horses, dogs and others	USA, Europe, Africa	Apparently little impact, but underresearched	Uncertain	(*64*)
Plague 4	*Yersinia pestis* (bacterium)	Humans, wide range of mammalian (especially rodent) hosts	Panglobal, notably India, SW USA	High mortality in prairie dog towns during epizootics leading to declines in endangered black-footed ferret	Enzootic foci are remnants of last panzootic outbreak in early 1900s	(*65*)
		Domestic animals–wildlife				
Canine distemper 3	Canine distemper virus (morbillivirus)	Wide range of carnivores	USA, Africa	Extinction of African wild dog and black-footed ferret populations; threat to Ethiopian wolf	Spill-over from domesticated dogs	(*7*, *24*)

common in sympatric domestic dogs has been identified from one such incident (*25*). The geographic expansion of human populations and the consequent encroachment of domestic dog carriers may explain the emergence and impact of rabies in wild dogs in the Serengeti (*25*).

Spill-over epizootic outbreaks represent a serious threat both to wildlife and, via reverse spill-over ("spill-back"), to sympatric populations of susceptible domesticated animals. Brucellosis was probably introduced into America with cattle. In Yellowstone National Park (United States), the presence of this disease in elk and bison is considered a potential threat to domesticated cattle grazing at the park boundaries (*20*). Other examples of spill-over infections include sarcoptic mange in foxes (Europe) and wombats (Australia) and bovine tuberculosis (global). The latter threatens to spill back to domestic livestock (*8*, *9*) and, ultimately, to humans.

Emergence Owing to Host or Parasite Translocations

The translocation of wildlife for conservation, agriculture, and hunting occurs on a global scale, with an inherent risk of exposure of wildlife species to exotic infectious agents

Table 1. (*continued*)

Disease and class of EID†	Pathogen	Hosts‡	Geography of emergence	Impact on wildlife populations	Factors associated with emergence	Refs.
		Humans–domestic animals–wildlife (continued)				
Canine parvovirus disease 1	Canine parvovirus	Canids	Europe, USA	Suspected cause of gray wolf population declines; threat to Ethiopian wolf	Evolution of novel strain, contact with domestic dogs	(*66*)
Varroasis 2	*Varroa jacobsoni* (mite)	Wild and domesticated honeybees	Panglobal except Australasia and C. Africa	Catastrophic mass mortality, e.g., 75% loss of feral colonies in California	Introduction of hosts into enzootic region	(*28*)
Neurotropic velogenic Newcastle disease 2	Newcastle disease virus (paramyxovirus)	Double-crested cormorants, pelicans, gulls, poultry	Canada, USA	High mortality rates (up to 80 to 90%)	Unknown	(*67*)
Sarcoptic mange 2	*Sarcoptes scabiei* (mite)	Mammals	Australia, UK, Sweden	Recent threat to wildlife in Sweden; emerging threat to wombats in Australia	Dispersal of infected wildlife; domestic dog–wildlife interactions	(*68*)
		Wild animals only				
Amphibian chytridiomycosis 1	*Batrachochytrium dendrobatidis* (fungus)	Range of amphibian species, including anurans and salamanders	Australia, Central and North America	Mass mortalities, population declines, local and possibly global extinctions	Unknown; evidence indicates introduced pathogen and possibly associated with climate change in C. America	(*40*, *41*)
Viral chorioretinitis "Kangaroo blindness" 1	Wallal virus and possibly Warrego virus; vector-borne orbivirus	Kangaroo spp.	Australia	Substantial mortalities	Unknown; possibly weather related	(*69*)
Crayfish plague 2	*Aphanomyces astaci* (fungus)	Crayfish	Europe	High mortality rates with population declines, threatening native species with extinction	Introduction of infected North American crayfish (in which the infection is enzootic and nonlethal)	(*70*)
		Captive wild animals				
Steinhausiosis	*Steinhausia* sp. (protozoan parasite)	*Partula* snails		Global extinction of *P. turgida*	Unknown	(*54*, *55*)
Avian malaria	*Plasmodium* spp. (protozoan parasites)	Birds		High mortality in susceptible species, e.g., penguins	Translocation of naïve animals to enzootic regions	(*71*)
Pneumonia	Ophidian paramyxovirus	Snakes		Epizootics with high mortality rates	Unknown	(*72*)

*Before this review, few wildlife diseases had been labeled "emerging" (*19*, *73*). The criteria used to distinguish emerging from established infectious diseases are described in the introduction and in Table 2. †EID are classified on the basis of their "emerging" characteristics, according to criteria listed in Table 2. EID of captive wild animals are not classified since geographic range is not relevant in these cases. ‡Not all hosts are listed. The identity of reservoir hosts for some EID remains uncertain.

(*4*, *8*, *9*). Translocation and introduction of animals to new geographic regions correspond to increased human global travel and commerce as underlying factors for infectious disease emergence (*2*, *14*). The translocation of fish, and possibly amphibians, may have driven the emergence of ranavirus epizootics as threats to freshwater fish and wild herpetofauna (*26*). Similarly, a rabies epizootic in the mid-Atlantic region of the United States resulted from translocation of infected raccoons from a southeastern U.S. enzootic focus (*27*). The introduction of potential hosts into new geographic areas without co-introduction of pathogens can also result in disease emergence. For example, varroasis, a disease of honeybees caused by the mite *Varroa jacobsoni*, spread globally (except Australia) after the European honeybee (*Apis mellifera*) was introduced into Asia (*28*).

This form of emergence is a particular concern to conservation programs that bring allopatric endangered species into close proximity or that alter basic host-parasite variables such as population density and structure (*8*, *9*, *11*, *13*). Molecular analyses of a newly discovered herpesvirus associated with disease in captive elephants indicate that a normally benign herpesvirus of the African elephant can be lethal to its Asian cousin (*29*). Another notable example is the exposure of zoo animals in the United Kingdom to food contaminated by the BSE agent (*30*). Scrapie-like spongiform encephalopathies thought to result from exposure to the BSE agent have been confirmed in 58 zoo animals of 17 species (*31*). Recommendations have been published to preempt the potentially disastrous consequences to wildlife, agriculture, and public health should BSE be introduced into free-living wildlife (*31*).

Risk factors for disease emergence in conservation programs are complex. For example, epizootic toxoplasmosis, with high mortality rates, has occurred in captive lemurs, New World primates, and Australian marsupials. These animals evolved in the absence of *Toxoplasma gondii*, and only recently, after human intervention (translocation), they have been exposed to the parasite (*32*). The feeding of contaminated neonate mice to captive callitrichid primates (marmosets and tamarins) led to the emergence of callitrichid hepatitis (*32*), caused by a variant of the zoonotic pathogen, lymphocytic choriomeningitis virus (LCMV). The zoonotic risk of LCMV is mirrored by the transfer of pathogens from humans to wildlife species. For example, measles contracted from humans threatens wild mountain gorillas habituated to tourists, and poliovirus has killed chimpanzees in the Gombe National Park in Tanzania (*33*).

Captive breeding programs aim to maintain genetically viable, healthy populations for subsequent release into the wild. The potential transfer of pathogens into previously unexposed wild populations in often sensitive, protected areas represents a serious challenge to conservation efforts (*8*, *9*, *13*). This can impinge on release programs even when no apparent disease is observed. The release of captive-reared field crickets (*Gryllus campestris*) was suspended in England after the discovery of unidentified, potentially exotic parasites that were not associated with ill-health, but that posed a disease threat to sympatric wild species at release sites (*34*). The loss of host-specific parasites from endangered species in captive breeding programs is also a substantial threat to biodiversity conservation. In addition to ethical obligations to conserve parasite assemblages along with their more favored hosts (*35*), the maintenance of established host-parasite relations may be important for the overall well-being of the host species both at an individual level (maintenance of immunity) and at a population level (maintenance of genetic diversity) (*8*, *9*, *11*–*13*).

Table 2. Definition and classification of EIDs of wildlife based on fundamental epizootiological parameters derived from (*1*, *2*). EIDs of humans are defined as diseases that are newly recognized, newly appeared in the population, or are rapidly increasing in incidence or geographic range (*1*, *2*). Here, and in Table 1, we classify EIDs according to their specific characteristics that are emerging or novel. E, emerging, new or increasing; R, recognized.

EID type	Infectious agent	Host species	Incidence or geographic range
1	E	E	E
2	R	E	E
3	R	E	R
4	R	R	E

Emergence Without Overt Human Involvement

Correlations between emergence of human diseases (such as cryptosporidiosis, hemorrhagic fevers, cholera, and malaria) and weather patterns [flooding, the El Niño Southern Oscillation (ENSO)] are common (*36*, *37*). These patterns may also cause changes in parasite prevalence and intensity and host mortality rates in wild animals such as the 3- to 4-year cycles of population crashes in feral sheep on the St. Kilda archipelago, Scotland (*38*), and major epizootics of AHS every 10 to 15 years in South Africa (*39*). There is increasing evidence that the frequency and severity of these events are influenced by anthropogenic effects on the climate.

A newly discovered fungal disease, cutaneous chytridiomycosis, has recently been identified as the cause of amphibian mortality linked to declines in Central American and Australian rain forests (*40*). The emergence of chytridiomycosis in amphibians radically changes our view of wildlife EIDs, because it is the first such disease to emerge in "pristine" sites, to infect a wide range of hosts, and to cause declines and possibly extinctions in disparate regions. Hypotheses for the relatively synchronous emergence of amphibian chytridiomycosis globally include human-assisted introduction to previously unexposed amphibian populations (*41*), or an alteration of preexisting host-parasite relations owing to climate change (*42*).

The Zoonotic Threat

Most human EIDs result from exposure to zoonotic pathogens, that is, those transmitted naturally between animals and humans, with or without establishment of a new life-cycle in humans. Wildlife play a key role in their emergence by providing a "zoonotic pool" from which previously unknown pathogens may emerge (*2*). This occurs classically for influenza virus, which causes pandemics in humans after periodic exchange of genes between the viruses of wild and domestic birds, pigs, and humans. Recent nucleic acid sequence analyses have demonstrated direct transmission of avian influenza to humans (*43*) and have identified potential nonhuman primate reservoirs from which HIV types 1 and 2 originated (*44*). Natural reservoir hosts for Ebola and Marburg viruses have proved more elusive (*17*), although fruit or insectivorous bats, insectivores, and rodents have been tentatively implicated. The link to bats is strengthened because (i) they can support replication of experimentally inoculated virus, (ii) human infection has occurred near bat-roosting sites, and (iii) Ebola virus subtypes have been identified in geographically dispersed regions (including Madagascar and the Philippines). Sequence analysis suggests that separate Ebola outbreaks are associated with distinct emergence events, occurring either directly from the primary reservoir, or via secondary or tertiary intermediate hosts. Similar chain events are thought to have occurred in Australia for Hendra virus (fruit bat reservoir, horses, and humans) and Menangle virus (fruit bat reservoir, domesticated pigs, and humans) (*16*), and in Malaysia and Singapore for Nipah virus (fruit bat reservoir), which causes a fatal disease of humans, dogs, and pigs (*45*). The involvement of fruit bats in this high-profile group of EIDs has implications for further zoonotic disease emergence. A number of species are endemic to remote oceanic islands, and these may harbor enzootic, potentially zoonotic, pathogens.

Searches for new zoonotic pathogens have become part of the strategy to counter emerging disease threats to humans, and knowledge from studies of known pathogens can assist in

this surveillance. Telford *et al.* (*46*) compared guilds of deer tick-transmitted zoonotic pathogens in Eurasian *Ixodes* spp. ticks with those described from America and discovered a novel flavivirus, "deer tick virus," related to the virulent Powassan virus. This work showed similar host-parasite guilds in wildlife host-vector assemblages separated since the Pleistocene, and has important implications for future targeting of surveillance efforts.

"Pathogen Pollution": Implications for Global Biodiversity

One of the costs of human domination of the Earth's ecosystem is increasing global biogeographical homogeneity caused by the widespread introduction of nonnative flora and fauna into new areas (*14*, *47*). This anthropogenic form of invasion, sometimes termed "biological pollution" (*14*, *47*, *48*) has caused loss of biodiversity globally, particularly on oceanic islands (*49*).

Similar loss of biodiversity occurs when disease is introduced into naïve populations. The introduction of smallpox, typhus, and measles by the conquistadors in the 15th and 16th centuries resulted in catastrophic depopulation and 50 million deaths among native South Americans (*4*). A number of epizootiological equivalents of these "first-contact" depopulations have occurred, but considering the global scale of anthropogenic domestic and feral animal introduction, their true extent has probably been grossly underestimated. MacPhee and Marx (*50*) implicate the introduction of infectious diseases in the striking loss of biodiversity after human colonization of continental landmasses and large islands over the past 40,000 years, including many of the Pleistocene megafaunal extinctions. If pathogens have been introduced on a global scale within recent human history, how many wildlife diseases currently considered native actually originated from these introduction events? Anthropogenic introduction of exotic pathogens, which we term here pathogen pollution (human-mediated pathogen invasion), is implicated in many wildlife EIDs listed in Table 1, often acting in consort with spill-over events to drive emergence.

Pathogen pollution poses a substantial threat to global biodiversity. First, it has the potential to cause catastrophic depopulation of the new and naïve host population. Second, when introduced diseases become enzootic, initial declines may be followed by chronic population depression, and if the threshold host density for disease transmission is lowered, local extinction may occur. In some cases, the success of invading host species may be enhanced by parasite-mediated competition ("apparent competition") due to the impact of co-introduced diseases on resident species (*10*). Disease co-introduction may also impact humans, either directly (Marburg virus importation into Germany) or via effects on domesticated animals (the introduction of AHS into Spain with zebra).

Although there are numerous examples of disease emergence after pathogen introduction (Table 1), there undoubtedly are many more that have not been identified as such. For example, the decline of red squirrels in Britain, recorded since 1900, may have been caused by a parapoxvirus transmitted from introduced grey squirrels in which it is benign (*51*). Whether the pathogen was co-introduced to Britain with the grey squirrel, or whether the establishment of this reservoir host in Britain led to an increased exposure of red squirrels to a preexisting pathogen, is unknown.

The mechanics of pathogen pollution involve international traffic in agricultural materials, domesticated animals, food crops, and timber, and in biologically contaminated wastes such as landfill and ballast water (*47*, *48*). Global hotspots of biodiversity and wilderness sites such as the Galápagos and Antarctica are not exempt (*52*). Evidence of introduced disease in Antarctic wildlife (antibodies to the domestic chicken pathogen, infectious bursal disease virus, in Antarctic penguins) has prompted legislation to maintain stricter controls against pathogen pollution (*52*).

The impact of pathogen pollution may be augmented by secondary or "knock-on" effects that are difficult to predict. High mortality of rabbits after the introduction of myxomatosis in the United Kingdom caused population declines in stoats, buzzards, and owls (*4*). Myxomatosis also led to local extinction of the endangered large blue butterfly, by reducing grazing pressure on heathlands which, in turn, removed the habitat for an ant species that assists developing butterfly larvae (*12*). The effect on rain forest ecology after disease-mediated local extinction of multispecies amphibian assemblages is yet to be assessed, but is likely to be substantial (*41*).

Vitousek *et al.* (*47*) suggest that introduction of alien species is the next most important cause of extinction to habitat loss. The introduction of pathogens might achieve a similar status. Introduced diseases have been implicated in the local extinction of a number of species (*7–11*, *18*, *24*, *25*) and the global (species) extinction of Hawaiian birds (*53*), the thylacine (*11*), Mascarene reptiles (*49*), Pleistocene megafauna (*50*), and others. In the first definitively proven example of extinction by infection, a microsporidian parasite extirpated the captive remnant population of the Polynesian tree snail, *Partula turgida* (*54*). Thus, the 20 or so other species of *Partula* occurring solely in captivity may be at greater risk of extinction than previously thought. This case highlights the inherent problems parasites present to the conservation community, in which there is reliance on captive propagation and reintroduction as a safeguard against extinction. Global extinction as a secondary effect of disease occurred after mass mortality of the eel grass (*Zostera marina*) on the U.S. Atlantic seaboard caused by the slime mold *Labyrinthula zosterae*. Here, a *Z. marina* eelgrass-specific limpet, *Lottia alveus*, was driven to extinction after more than 90% loss of its habitat (*55*). These two cases also highlight the consequences of ignoring diseases of invertebrates, which are the most speciose form of life (*47*) and are crucial components of most ecosystems.

Perspectives

There is a clear economic cost of wildlife EIDs. For example, in 1994, postexposure prophylaxis for 665 people who had potential contact with a single rabid kitten in a pet store in New Hampshire cost $1.1 million, and it has been estimated that the economic burden of Lyme disease treatment in the United States may be around $500 million per annum (*56*). The cost of importing AHS into Spain was estimated at $20 million (*23*). In Australia, a recent epizootic of pilchards reduced fisheries production by around A$12 million over 3 years (*57*). The economic impacts of zoonotic EIDs may be difficult to predict and may have complex consequences. For example, the recent proposal to ban blood donation in the United States by persons who have spent longer than 6 months cumulatively in the United Kingdom during 1980–96 and are considered as potential carriers of the BSE agent, will reduce the U.S. blood supply by 2.2% (*58*). The cost of introduced disease to human, livestock, and crop plant health is over $41 billion per year in the United States (*48*). Although the value of biodiversity and significance of disease threats can be calculated (*59*), the cost of global biodiversity loss due to disease is yet to be assessed.

There are few regulations concerning exotic disease threats to wild animals, and few systems for surveillance are in place. Current measures for the detection and control of human and livestock EIDs are inadequate for the identification of similar threats to wildlife. The conservation community has drawn up guidelines to prevent the release of animals carrying exotic pathogens to novel areas (*8*, *9*). These recommendations are currently underused: of almost 700 terrestrial vertebrate translocations (within conservation programs) per year between 1973 and 1986 in the United States, Australia, Canada, and New Zealand, 24% occurred without any disease screening, and fewer than 25% involved investigations into causes of death of the translocated animals (*60*).

Future strategies for wildlife EID surveil-

lance and control may adapt techniques now used to study EIDs of humans and domestic animals such as satellite imaging, used in analyzing ENSO-related cholera outbreaks and forecasting ENSO-related Rift Valley fever epidemics (*37*). An increasing use of moderated Internet newsgroups in rapidly disseminating quality information on outbreaks is evident, and some (ProMED, *61*) regularly include data on plant and wildlife EIDs. Control measures for wildlife EIDs have largely been attempted as part of a strategy to prevent spread to humans (rabies control) or domesticated animals (culling of wildlife reservoir hosts). Recent attempts to control wild dog rabies by vaccination of domesticated dogs adjacent to the Serengeti National Park, and the vaccination of mountain gorillas against measles and of chimpanzees against poliovirus suggest a growing trend (*25*, *34*). Woodroffe (*9*) predicted an increasing role of population management, building on modeling studies (*13*, *20*), as an alternative, or complement, to direct veterinary intervention.

Important ethical differences exist between domesticated animal and human EIDs, where many diseases are notifiable and control measures easily conducted, and wildlife EIDs, for which few notifiable diseases exist and control is often politicized and underfunded. New initiatives are required. McSweegan (*62*) proposed that infectious disease impact plans be submitted for large-scale developmental projects. Similarly, wildlife disease impact plans could be incorporated into environmental impact statements. In addition, ecological studies, which have demonstrated the extent of parasite influence on community structure and biodiversity via host population regulation and apparent competition (*10*), may also allow prediction of the combination of parasite, host, and environmental parameters most likely to lead to disease emergence.

Future research on wildlife EIDs will need to adopt a multidisciplinary approach to identify underlying causes and to control their spread. Efforts to increase surveillance for known pathogens and to identify previously unknown infectious agents will be increased. Investigations into the ecology, pathology, and population biology of host-parasite systems will be approached from individual, population, and environmental perspectives. This integrative approach has been successfully applied to human EIDs (*16*, *63*) and wildlife EIDs that threaten public or domestic animal health (*27*, *20*). For wildlife EIDs this integration will involve a synthesis of both classical and cutting edge technologies from diverse disciplines.

References and Notes

1. J. Lederberg, R. E. Shope, S. C. Oakes Jr., Eds., *Emerging Infections: Microbial Threats to Health in the United States* (Institute of Medicine, National Academy Press, Washington, DC, 1992); B. W. J. Mahy and F. A. Murphy, in *Topley and Wilson's Microbiology and Microbial Infections*, vol. 1, *Virology*, B. W. J. Mahy and L. Collier, Eds. (Arnold, London, 1997), chap. 47; S. Binder *et al.*, *Science* **284**, 1311 (1999).
2. S. S. Morse, in *Emerging Viruses*, S. S. Morse, Ed. (Oxford Univ. Press, New York, 1993), chap. 2; R. M. Krause, *J. Infect. Dis.* **170**, 265 (1994).
3. Marine EIDs are dealt with in a parallel paper: C. D. Harvell *et al.*, *Science* **285**, 1505 (1999).
4. Noninfectious emerging diseases of wildlife and emerging plant diseases are not reviewed here. R. M Anderson and R. M. May [*Philos. Trans. R. Soc. London Ser. B* **314**, 533 (1986)] give notable examples of plant diseases that could be considered emerging using the criteria in (*1*, *2*).
5. An expanded version of Table 1 (Web table 1) is available to *Science* Online subscribers at www.sciencemag.org/feature/data/1041321.shl.
6. W. Plowright, *Symp. Zool. Soc. London* **50**, 1 (1982); A. P. Dobson and P. J. Hudson, *Trends Ecol. Evol.* **1**, 11 (1986).
7. T. Thorne and E. S. Williams, *Conserv. Biol.* **2**, 66 (1988).
8. K. L. Viggers, D. B. Lindenmayer, D. M. Spratt, *Wildl. Res.* **20**, 687 (1993); M. H. Woodford, *J. Zoo Wildl. Med.* **24**, 265 (1993); A. A. Cunningham, *Conserv. Biol.* **10**, 349 (1996).
9. R. Woodroffe, *Anim. Conserv.* **2**, 185 (1999).
10. R. M. Anderson and R. M. May, *Nature* **280**, 361 (1979); P. Hudson and J. Greenman, *Trends Ecol. Evol.* **13**, 387 (1998); D. M. Tompkins and M. Begon, *Parasitol. Today* **15**, 311 (1999).
11. H. McCallum and A. Dobson, *Trends Ecol. Evol.* **10**, 190 (1995).
12. A. P. Dobson and R. M. May, in *Conservation Biology: The Science of Scarcity and Diversity*, M. Soulé Ed. (Sinauer, Sunderland, MA, 1986), chap. 16.
13. R. M. May, *Conserv. Biol.* **2**, 28 (1988); A. M. Lyles and A. P. Dobson, *J. Zoo Wildl. Med.* **24**, 315 (1993); M. E. Scott, *Conserv. Biol.* **2**, 40 (1988); L. A. Real, *Bioscience* **46**, 88 (1996); G. Hess, *Ecology* **77**, 1617 (1996).
14. Causal themes underlying the emergence of human EIDs are closely paralleled by factors driving the emergence of wildlife EIDs (for example, international travel is paralleled by the international movement of livestock and other animals). The "globalization" of agriculture, trade and human population movements [D. P. Fidler, *Emerg. Infect. Dis.* **2**, 77 (1996); A. J. McMichael *et al.*, *Bioscience* **49**, 206 (1999)] can be equated, for wildlife EIDs, with increasing biogeographical homogeneity resulting from human influence on ecosystems [S. L. Pimm *et al.*, *Science* **269**, 347 (1995)].
15. S. J. Schrag and P. Wiener, *Trends Ecol. Evol.* **10**, (1995).
16. K. Murray *et al.*, *Science* **268**, 94 (1995); J. S. Mackenzie, *Emerg. Infect. Dis.* **5**, 1 (1999).
17. H.-D. Klenk, Ed., *Curr. Top. Microbiol. Immunol.* **235** (1999); T. P. Monath, *J. Infect. Dis.* **179**, S127 (1999); H. Leirs *et al.*, *J. Infect. Dis.* **179**, S155 (1999); M. Hagmann, *Science* **286**, 654 (1999).
18. D. W. Macdonald, *Nature* **360**, 633 (1992); K. A. Alexander, P. W. Kat, L. A. Munson, A. Kalake, M. J. G. Appel, *J. Zoo Wildl. Med.* **27**, 426 (1996).
19. J. K. Kirkwood, *Vet. Rec.* **142**, 468 (1998); T. W. Pennycott *et al.*, *Vet. Rec.* **143**, 155 (1998); J. R. Fischer, D. E. Stallknecht, M. P. Luttrell, A. A. Dhondt, K. A. Converse, *Emerg. Infect. Dis.* **3**, 69 (1997).
20. A. Dobson and M. Meagher, *Ecology* **77**, 1026 (1996); M. E. Meyer and M. Meagher, *J. Wildl. Dis.* **31**, 579 (1995).
21. A. G. Barbour and D. Fish, *Science* **260**, 1610 (1993).
22. D. Spratt, *Int. J. Parasitol.* **28**, 925 (1998); G. C. Cook, *J. R. Soc. Med.* **85**, 688 (1992); J. McCurry, *Lancet* **350**, 1825 (1997); P. R. Epstein, *Lancet* **351**, 1737 (1998).
23. D. G. A. Meltzer, *J. Zoo Wildl. Med.* **24**, 237 (1993); P. S. Mellor and J. Boorman, *Ann. Trop. Med. Parasitol.* **89**, 1 (1995).
24. J. R. Ginsberg, G. M. Mace, S. Albon, *Proc. R. Soc. London Ser. B.* **262**, 221 (1995); M. E. Roelke-Parker *et al.*, *Nature* **379**, 441 (1996); K. Laurenson, *Anim. Conserv.* **1**, 273 (1998).
25. P. W. Kat, K. A. Alexander, J. S. Smith, L. Munson, *Proc. R. Soc. London Ser. B.* **262**, 229 (1995); S. Cleaveland, *Trans. R. Soc. Trop. Med. Hyg.* **92**, 131 (1998); S. Cleaveland and C. Dye, *Parasitology* **111**, S33 (1995).
26. A. A. Cunningham *et al.*, *Philos. Trans. R. Soc. London Ser. B* **351**, 1529 (1996); J. K. Jancovich, E. W. Davidson, J. F. Morado, B. L. Jacobs, J. P. Collins, *Dis. Aquat. Org.* **31**, 161 (1997); R. J. Whittington, C. Kearns, A. D. Hyatt, S. Hengstberger, T. Rutzou, *Austral. Vet. J.* **73**, 112 (1996); R. P. Hedrick and T. S. McDowell, *Vet. Res.* **26**, 423 (1995).
27. C. E. Rupprecht, J. S. Smith, M. Fekadu, J. E. Childs, *Emerg. Infect. Dis.* **1**, 107 (1995).
28. B. P. Oldroyd, *Trends Ecol. Evol.* **14**, 312 (1999).
29. L. K. Richman *et al.*, *Science* **283**, 1171 (1999).
30. J. Collinge *et al.*, *Nature* **383**, 685 (1996); R. M. Anderson *et al.*, *Nature* **382**, 779 (1996); M. E. Bruce *et al.*, *Nature* **389**, 498 (1997).
31. J. K. Kirkwood and A. A. Cunningham, *Proc. Am. Assoc. Zoo Vet.* 26 (1992); J. K. Kirkwood and A. A. Cunningham, in *Zoo & Wild Animal Medicine, Current Therapy 4*, M. E. Fowler and R. E. Miller, Eds. (Saunders, Philadelphia, 1999), pp. 662–663; N. Bons *et al.*, *Proc. Natl. Acad. Sci., U.S.A.* **96**, 4046 (1999); J. K. Kirkwood and A. A. Cunningham, paper presented at the World Veterinary Congress, Lyon, France, 23 to 26 September 1999, in press.
32. A. A. Cunningham, D. Buxton, K. M. Thomson, *J. Comp. Pathol.* **107**, 207 (1992); J. K. Frenkel, *Am. Zool.* **29**, 455 (1989); C. Pertz, R. R. Dubielzig, D. S. Lindsay, *J. Zoo Wildl. Med.* **28**, 491 (1997); R. J. Montali *et al.*, *Am. J. Pathol.* **148**, 1141 (1995).
33. J. M. Hime *et al.*, *Vet. Rec.* **97**, 392 (1975); T. M. Butynski and J. Kalina, in *Conservation of Biological Resources*, E. J. Milner-Gulland and R. Mace, Eds. (Blackwell Science, Oxford, 1998), pp. 294–313; J. Goodall, *In the Shadow of Man* (Weidenfeld & Nicholson, London, rev. ed., 1988), pp. 214–224.
34. A. A. Cunningham, *Mem. Mus. Victoria* **56**, 647 (1997).
35. E. A. Harris, *Parasitology* **87**, R29 (1983); D. A. Windsor, *Nature* **348**, 104 (1990); N. E. Stork and C. H. C. Lyal, *Nature* **366**, 307 (1993); M. E. Gompper and E. S. Williams, *Conserv. Biol.* **12**, 730 (1998).
36. J. K. Griffiths, *Adv. Parasitol.* **40**, 37 (1998).
37. R. T. Trevejo *et al.*, *J. Infect. Dis.* **178**, 1457 (1998); J. M. Bouma, *JAMA* **278**, 1772 (1997); T. J. Doyle, R. T. Bryan, C. J. Peters, *Infect. Dis. Clin. N. Am.* **12**, 95 (1998); R. R. Colwell, *Science* **274**, 2025 (1996); K. J. Linthicum *et al.*, *Science* **285**, 397 (1999).
38. B. T. Grenfell *et al.*, *Nature* **394**, 674 (1998).
39. M. Baylis, P. S. Mellor, R. Meiswinkel, *Nature* **397**, 574 (1999).
40. L. Berger *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 9031 (1998); V. Morrell, *Science* **284**, 728 (1999).
41. P. Daszak *et al.*, *Emerg. Infect. Dis.* **85**, 735 (1999).
42. J. A. Pounds, M. P. L. Fogden, J. H. Campbell, *Nature* **398**, 611 (1999).
43. K. Subbarao *et al.*, *Science* **279**, 393 (1998).
44. F. Gao *et al.*, *Nature* **397**, 385 (1999).
45. N. I. Paton *et al.*, *Lancet* **354**, 1253 (1999); K. B. Chua *et al.*, *Lancet* **354**, 1257 (1999); J. Aziz *et al.*, paper presented at the 11th International Congress of Virology, Sydney, Australia, 9–13 August, 1999.
46. S. R. Telford *et al.*, *Emerg. Infect. Dis.* **3**, 165 (1997); G. D. Ebel *et al.*, *Emerg. Infect. Dis.* **5**, 570 (1999).
47. P. M. Vitousek *et al.*, *Am. Sci.* **84**, 468 (1996); P. M. Vitousek *et al.*, *Science* **277**, 494 (1997).
48. D. Pimentel, L. Lach, R. Zuniga, D. Morrison, *Bioscience*, in press; D. M. Bartley, *Rev. Sci. Tech. Off. Int. Epizoot.* **15**, 387 (1996).
49. D. W. Steadman, *Science* **267**, 1123 (1995); G. H. Rodda, T. H. Fritts, D. Chiszar, *Bioscience* **47**, 565 (1997); A. S. Cheke, in *Studies of Mascarene Island Birds*, A. W. Diamond, Ed. (Cambridge Univ. Press, Cambridge, UK, 1987), chap. 1.
50. R. D. E. MacPhee and P. A. Marx, in *Natural Change and Human Impact in Madagascar*, S. M. Goodman and B. D. Patterson, Eds. (Smithsonian Institution Press, Washington, DC, 1997), chap. 7.
51. A. W. Sainsbury, P. Nettleton, J. Gurnell, in *The Conservation of Red Squirrels*, Sciurus vulgaris *L.*, J. Gurnell and P. W. W. Lurz, Eds. (Peoples Trust for Endangered Species, London, 1997), pp. 105–108.
52. *Symposium on Invasive Species on Oceanic Islands*, Galápagos Conservation Trust, Shaftsbury, Dorset,

UK, 1996); K. R. Kerry, M. J. Riddle, J. R. Clarke, *Diseases of Antarctic Wildlife* (Australian Antarctic Division, Kingston, Tasmania, 1999); H. Gardner, K. Kerry, M. Riddle, S. Brouwer, L. Gleeson, *Nature* **387**, 245 (1997).
53. R. E. Warner, *Condor* **70**, 101 (1968); C. van Riper, S. G. van Riper, M. L. Goff, M. Laird, *Ecol. Monogr.* **56**, 327 (1986).
54. A. A. Cunningham and P. Daszak, *Conserv. Biol.* **12**, 1139 (1998).
55. P. Daszak and A. A. Cunningham, *Trends Ecol. Evol.* **14**, 279 (1999).
56. E. Maes, P. Lecomte, N. Ray, *Curr. Ther.* **20**, 993 (1998); D. L. Noah *et al.*, *Am. J. Publ. Health* **86**, 1149 (1996).
57. A. D. Hyatt *et al.*, *Dis. Aquat. Org.* **28**, 1 (1997).
58. A. Ault, *Lancet* **353**, 2050 (1999).
59. D. S. Wilcove, D. Rothstein, J. Dubow, A. Phillips, E. Losos, *Bioscience* **48**, 607 (1998); R. Costanza *et al.*, *Nature* **387**, 253 (1997); D. Pimentel *et al.*, *Bioscience* **47**, 747 (1997).
60. B. Griffith, M. Scott, J. Carpenter, C. Reed, *J. Zoo Wildl. Med.* **24**, 231 (1993).
61. The Program for Monitoring Emerging Diseases, available at http://www. promedmail.org
62. E. McSweegan, *Emerg. Infect. Dis.* **2**, 103 (1996).
63. D. M. Engelthaler *et al.*, *Emerg. Infect. Dis.* **5**, 87 (1999); J. N. Mills, T. G. Ksiazek, C. J. Peters, J. E. Childs, *Emerg. Infect. Dis.* **5**, 135 (1999).
64. W. R. Davidson, J. E. Dawson, S. A. Ewing, in *Infectious Diseases of Wild Mammals*, B. Williams, I. Barker, T. Thorne, Eds. (Iowa State Univ. Press, Ames, IA, in press); S. R. Telford *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **93**, 6209 (1996).
65. J. F. Cully, A. M. Barnes, T. J. Quan, G. Maupin, *J. Wildl. Dis.* **33**, 706 (1997).
66. I. McCandlish, H. Thompson, C. Cornwell, E. Fisher, *Vet. Rec.* **105**, 180 (1979); C. R. Parrish *et al.*, *Science* **230**, 1046 (1985).
67. G. Wobeser *et al.*, *Can. Vet. J.* **34**, 353 (1993); C. U. Meteyer *et al.*, *Avian Dis.* **41**, 171 (1997).
68. E. Lindström *et al.*, *Ecology* **75**, 1042 (1994); L. F. Skerratt, R. Martin, K. Handasyde, *Austral. Vet. J.* **76**, 408 (1998).
69. P. T. Hooper *et al.*, *Aust. Vet. J.* **77**, 529 (1999).
70. D. J. Alderman, *Rev. Sci. Tech. Off. Int. Epizoot.* **15**, 603 (1996).
71. R. Cranfield, M. Shaw, F. Beall, M. Skjoldager, *Proc. Am. Assoc. Zoo Vet.* **1990**, 243 (1990).
72. E. R. Jacobson, *J. Zoo Wildl. Med.* **24**, 245 (1993).
73. V. F. Nettles, *ASM News* **62**, 589 (1996); *World Animal Health in 1997* (Office International des Epizooties, Paris, France, 1997); Anonymous, *Vet. Rec.* **143**, 378 (1998).
74. We thank B. W. J. Mahy, C. C. Brown, J. E. Dawson and J. K. Kirkwood for critical reviews of this manuscript; J. P. O'Connor for editorial assistance; J. E. Dawson, P. T. Hooper, K. R. Kerry, B. P. Oldroyd, D. Pimentel, M. J. Riddle and S. R. Telford for access to unpublished data; and M. A. Farmer, J. R. Fischer, C. S. Goldsmith, C. D. Humphrey, T. G. Ksiazek, R. McLean, D. Porter, J. W. Porter, W.-J. Shieh, T. Whistler, and S. R. Zaki for helpful discussions.