critical to test the efficacy of specific disease prevention strategies applied not only within donor and recipient communities, but also in the realm where they intersect.

References and Notes

1. J. O. Lloyd-Smith *et al.*, *Science* **326**, 1362 (2009).
2. C. E. Rupprecht, C. A. Hanlon, T. Hemachudha, *Lancet Infect. Dis.* **2**, 327 (2002).
3. V. P. Hsu *et al.*, *Emerg. Infect. Dis.* **10**, 2082 (2004).
4. S. Riley *et al.*, *Science* **300**, 1961 (2003).
5. A. Moya, E. C. Holmes, F. González-Candelas, *Nat. Rev. Microbiol.* **2**, 279 (2004).
6. M. Anishchenko *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **103**, 4994 (2006).
7. H. D. Song *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **102**, 2430 (2005).
8. C. R. Parrish *et al.*, *Microbiol. Mol. Biol. Rev.* **72**, 457 (2008).
9. T. Kuiken *et al.*, *Science* **312**, 394 (2006).
10. J. D. Blanton, K. Robertson, D. Palmer, C. E. Rupprecht, *J. Am. Vet. Med. Assoc.* **235**, 676 (2009).
11. D. A. Brass, in *Rabies in Bats: Natural History and Public Health Implications*, D. A. Brass, Ed. (Livia Press, Ridgefield, CT, 1994), pp. 151–162.
12. J. S. Smith, L. A. Orciari, P. A. Yager, *Semin. Virol.* **6**, 387 (1995).
13. G. J. Hughes, L. A. Orciari, C. E. Rupprecht, *J. Gen. Virol.* **86**, 1467 (2005).
14. O. R. P. Bininda-Emonds *et al.*, *Nature* **446**, 507 (2007).
15. Materials and methods are available as supporting material on *Science* Online.
16. D. M. de Vienne, M. E. Hood, T. Giraud, *J. Evol. Biol.* **22**, 2532 (2009).
17. G. S. Gilbert, C. O. Webb, *Proc. Natl. Acad. Sci. U.S.A.* **104**, 4979 (2007).
18. T. J. Davies, A. B. Pedersen, *Proc. Biol. Sci.* **275**, 1695 (2008).
19. G. M. Baer, J. H. Shaddock, R. Quirion, T. V. Dam, T. L. Lentz, *Lancet* **335**, 664 (1990).
20. S. Finke, K. K. Conzelmann, *Virus Res.* **111**, 120 (2005).

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Materials and Methods
SOM Text
Fig. S1
Tables S1 to S9
References

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An Emerging Disease Causes Regional Population Collapse of a Common North American Bat Species

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White-nose syndrome (WNS) is an emerging disease affecting hibernating bats in eastern North America that causes mass mortality and precipitous population declines in winter hibernacula. First discovered in 2006 in New York State, WNS is spreading rapidly across eastern North America and currently affects seven species. Mortality associated with WNS is causing a regional population collapse and is predicted to lead to regional extinction of the little brown myotis (*Myotis lucifugus*), previously one of the most common bat species in North America. Novel diseases can have serious impacts on naïve wildlife populations, which in turn can have substantial impacts on ecosystem integrity.

Emerging infectious diseases are increasingly recognized as direct and indirect agents of extinction of free-ranging wildlife (*1*–*4*). Introductions of disease into naïve wildlife populations have led to serious declines or local extinctions of different species in the past few decades, including amphibians from chytridiomycosis (*5*, *6*), rabbits from myxomatosis in the United Kingdom (*7*), Tasmanian devils from infectious cancer (*3*), and birds in North America from West Nile virus (*8*). Here we demonstrate that white-nose syndrome (WNS), an emerging infectious disease, is causing unprecedented mortality among hibernating bats in eastern North America and has caused a population collapse that is threatening regional extinction of the little brown myotis (*Myotis lucifugus*), a once widespread and common bat species.

WNS is associated with a newly described psychrophilic fungus (*Geomyces destructans*) that grows on exposed tissues of hibernating bats, apparently causing premature arousals, aberrant behavior, and premature loss of critical fat reserves (*9*, *10*) (Fig. 1). The origin of WNS and its putative pathogen, *G. destructans*, is uncertain (*9*). A plausible hypothesis for the origin of this disease in North America is introduction via human trade or travel from Europe, based on recent evidence that *G. destructans* has been observed on at least one hibernating bat species in Europe (*11*). Anthropogenic spread of invasive pathogens in wildlife and domestic animal populations, so-called pathogen pollution, poses substantial threats to biodiversity and ecosystem integrity and is of major concern in conservation efforts (*1*, *2*).

WNS has spread rapidly and now occurs throughout the northeastern and mid-Atlantic regions in the United States and in Ontario and Québec provinces in Canada and currently affects at least seven species of hibernating bats (Fig. 2). Many species of bats in temperate North America hibernate in caves and mines (*12*) in aggregations of up to half a million individuals in a single cave (*13*). In late spring, these winter aggregations typically disperse into smaller sex-segregated groups of conspecifics, when adult females form maternity colonies and adult males mostly roost alone (*14*, *15*). From August to October, females and males assemble at hibernacula or swarming sites to mate before hibernating (*16*, *17*). The mechanisms for the persistence and transmission of *G. destructans* during summer and fall months are unknown, but spread of the fungus to new geographic regions and to other species may result from social and spatial mixing of individuals across space and time.

During the past 4 years, WNS has been confirmed in at least 115 bat hibernacula in the United States and Canada and has spread over 1200 km from Howe Cave near Albany, New York, where it was first observed in February

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2006 (*9*) (Fig. 2). Decreases in bats at infected hibernacula range from 30 to 99% annually, with a regional mean of 73%, and all surveyed sites have become infected within 2 years of the disease arriving in their region (Fig. 3, A to C). Such sharp declines and rapid spread raise serious concerns about the impact of WNS on the population viability of affected bat species.

We investigated the impacts of disease-associated mortality on the regional population of little brown myotis in the northeastern United States by comparing trends in pre- and post-WNS populations and simulating 100 years of post-WNS population dynamics to assess the consequences of the introduction of the disease for bat population viability (*18*). We used a population matrix model parameterized with survival and breeding probabilities estimated from 16 years (1993–2008) of mark and recapture data at a maternity site of little brown myotis (*19*) to estimate population growth before WNS (table S1). We also calculated geometric mean growth rates from winter count surveys of this species conducted over the past 30 years at 22 hibernacula ranging across five states in the northeastern United States to determine regional population trends before the emergence of WNS (table S2).

Deterministic population growth calculated from the population matrix model of mean vital rates was positive [yearly population growth rate (λ) = 1.008], demonstrating that population growth was stable or increasing before the emergence of WNS. Estimates of long-term growth rates over the past 30 years indicate that 86% of hibernacula (n = 19 out of 22) had stable or increasing populations (λ = >1). Regional mean growth equaled 1.07 (range: 0.98 to 1.2) (table S2), suggesting that the regional population was growing before WNS and that vital rates estimated from the maternity site represent regional patterns. The growth of hibernating populations over the past 30 years may be in response to conservation measures, such as protective gating of mines and caves (*20*), the installation of bat houses (*21*), and the potential amelioration of impacts from pesticides banned in the 1970s (*22*).

To assess the impact of disease-related mortality on population viability, we simulated population dynamics using a stochastic population model that included demographic data from both infected and susceptible (uninfected) populations (*18*). We performed 1000 simulations of 100 years of growth from a starting population of 6.5 million bats, using means, variances, and correlations from vital rates (*19*) that incorporated environmental variability (*23*). The probability of extinction for each year was defined as the proportion of 1000 runs for which the simulated population dropped below a quasi-extinction threshold during that year. Quasi-extinction was specified as 0.01% of the starting population (that is, 650 bats). Defining extinction thresholds at low population sizes accounts for processes such as demographic stochasticity and potential Allee effects (*23*–*26*).

In the simulation model, the susceptible population retained pre-WNS vital rates estimated from the 16-year mark and recapture data (*19*), and infected populations were given vital rates associated with annual declines calculated from infected hibernacula where consecutive yearly counts were available (n = 22) (*18*). The increase of prevalence of WNS was estimated as the percentage of uninfected hibernacula that became infected each year (2007, 5%; 2008, 49%; 2009, 59%) and was incorporated into the simulation as the proportion of the susceptible population that becomes infected each year.

Because of the inherent uncertainty in predicting the dynamics of a recently emergent disease, we evaluated the potential for disease fadeout and its influence on population viability. We estimated annual declines for each of 3 years after infection and constructed nine a priori models to test hypotheses regarding the influence of density and time since infection on population growth rates at infected hibernacula (table S3). From these estimates, there is little evidence of density-dependent declines, although model results suggest that the rate of decline ameliorates with the time since infection (Fig. 3D and table S3). To incorporate this time amelioration effect into the simulation model, we used predicted values of population growth from a nonlinear model [$\lambda = 1 - 1.16 \times \exp(-0.31 \times t)$, where t = years since infection] for each of 16 years after infection, when predicted population growth stabilized (λ = 1) (Fig. 3D).

We simulated population growth for five scenarios related to this time amelioration effect, including declines ameliorated according to predicted values (Fig. 3D) at each yearly time step and that persisted at 45% (3rd-year actual mean), 20% (6th-year predicted mean), 10% (8th-year predicted mean), 5% (10th-year predicted mean), and 2% (13th-year predicted mean) per year (Fig. 4). By comparing the probabilities of extinction over 100 years for these five scenarios, we evaluated the vulnerability of the regional population to extinction,

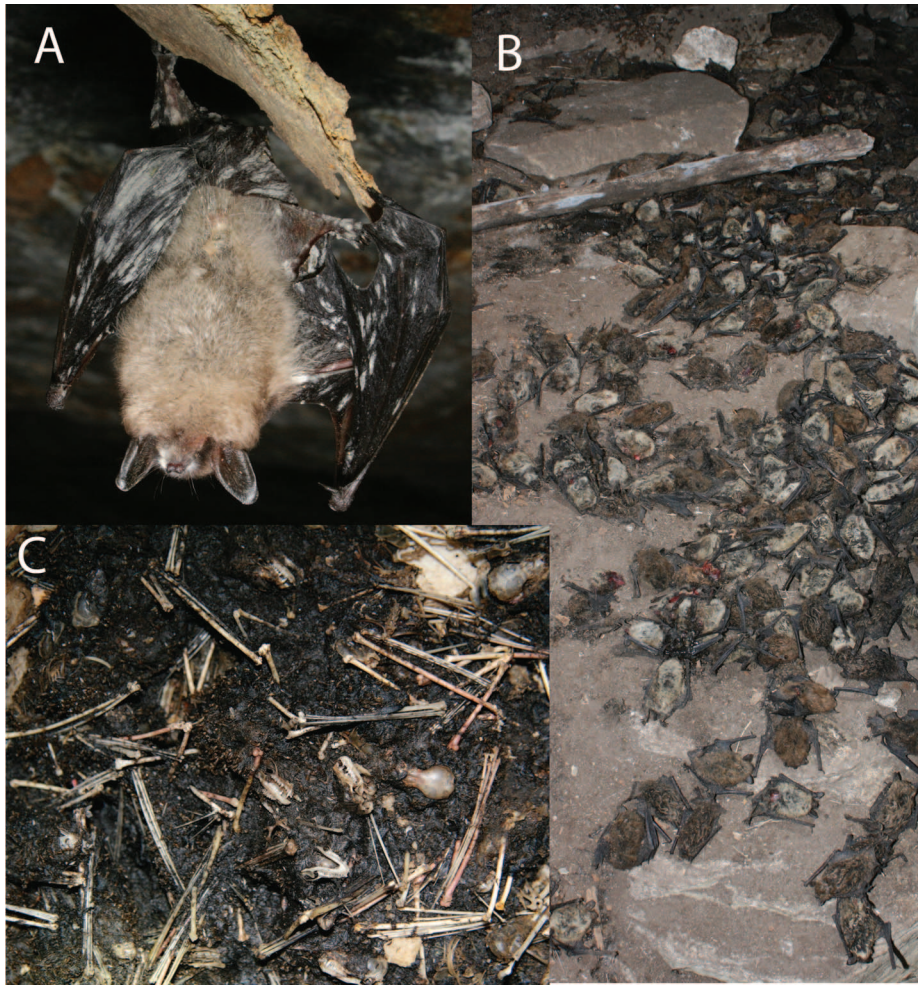

Fig. 1. (**A**) Photograph of hibernating little brown myotis infected with WNS. White fungus is visible on wings, ears, muzzle, and other exposed skin tissues. [Photo: Ryan Von Linden] (**B**) Bat carcasses piled on a cave floor, illustrating mass mortality at hibernacula infected with WNS. [Photo: Alan Hicks] (**C**) Skulls, bones, and decomposed carcasses covering the cave floor after multiple years of infection. [Photo: Marianne Moore]

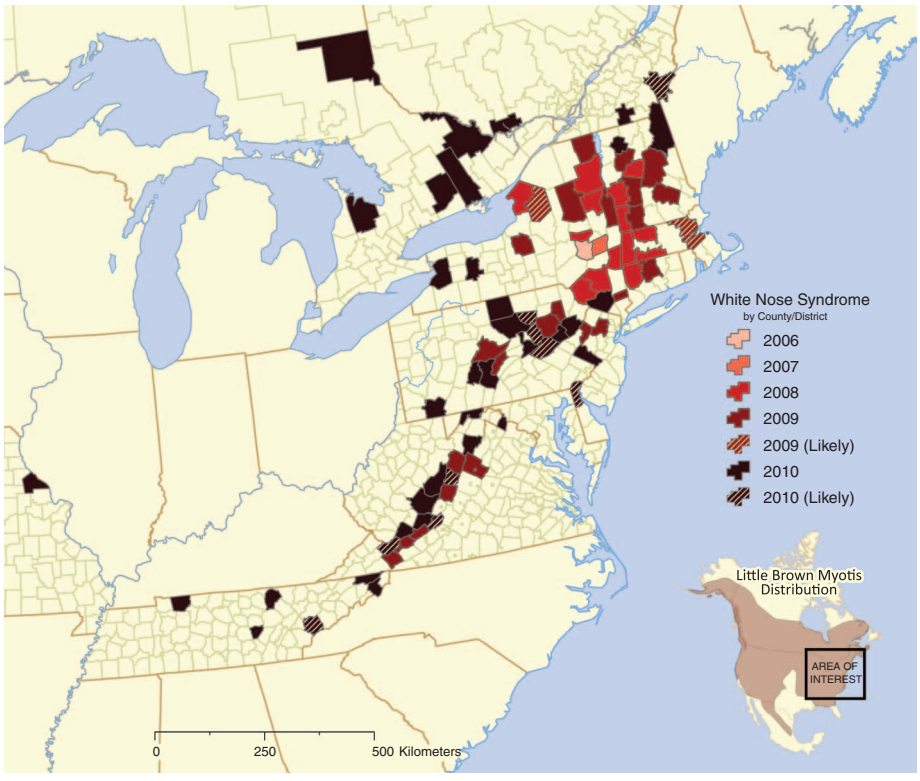

Fig. 2. Map of current distribution and spread of WNS across eastern North America.

given the uncertainty in how declines from disease mortality may persist in the future.

Using vital rates derived from mean declines in the first 3 years of infection and persisting at the observed third-year mean decline of 45% per year thereafter (Fig. 3D), we expect a 99% chance of regional extinction of little brown myotis within the next 16 years (Fig. 4A). If declines continue to ameliorate with time since infection, timelines to probable extinction lengthen but remain greater than 90% by 65 years, even if declines ameliorate and stabilize at 10% per year (Fig. 4A). Model results indicate that annual declines from WNS would have to ameliorate to less than 5% per year to significantly reduce the chance of extinction over 100 years (Fig. 4A). Even if disease mortality lessens over time, the regional population is expected to collapse from an estimated starting population of 6.5 million bats to fewer than 65,000 (1% of the pre-WNS population) in less than 20 years (Fig. 4B).

Our results paint a grim picture of a once-healthy population of an abundant and widely distributed species now experiencing unprecedented losses from WNS and facing a serious threat of regional extinction within the next 16 years (Fig. 4). Such a severe population decline, especially if the disease spreads farther south and west of its current distribution in eastern North America, may result in unpredictable changes in ecosystem

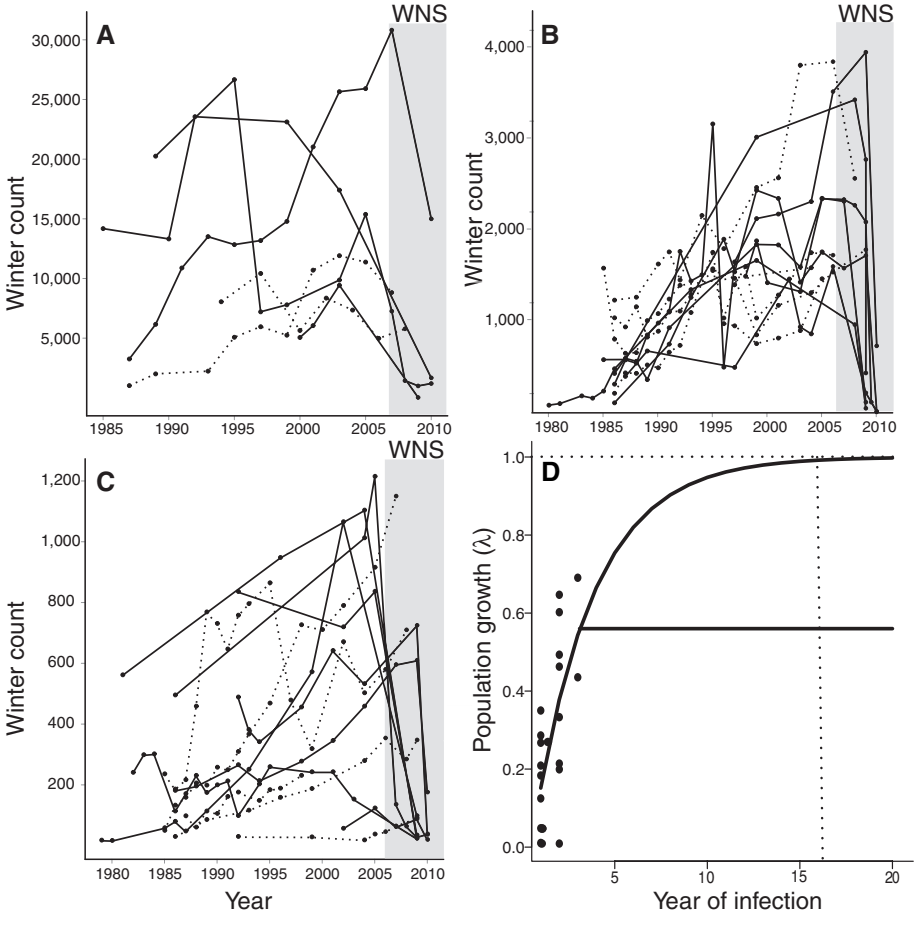

Fig. 3. (**A** to **C**) Population trends of little brown myotis over the past 30 years at (A) small (<1500 bats), (B) medium (<5000 bats), and (C) large (>5000 bats) hibernating colonies in the northeastern United States. Solid lines represent sites with bats infected with WNS; dotted lines represent uninfected sites. Hibernacula infected with WNS experienced a significant reduction in numbers as compared to the lowest available count from the past 30 years (Wilcoxon test = 190; $P < 0.002$). Large decreases in winter counts at a few hibernacula in the mid-1990s were related to winter flood events. (**D**) Population growth (λ) at hibernacula (black circles) by year since infection. The curved fitted line represents the nonlinear time-dependent model, showing amelioration of mortality from WNS until population growth reaches equilibrium at $\lambda = 1$ in 16 years since the first year of infection (vertical dotted line). The hockey-stick line represents declines from WNS persisting at the third-year mean of 45% per year, after a first-year decline of 85% and a second-year decline of 62%.

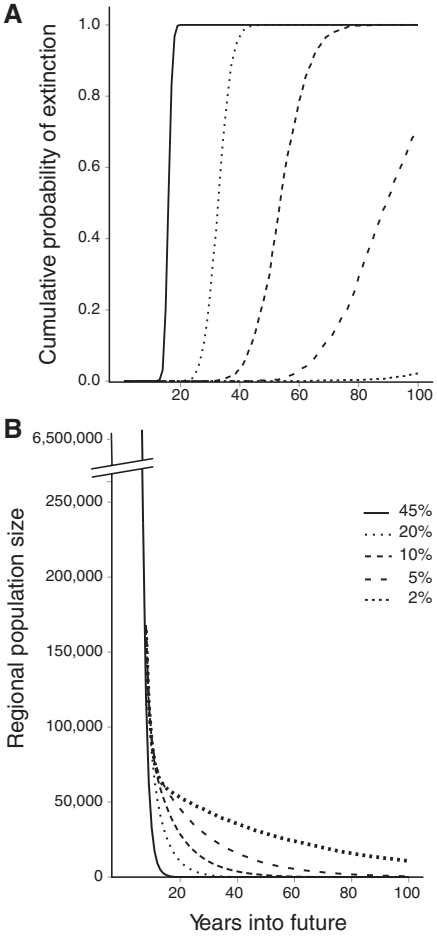

Fig. 4. (**A**) Cumulative probability of regional extinction of little brown myotis for five scenarios of time-dependent amelioration of disease mortality from WNS, based on matrix model simulation results. Each scenario represents predicted time-dependent declines for a specified number of years after infection and then holds the decline rate constant at either 45, 20, 10, 5, or 2% to demonstrate the impact of amelioration on the probability of extinction over the next 100 years. (**B**) Population size in each year averaged across 1000 simulations for each of the five scenarios of time-dependent amelioration of mortality from WNS.

structure and function (*27*, *28*). The rapid geographic spread of WNS since 2006, coupled with the severity and rapidity of population declines, support the hypothesis of introduction of a novel pathogen into a naïve population and demonstrate the seriousness of pathogen pollution as a conservation issue (*1*). Our analysis focused on little brown myotis in the northeastern United States, but several other bat species are experiencing similar mortality from WNS and may also be at significant risk of population collapse or extinction. This rapid decline of a common bat species from WNS draws attention to the need for increased research, monitoring, and management to better understand and combat this invasive wildlife disease (*1*).

References and Notes

1. P. Daszak, A. A. Cunningham, A. D. Hyatt, *Science* **287**, 443 (2000).
2. H. McCallum, A. Dobson, *Trends Ecol. Evol.* **10**, 190 (1995).
3. H. McCallum, *Trends Ecol. Evol.* **23**, 631 (2008).
4. A. M. Kilpatrick, C. J. Briggs, P. Daszak, *Trends Ecol. Evol.* **25**, 109 (2010).
5. L. Berger *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 9031 (1998).
6. K. R. Lips *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **103**, 3165 (2006).
7. F. Fenner, *FEMS Microbiol. Rev.* **24**, 123 (2000).
8. S. L. LaDeau, A. M. Kilpatrick, P. P. Marra, *Nature* **447**, 710 (2007).
9. D. S. Blehert *et al.*, *Science* **323**, 227 (2009).
10. A. Gargas, M. T. Trest, M. Christensen, T. J. Volk, D. S. Bleher, *Mycotaxon* **108**, 147 (2009).
11. S. J. Puechmaille *et al.*, *Emerg. Infect. Dis.* **16**, 290 (2010).
12. T. J. O'Shea, M. A. Bogan, *Monitoring Trends in Bat Populations of the United States and Territories: Problems and Prospects* (Biological Resources Discipline, Information and Technology Report USGS/BRD/ITR-2003-003, U.S. Geological Survey, Washington, DC, 2003).
13. R. Barbour, W. Davis, *Bats of America* (Univ. Press of Kentucky, Lexington, KY, USA, 1969).
14. T. H. Kunz, L. F. Lumsden, in *Bat Ecology,* T. H. Kunz, M. B. Fenton, Eds. (Univ. of Chicago Press, Chicago, IL, 2003), pp. 3–89.
15. T. H. Kunz, D. S. Reynolds, in (*12*), pp. 9–20.
16. W. H. Davis, H. B. Hitchcock, *J. Mammal.* **46**, 296 (1965).
17. D. W. Thomas, M. B. Fenton, R. M. R. Barclay, *Behav. Ecol. Sociobiol.* **6**, 129 (1979).
18. Information on materials and methods is available on *Science* Online.
19. W. F. Frick, D. S. Reynolds, T. H. Kunz, *J. Anim. Ecol.* **79**, 128 (2010).
20. E. T. Posluszny, C. Butchkoski, in *Proceedings of Bat Conservation and Mining: A Technical Interactive Forum* (Bat Conservation International and U.S. Department of the Interior, Office of Surface Mining, St. Louis, MO, 2000), pp. 159–168.
21. M. D. Tuttle, D. Hensley, *Bats* **11**, 3 (1993).
22. K. N. Geluso, J. S. Altenbach, D. E. Wilson, *Science* **194**, 184 (1976).
23. W. F. Morris, D. F. Doak, *Quantitative Conservation Biology: Theory and Practice of Population Viability Analysis* (Sinauer, Sunderland, MA, 2002).
24. F. Courchamp, T. Clutton-Brock, B. Grenfell, *Trends Ecol. Evol.* **14**, 405 (1999).
25. P. A. Stephens, W. J. Sutherland, *Trends Ecol. Evol.* **14**, 401 (1999).
26. F. Courchamp, B. Grenfell, T. Clutton-Brock, *Proc. Biol. Sci.* **266**, 557 (1999).
27. K. J. Gaston, *Science* **327**, 154 (2010).
28. G. W. Luck, G. C. Daily, P. R. Ehrlich, *Trends Ecol. Evol.* **18**, 331 (2003).

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Supporting Online Material

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Materials and Methods
Figs. S1 and S2
Tables S1 to S3
References

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Sex-Specific Parent-of-Origin Allelic Expression in the Mouse Brain

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Genomic imprinting results in preferential gene expression from paternally versus maternally inherited chromosomes. We used a genome-wide approach to uncover sex-specific parent-of-origin allelic effects in the adult mouse brain. Our study identified preferential selection of the maternally inherited X chromosome in glutamatergic neurons of the female cortex. Moreover, analysis of the cortex and hypothalamus identified 347 autosomal genes with sex-specific imprinting features. In the hypothalamus, sex-specific imprinted genes were mostly found in females, which suggests parental influence over the hypothalamic function of daughters. We show that *interleukin-18*, a gene linked to diseases with sex-specific prevalence, is subject to complex, regional, and sex-specific parental effects in the brain. Parent-of-origin effects thus provide new avenues for investigation of sexual dimorphism in brain function and disease.

Genomic imprinting is an epigenetic mode of gene regulation involving preferential expression of the paternally or maternally inherited allele (*1*). Sexual dimorphism is a central characteristic of mammalian brain function and behavior that influences major neurological diseases in humans (*2*). Here we address the potential existence of differential genomic imprinting in the brain according to the sex of individuals. Imprinting refers to gene expression differences between maternal and paternal chromosomes (*3*) and is also used more strictly to define complete allele-specific silencing (*4*). Our analysis encompasses sex differences in parent-

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REVIEW: WILDLIFE ECOLOGY

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

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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-

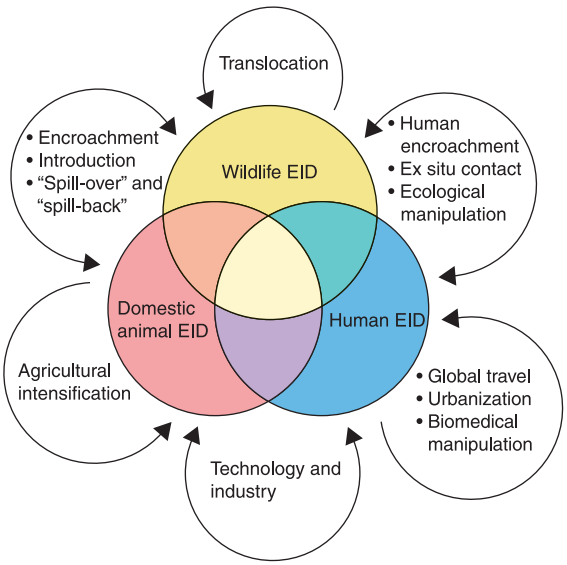

Fig. 1. The host-parasite ecological continuum (here parasites include viruses and parasitic prokaryotes). Most emerging diseases exist within a host and parasite continuum between wildlife, domestic animal, and human populations. Few diseases affect exclusively any one group, and the complex relations 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.

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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.

CHINA

After Long March, Scientists Create 'Chinese NIH'

BEIJING—Scientists here rang in the New Year with the debut of China's first biomedical research fund. Last week, the National Natural Science Foundation of China (NSFC) launched a medical department that expects to disburse about 1 billion renminbi ($150 million) in government grants in 2010.

The department should be a shot in the arm for unraveling disease mechanisms, modernizing traditional Chinese medicine, and moving results from bench to bedside. "It will promote a speedy transition of basic research into clinical application," says Pei Duanqing, director general of the Guangzhou Institute of Biomedicine and Health of the Chinese Academy of Sciences.

For backers of basic biomedical research, the new department is a decisive victory in a decade-long ideological struggle. In 2001, when NSFC first declared its intention to create a medical department, "some people believed that there was no basic research in medical science," says NSFC President Chen Yiyu. That unfavorable climate compelled many scientists to work abroad. In the early 1990s, says Ma Yue, a "poor atmosphere" and a shortage of grants made it "hard to do medical research." Ma left for the United States in 1994 and returned here in 2006 to conduct stem cell research at the Institute of Biophysics of the Chinese Academy of Sciences.

The prevailing winds shifted in 2008, when hematologist Chen Zhu was appointed health minister. He has campaigned vigorously for creation of an agency akin to the U.S. National Institutes of Health (NIH) (*Science*, 28 March 2008, p. 1748). Although Chen Zhu has not forsaken that goal, he threw his weight behind NSFC's effort. The health minister was "instrumental" in helping to get the medical department off the ground, says Chen Yiyu.

Unlike NIH, NSFC's medical department will not have an intramural research program. Nevertheless, says Stephen Roper, a biophysicist at the University of Miami in Florida, "the target of NSFC and NIH is the same: apply basic research to solving ongoing human disease problems."

Chen Yiyu has tapped Wang Hong-Yang, an expert on hepatitis-induced liver cancer, as the medical department's first director. Wang, director of the International Cooperation Laboratory on Signal Transduction at the Second Military Medical University in Shanghai, will spend a third of her time here overseeing the new department. "My job is to clarify the research directions and make sure the best medical scientists get funded," she says.

That's music to the ears of Huang Liquan of the Monell Chemical Senses Center in Philadelphia, Pennsylvania. The medical department's initial budget "is an excellent start," says Huang, who believes the new entity will usher in a much wider range of opportunities for cooperation between Chinese and U.S. scientists on basic biomedical research. **–LI JIAO**

Li Jiao is a writer in Beijing. With reporting by Richard Stone.

ECOLOGY

Europe's Bats Resist Fungal Scourge of North America

The same fungus that has devastated bat colonies in the northeastern United States has been identified for the first time in Europe—in a healthy bat. "The astonishing thing is that [the fungus] affects North American bats so devastatingly, but that European bats can get along with it," says Christian Voigt, a bat physiologist at the Leibniz Institute for Zoo and Wildlife Research (IZW) in Berlin.

Survivor. This French bat was not killed by fungus on its nose (arrow).

White-nose syndrome was first identified in a cave in upstate New York in 2006. Since then, it has spread across nine states and caused unprecedented mortalities. Affected bats emerge from hibernation too frequently and lose body fat, and many starve to death. Last year, a group led by microbiologist David Blehert of the U.S. Geological Survey in Madison, identified the fungus associated with the syndrome as *Geomyces destructans*, but many puzzles remain about the nature of the disease, such as whether the bats' immune systems were compromised (*Science*, 29 May 2009, p. 1134).

European researchers watched the U.S. outbreak with alarm. "I thought, 'Oh my God, we've got a huge nightmare on our hands,' " recalls Kate Jones of the Zoological Society of London. So far, no mass casualties have been detected among Europe's species, but researchers did find anecdotal reports of bats with white fungus that no one had paid attention to previously.

On 12 March, Sébastien Puechmaille of University College Dublin (UCD) spotted a mouse-eared bat (*Myotis myotis*) covered with fungus in a cave 130 kilometers northeast of Bordeaux, France. Microscopic examination of the spores and two molecular markers showed that it was *G. destructans*, the team reported online 29 December in *Emerging Infectious Diseases*. Another group, led by Gudrun Wibbelt of IZW, has also identified the fungus in bats from three other European countries, none reporting bat deaths. Their results have been submitted to the same journal.

Now the challenge is to figure out why most European bats are not infected and why those that are remain healthy—and whether that knowledge can be used to help ailing bat populations in the United States. One scenario is that *G. destructans* has been present in Europe for a long time, and European bat species have evolved immunity, says Emma Teeling of UCD, the senior author of the December paper. Or perhaps the fungus evolved greater virulence after arriving in North America, a possibility that could be investigated with further sequencing.

Whatever the explanation, the European reports are "great news," says Alan Hicks, a mammal specialist with New York's Department of Environmental Conservation in Albany, who has charted the decline of the state's once-massive bat colonies. Eventually, an understanding of these differences could help lead to the development of a vaccine or treatments for endangered bats, Blehert says. Meanwhile, researchers are beginning once again to survey hibernating bats in the Northeast United States. Hicks says the signs so far are that deaths are continuing. **–ERIK STOKSTAD**

CREDIT: PASCAL VERDEYROUX, *EMERGING INFECTIOUS DISEASES* (ADVANCED ONLINE EDITION, 2010)

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A Devil of a Disease

Tasmanian devils are being wiped out by a deadly facial cancer that may spread when the animals fight each other

Geoff King, a farmer in Northwest Tasmania, sees a lot of fights at dinner. That's because he also runs a "devil restaurant," a tour in which customers watch the island's most famous animal, the Tasmanian devil, devour carcasses left out for it. Known as Taz in the cartoon incarnation of the marsupial, the Tasmanian devil is in reality a relatively shy scavenger. But at suppertime, and during the mating season, devils engage in the fighting and biting that have made them legendary. That violence may now be the death of the devils—but in a most unusual way.

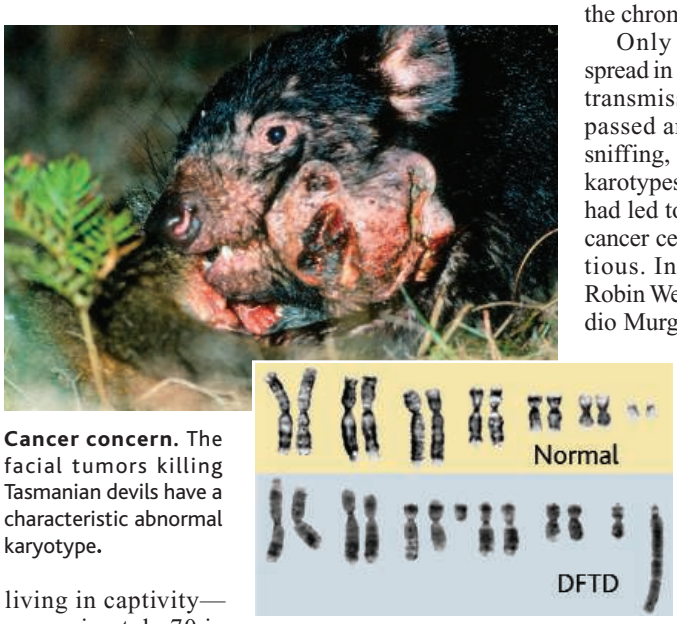
A disfiguring and deadly facial cancer has slashed Tasmanian devil numbers by up to one-half in the past decade. "It's an aggressive cancer that is spreading rapidly and killing animals within 6 months," says Menna Jones, a zoologist at the University of Tasmania in Hobart. Although several hypotheses are still in the running, clues are emerging that the devils may be transferring tumor cells directly from animal to animal during fights. While research into the unusual cancer, known as devil facial tumor disease (DFTD), continues, biologists this month outlined a management strategy aimed at safeguarding the survival of the species.

In DFTD, tumors grow on an animal's face and muzzle so that the devil eventually cannot feed. Although the facial tumors were first recorded by a wildlife photographer in 1996, the true threat only became apparent in 2000 when the same tumors were found in statewide surveys. Research picked up momentum in November 2003, when the Tasmanian government dealt out a $1.8 million funding package to tackle DFTD.

Field research indicates that between one-half and one-third of the 150,000 devils that lived in Tasmania 10 years ago have been lost. According to a report released in January, the disease is now present across at least 65% of the island. And that may be a low estimate; with no diagnostic tests, scientists can only record the disease in obviously sick animals. Instead of breeding four to five times in their life, devils have been reduced to breeding only once before they succumb to the disease, says Jones.

Although there is no immediate threat of extinction, biologists fear that devils may become "functionally extinct" and no longer perform their role as a bush janitor. Already farmers are noting that dead stock is not cleaned up from their farms, says wildlife biologist Nick Mooney of the Department for Primary Industries, Water, and Environment (DPIWE). His biggest worry is that illegally introduced foxes, which were discovered on the island in 2001, may take over the devils' ecological niche.

The disease management strategy focuses on isolating devils that are already living in captivity—approximately 70 in zoos on the Australian continent and 100 in parks in Tasmania—from wild populations afflicted with the disease. So far there is no indication that devils in captivity are catching DFTD. Wildlife managers will also capture young, apparently healthy devils to establish further insurance populations. Should these devils develop tumors in quarantine, this would provide further opportunities to study the disease. Finally, scientists will experiment with strategies to suppress the disease's spread in the wild, such as removing affected animals in order to protect nearby healthy populations.



Cancer concern. The facial tumors killing Tasmanian devils have a characteristic abnormal karyotype.

"It's an excellent example of a sensible response to a new wildlife disease about which we know very little," says Andrew Dobson, a population ecologist at Princeton University who studies wildlife diseases.

At first, researchers assumed that a virus was behind the spread of DFTD, as similar viral conditions are known in cats and other animals. But efforts over the past year to detect virus particles in tumors have come up empty, prompting research into whether cancer cells themselves spread the disease. "Field observations are consistent with direct biting transmission, and we are waiting for the lab work," says Jones.

The lab work so far is provocative but not conclusive. The tumors have been characterized as a neuroendocrine cancer, and tumors studied so far have identical chromosomal rearrangements. That suggests that all the animals with DFTD are being affected by the same cancer cell line. "That's the hypothesis that I would put my money on," says Jonathan Stoye, a virologist at the National Institute for Medical Research in London, who is impressed by the chromosomal evidence.

Only one known cancer is spread in a similar fashion. Canine transmissible venereal tumor is passed among dogs during sex, sniffing, and licking. The similar karotypes of these canine tumors had led to the suggestion that the cancer cells themselves are infectious. Indeed, viral oncologist Robin Weiss and his student Claudio Murgia at University College London have recently carried out experiments—soon to be submitted for publication—that demonstrate that these tumors are caused by a single transmissible cancerous cell line. Weiss suggests that profiling the nuclear and mitochondrial genomes of DFTD tumor cells could confirm whether they, too, are a transmissible cell line.

If direct contact is required for transmission of DFTD, then removal of sick devils would be a very effective way of controlling the disease. But if a virus does turn out to be the culprit, other animals could be asymptomatic reservoirs for the disease. Researchers are continuing to investigate possible causes, from a virus to environmental and human-made toxins, says Stephen Pyecroft, a veterinary pathologist with DPIWE.

Tasmania's government and opposition parties have been quibbling over whether to list the devil as a threatened species, but with the data in hand, it is now expected that nomination to threatened species status will go ahead later this year. Worried Tasmanians have donated an additional $50,000 to study DFTD and to make sure the devil does not go the same way as the island's other iconic animal: the now-extinct Tasmanian tiger.

–Adam Bostanci

Adam Bostanci is a science writer in Exeter, U.K.

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Prev | Table of Contents | Next

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- NEWS FOCUS

INFECTIOUS DISEASE

The Enigma of West Nile

Martin Enserink

A year after it invaded New York City, there's still much that scientists, don't know about the West Nile virus. But they're sure it will keep spreading.

Related Resources

In *Science* Magazine

NEWS FOCUS
INFECTIOUS DISEASE
West Nile Drugs, Vaccine Still Years Away
Martin Enserink
Science 24 November 2000: 1483.

When the West Nile virus gained a foothold in New York City last summer, it found a land of endless opportunities. It had its pick of dozens of bird species that had never been in contact with the virus before; who knew how many might be hosts in which the virus could live? There are more than 100 mosquito species in the United States—how many could transmit the virus from one bird to another? How fast would the newcomer colonize the entire continent?

Fifteen months after the 1999 West Nile outbreak, which sickened 62 mostly elderly people and killed seven, scientists now have some answers. They are not reassuring. This summer, the human toll has been relatively mild, with just 18 cases and one death. But the virus has been found in more than 60 bird species and about a dozen mammals; in a little more than a year, it has spread to 11 states along the East Coast and the District of Columbia. “There's a good chance it will reach the West Coast within 5 years,” predicts vertebrate ecologist Nicholas Komar of the Centers for Disease Control and Prevention (CDC) in Fort Collins, Colorado. And with no natural barriers to stop it, he adds, it's just a matter of time before citizens of Buenos Aires should start worrying.

Yet researchers are still hard pressed to predict how abundant the virus will eventually become or how serious a public health threat it will pose. Like St. Louis encephalitis, which occasionally flares up in the southern United States, West Nile virus is primarily a bird virus that is spread by mosquitoes. Humans, as well as horses and several other mammals, are “dead-end hosts.” They become infected when a mosquito bites an infected bird and then a human. But the disease stops there; unlike malaria, say, mosquitoes don't transmit the West Nile virus from person to person. That puts a natural limit on the human epidemic; but the complex dynamics of birds, mosquitoes, and humans also cause erratic outbreak patterns. “People have studied St. Louis encephalitis for 50 years, and outbreaks are still unpredictable,” says Lyle Petersen, a CDC physician who studies the West Nile virus. “They just sort of happen.”

North or south?

After its surprise debut last year, some researchers said there was a 50-50 chance that West Nile would never make it in its new home. Except for one infected crow found in Baltimore, the virus seemed confined to an 80-kilometer radius around New York City, and as temperatures dropped and mosquito populations dwindled, they said, it might well die out. Alternately, some researchers predicted that migrating birds would carry the virus south as they escaped the New York winter; it would likely show up in Florida or the Caribbean in spring. Neither scenario proved right. This winter, after searching for mosquitoes in underground sewers and abandoned buildings in New York, CDC researchers discovered a few overwintering mosquitoes, and one sample was infected with the virus, dashing any hopes that the virus would simply disappear. Nor did the southward migration occur—at least not initially. The virus has mostly traveled north this past summer. From July on, increasing numbers of infected birds were found in upstate New York, Connecticut, Rhode Island, Massachusetts, Vermont, and New Hampshire. “That took most people by surprise,” says Linda Glaser, a researcher with the U.S.

Geological Survey's National Wildlife Health Center in Madison, Wisconsin. Only late this summer did the virus head south. In early October, a dead crow in Virginia tested positive; so did one from Chatham County in North Carolina a few weeks later. Chatham, some 800 kilometers from New York City, is now the southernmost point where the virus has been found.

Ideal hosts

As some researchers tracked the virus in the field, others have been studying its behavior in the lab, trying to determine how it spreads so rapidly. Crows are the virus's most conspicuous hosts because they have been dying en masse. But that doesn't mean they're the most helpful to the virus, says Komar. An ideal host would let the virus replicate for a long time but stay healthy enough to be fed on by mosquitoes. When the host dies quickly, as do crows, the virus goes with it.

Dozens of other bird species tested positive last year for West Nile antibodies, and Komar has studied how well the virus replicates in seven of them. Blue jays were “off the charts,” says Komar; they had over a trillion viral particles per milliliter of blood when the infection peaked—similar to what has been found in crows. The humble house sparrow also came in high, although its viral load was a 1000 times lower than the blue jay's. But because house sparrows are so ubiquitous, they may be the virus's prime replication machine, suspects Komar.

Meanwhile, a team led by Michael Turell of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) in Fort Detrick, Maryland, has been trying to identify the virus's insect accomplices. The team collected two dozen species of mosquitoes in New York City, Massachusetts, and Virginia and then turned them loose on infected chickens. Two weeks later, they tested whether the mosquitoes themselves had become infected and whether they could transmit the infection to other chickens. Three *Aedes* species turned out to be highly susceptible to West Nile infection, and several others —including *Culex pipiens*, which was first implicated in the outbreak—were moderately efficient vectors.

But lab tests aren't the final word, says USAMRIID's Monica O'Guinn. Each species' role in spreading disease also depends on such factors as population density and feeding habits, about which relatively little is known; these in turn may depend on geography or weather. Some mosquito species are most likely to fuel the virus's avian life cycle, as they primarily feed on birds; others bite both birds and humans and might serve as the “bridge species” that makes people sick.

No early warning

With so many variables in play, the dynamics of the outbreak have been difficult to understand, let alone predict. It's “somewhat of an enigma,” for instance, why the virus made such impressive strides across the U.S. map this summer yet sickened only 18 people, Petersen says. He speculates that certain conditions might have favored an explosion in bird transmission but not human transmission. Some attribute at least part of the low case rate to intense spraying of insecticides. Increased public awareness may also have played a role. In New York City, for instance, the public was bombarded with the message that elderly people, especially, should protect themselves from mosquito bites, says assistant commissioner Marcelle Layton of the city's department of health.

Another riddle of the 2000 outbreak is why an early warning system for viral activity was such a fiasco. In several states, researchers bled so-called sentinel chickens weekly and tested them for West Nile antibodies. For other insect-borne viral diseases, such as St. Louis encephalitis, chickens become infected before people do and are a time-proven indicator. But very few chickens became seropositive for West Nile virus this summer, and not one did so before the first human cases.

Dead birds, on the other hand, are too sensitive an indicator; they have been found in many states where there has not been a single human case, and spraying insecticides would have been premature. CDC researchers are now focusing their efforts on developing surveillance indicators that are a better predictor of human cases, says CDC's Petersen, so that public health authorities can take precautions once the risk becomes substantial. For instance, researchers are now combing through the data gathered this year in Staten Island, the New York borough where there was a cluster of cases. The hope, says Petersen, is that these will reveal a pattern that could have foreboded the epidemic. Researchers found high numbers of infected *Culex salinarius* mosquitoes in the area; they may prove to be significant. “But in all likelihood, it may be a couple of years before we can adequately predict the risk,” he says.

For that reason alone, Petersen won't speculate where the disease will next crop up—but he knows it will. And, because no drugs or a vaccine exists (see sidebar on p. 1483), West Nile is bound to claim new human victims. “We know it's going to be more than just a couple, and we know it's not going to be hundreds of thousands,” says Peterson. “But we can't say much more with any certainty.”

The editors suggest the following Related Resources on *Science* sites

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Martin Enserink
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Summary **Full Text**

CONSERVATION

Economic Importance of Bats in Agriculture

Insectivorous bat populations, adversely impacted by white-nose syndrome and wind turbines, may be worth billions of dollars to North American agriculture.

Justin G. Boyles,[1]* Paul M. Cryan,[2] Gary F. McCracken,[3] Thomas H. Kunz[4]

White-nose syndrome (WNS) and the increased development of wind-power facilities are threatening populations of insectivorous bats in North America. Bats are voracious predators of nocturnal insects, including many crop and forest pests. We present here analyses suggesting that loss of bats in North America could lead to agricultural losses estimated at more than $3.7 billion/year. Urgent efforts are needed to educate the public and policy-makers about the ecological and economic importance of insectivorous bats and to provide practical conservation solutions.

Infectious Disease and Wind Turbines

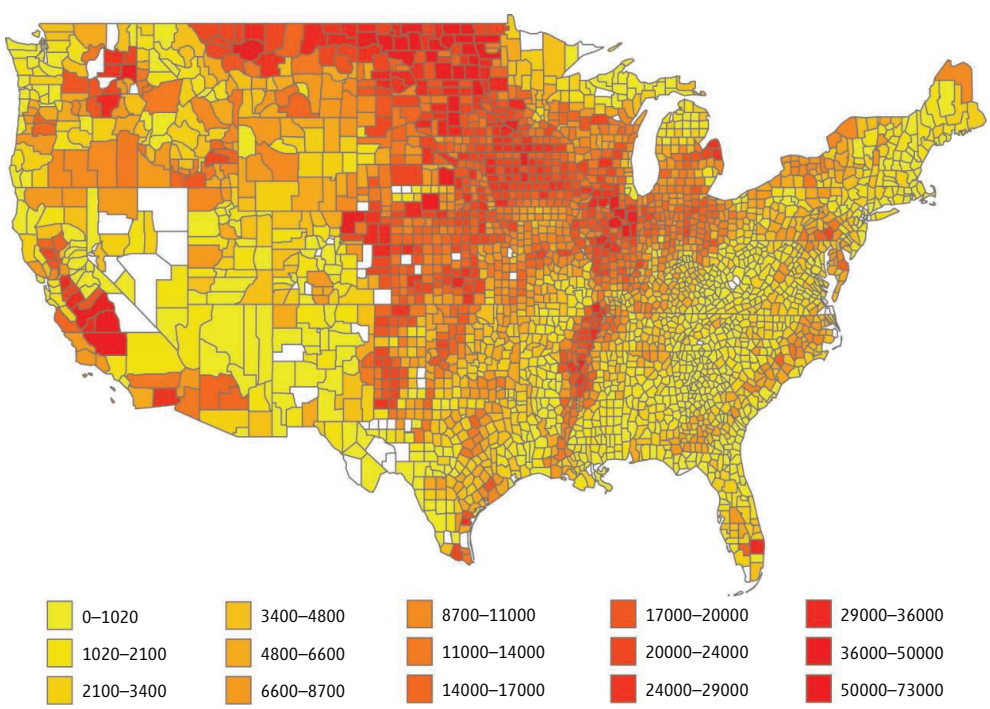
Insectivorous bats suppress populations of nocturnal insects (*1*, *2*), but bats in North America are under severe pressure from two major new threats. WNS is an emerging infectious disease affecting populations of hibernating cave-dwelling bats throughout eastern North America (*3*). WNS is likely caused by a newly discovered fungus (*Geomyces destructans*). This fungus infects the skin of bats while they hibernate and is thought to trigger fatal alterations in behavior and/or physiology (e.g., premature depletion of energy reserves) (*3*, *4*). Since February 2006, when WNS was first observed on bats in upstate New York, *G. destructans* has spread west of the Appalachian Mountains and into Canada. To date, over one million bats have probably died, and winter colony declines in the most affected region exceed 70% (*5*). Populations of at least one species (little brown bat, *Myotis lucifugus*) have declined so precipitously that regional extirpation and extinction are expected (*5*).

At the same time, bats of several migratory tree-dwelling species are being killed in unprecedented numbers at wind turbines across the continent (*6*, *7*). Why these species are particularly susceptible to wind turbines remains a mystery, and several types of attraction have been hypothesized (*6*). There are no continental-scale monitoring programs for assessing wildlife fatalities at wind turbines, so the number of bats killed across the entire United States is difficult to assess. However, by 2020 an estimated 33,000 to 111,000 bats will be killed annually by wind turbines in the Mid-Atlantic Highlands alone (*7*). Obviously, mortality from these two factors is substantial and will likely have long-term cumulative impacts on both aquatic and terrestrial ecosystems (*5*, *7*). Because of these combined threats, sudden and simultaneous population declines are being witnessed in assemblages of temperate-zone insectivorous bats on a scale rivaled by few recorded events affecting mammals.

Economic Impact

Although much of the public and some policy-makers may view the precipitous decline of bats in North America as only of academic interest, the economic consequences of losing so many bats could be substantial. For example, a single colony of 150 big brown bats (*Eptesicus fuscus*) in Indiana has been estimated to eat nearly 1.3 million pest insects each year, possibly contributing to the disruption of population cycles of agricultural pests (*8*). Other estimates suggest that a single little brown bat can consume 4 to 8 g of insects each night during the active season (*9*, *10*), and when extrapolated to the one million bats estimated to have died from WNS, between 660 and 1320 metric tons of insects are no longer being consumed each year in WNS-affected areas (*11*).

Estimating the economic importance of bats in agricultural systems is challenging, but published estimates of the value of pest suppression services provided by bats ranges



The worth of insectivorous bats. Estimated annual value of insectivorous bats in the agricultural industry at the county level. Values (×$1000 per county) assume bats have an avoided-cost value of ~$74/acre of cropland (*12*). (See SOM for details.)

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from about $12 to $173/acre (with a most likely scenario of $74/acre) in a cotton-dominated agricultural landscape in south-central Texas (*12*). Here, we extrapolate these estimates to the entire United States as a first assessment of how much the disappearance of bats could cost the agricultural industry [see supporting online material (SOM)].

Assuming values obtained from the cotton-dominated agroecosystem in Texas, and the number of acres of harvested cropland across the continental United States in 2007 (*13*), we estimate the value of bats to the agricultural industry is roughly $22.9 billion/year. If we assume values at the extremes of the probable range (*12*), the value of bats may be as low as $3.7 billion/year and as high as $53 billion/year. These estimates include the reduced costs of pesticide applications that are not needed to suppress the insects consumed by bats (*12*). However, they do not include the "downstream" impacts of pesticides on ecosystems, which can be substantial (*14*), or other secondary effects of predation, such as reducing the potential for evolved resistance of insects to pesticides and genetically modified crops (*15*). Moreover, bats can exert top-down suppression of forest insects (*1*, *2*), but our estimated values do not include the benefit of bats that suppress insects in forest ecosystems because economic data on pest-control services provided by bats in forests are lacking. Even if our estimates are halved or quartered, they clearly show how bats have enormous potential to influence the economics of agriculture and forestry.

Although adverse impacts of WNS on bat populations have occurred relatively rapidly, impacts of wind energy development appear to pose a more chronic, long-term concern. WNS has caused rapid and massive declines of hibernating bats in the northeastern United States, where this disease has persisted for at least 4 years (*5*). Thus, the coming growing season may be the first in which the adverse effects of this disease will become noticeable. Because of regional differences in crop production, the agricultural value of bats in the U.S. Northeast may be comparatively small relative to much of the United States (see the figure) (SOM). However, evidence of the fungus associated with WNS was recently detected in the Midwest and Great Plains, where the estimates of the value of bats to agriculture are substantial (see the figure). Additionally, because this region has the highest onshore wind capacity in North America, increased development of wind energy facilities and associated bat fatalities in this region can be expected (*16*). Thus, if mortality of bats associated with WNS and wind turbines continues unabated, we can expect noticeable economic losses to North American agriculture in the next 4 to 5 years.

Policy

A recently stated goal of the United Nations Environment Programme is to demonstrate the value of biodiversity to policy-makers and the public (*17*). In keeping with this goal, we hope that the scale of our estimates and the importance of addressing this issue will resonate both with the general public and policy-makers. Bats provide substantial ecosystem services worldwide, and their benefits to human economies are not limited to North America. For example, pioneering research in tropical ecosystems shows the importance of plant-visiting bats in the pollination of valuable fruit crops (*18*, *19*). Although the economic impacts of mass mortality of bats associated with WNS appear to be confined, at present, to North America, wind turbines are also causing bat fatalities in Europe (*20*), and the potential for WNS to spread to other parts of the world is unknown.

We suggest that a wait-and-see approach to the issue of widespread declines of bat populations is not an option because the life histories of these flying, nocturnal mammals—characterized by long generation times and low reproductive rates—mean that population recovery is unlikely for decades or even centuries, if at all. Currently, there are no adequately validated or generally applicable methods for substantially reducing the impacts of WNS or wind turbines on bat populations. To date, management actions to restrict the spread of WNS have been directed primarily toward limiting anthropogenic spread (e.g., cave and mine closures and fungal decontamination protocols) (*21*). Other proactive solutions for understanding and ameliorating the effects of WNS include developing improved diagnostics to detect early-stage infections and fungal distribution in the environment; defining disease mechanisms; investigating the potential for biological or chemical control of the fungus; and increasing disease resistance through habitat modification, such as creation of artificial or modified hibernacula that are less conducive to disease development and transmission (*11*, *22*). Other approaches, such as culling of infected bats have been widely discussed and dismissed as viable options for control (*23*). New research also shows that altering wind turbine operations during high-risk periods for bats significantly reduces fatalities (*24*, *25*). Specific action on these issues will benefit from scientific research carefully aimed at providing practical conservation solutions for bats in the face of new threats and at assessing their economic and ecological importance. We as scientists should also make concerted efforts to develop and use more effective methods for educating the public and policy-makers about the ecosystem services provided by bats.

Bats are among the most overlooked, yet economically important, nondomesticated animals in North America, and their conservation is important for the integrity of ecosystems and in the best interest of both national and international economies. In our opinion, solutions that will reduce the population impacts of WNS and reduce the mortality from wind-energy facilities are possible in the next few years, but identifying, substantiating, and applying solutions will only be fueled in a substantive manner by increased and widespread awareness of the benefits of insectivorous bats among the public, policy-makers, and scientists.

References

1. M. B. Kalka, A. R. Smith, E. K. V. Kalko, *Science* **320**, 71 (2008).
2. K. Williams-Guillén, I. Perfecto, J. Vandermeer, *Science* **320**, 70 (2008).
3. D. S. Blehert *et al.*, *Science* **323**, 227 (2009).
4. P. M. Cryan, C. U. Meteyer, J. G. Boyles, D. S. Blehert, *BMC Biol.* **8**, 135 (2010).
5. W. F. Frick *et al.*, *Science* **329**, 679 (2010).
6. P. M. Cryan, R. M. R. Barclay, *J. Mammal.* **90**, 1330 (2009).
7. T. H. Kunz *et al.*, *Front. Ecol. Environ* **5**, 315 (2007).
8. J. O. Whitaker, Jr., *Am. Midl. Nat.* **134**, 346 (1995).
9. E. L. P. Anthony, T. H. Kunz, *Ecology* **58**, 775 (1977).
10. A. Kurta, G. P. Bell, K. A. Nagy, T. H. Kunz, *Physiol. Zool.* **62**, 804 (1989).
11. J. G. Boyles, C. K. R. Willis, *Front. Ecol. Environ* **8**, 92 (2010).
12. C. J. Cleveland *et al.*, *Front. Ecol. Environ* **4**, 238 (2006).
13. USDA, *2007 Census of Agriculture: United States Summary and State Data*, vol. 1, *Geographic Area Series* (AC-07-A-51, USDA, Washington, DC, 2009).
14. D. Pimentel, in *Integrated Pest Management: Innovation-Development Process*, R. Peshin and A. K. Dhawan, Eds. (Springer Media, Houten, Netherlands, 2009), pp. 89–111.
15. P. Federico *et al.*, *Ecol. Appl.* **18**, 826 (2008).
16. D. L. Elliot, C. G. Holladay, W. R. Barchet, H. P. Foote, W. F. Sandusky, *Wind Energy Resource Atlas of the United States* (Solar Energy Research Institute, U.S. Department of Energy, Golden, CO, 1986).
17. The Economics of Ecosystems and Biodiversity, www.teebweb.org/.
18. S. Bumrungsri, E. Sripaoraya, T. Chongsiri, K. Sridith, P. A. Racey, *J. Trop. Ecol.* **25**, 85 (2009).
19. S. Bumrungsri *et al.*, *J. Trop. Ecol.* **24**, 467 (2008).
20. J. Rydell *et al.*, *Acta Chiropt.* **12**, 261 (2010).
21. U.S. Fish and Wildlife Service, www.fws.gov/whitenosesyndrome/.
22. J. Foley, D. Clifford, K. Castle, P. Cryan, R. S. Ostfeld, *Conserv. Biol.* **25**, 223 (2011).
23. T. G. Hallam, G. F. McCracken, *Conserv. Biol.* **25**, 189 (2011).
24. E. F. Baerwald, J. Edworthy, M. Holder, R. M. R. Barclay, *J. Wildl. Manage.* **73**, 1077 (2009).
25. E. Arnett *et al.*, *Front. Ecol. Environ* **16**, (2010). 10.1890/100103

Supporting Online Material

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