Effects of Host Diversity on Infectious Disease

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Abstract

The dynamics of infectious diseases can be affected by genetic diversity within host populations, species diversity within host communities, and diversity among communities. In principle, diversity can either increase or decrease pathogen transmission and disease risk. Theoretical models and laboratory experiments have demonstrated that a dilution effect (decreased disease risk with increasing diversity) can occur under a wide range of conditions. Field studies of plants, aquatic invertebrates, amphibians, birds, and mammals demonstrate that the phenomenon indeed does occur in many natural systems. A dilution effect is expected when (*a*) hosts differ in quality for pathogens or vectors; (*b*) higher quality hosts tend to occur in species-poor communities, whereas lower quality hosts tend to occur in more diverse communities; and (*c*) lower quality hosts regulate abundance of high-quality hosts or of vectors, or reduce encounter rates between these hosts and pathogens or vectors. Although these conditions characterize many disease systems, our ability to predict when and where the dilution effect occurs remains poor. The life-history traits that cause some hosts to be widespread and resilient might be correlated with those that promote infection and transmission by some pathogens, supporting the notion that the dilution effect might be widespread among disease systems. Criticisms of the dilution effect have focused on whether species richness or species composition (both being metrics of biodiversity) drives disease risk. It is well established, however, that changes in species composition correlate with changes in species richness, and this correlation could explain why the dilution effect appears to be a general phenomenon.

INTRODUCTION

At their simplest, infectious diseases involve only two species—a specialist pathogen and its sole host. The simplicity of these systems allows the development of ecological theory to understand the effects of variable host abundance, physiology, and behavior on pathogen transmission and disease dynamics within this two-species system (Anderson & May 1979, 1981). Models consisting of one host and one pathogen have been useful in allowing ecologists to isolate the effects on disease dynamics of, for instance, the length of the infectious period, the probability that an infectious and a susceptible individual make contact, and the probability that a pathogen is transmitted given contact (Anderson & May 1991). But these insights have required considerable simplifications of real host-pathogen systems. First, the models assume that host populations are homogeneous with respect to susceptibility to pathogen transmission, maintenance, and proliferation, but this is rarely the case. Most host populations are genetically heterogeneous in ways that affect their interactions with pathogens. Second, pathogens and parasites are allowed to infect only one host species in these models, but even many pathogens and parasites that are considered host specialists typically infect multiple host species. Some specialize on a particular host species but can spill over and temporarily invade others, whereas others readily proliferate within several or even many host species within a community. As a consequence, host species can differ strongly with respect to susceptibility to pathogen transmission, maintenance, and proliferation. Third, simple models assume that host species are affected only by their interaction with the specialist pathogen, but real host species occur within ecological communities. Host interactions with pathogens can be affected strongly by the presence of interacting species, including predators, competitors, and other parasites, within these communities (Holt & Roy 2007, Ostfeld & Holt 2004, Packer et al. 2003).

This review examines recent scientific studies that explore how disease dynamics are affected by variation in genetic diversity within a host species, variation among host species within communities, and variation among ecological communities. These three levels of variation—of diversity—correspond to the three levels invoked in leading definitions of the term biodiversity (Redford & Richter 1999). Indeed, current usage of the term biodiversity generally invokes genetic diversity, species diversity, and community diversity (we replace the more commonly used term ecosystem with community to reflect the notion that the abiotic component of ecosystems is not explicitly considered part of biodiversity (see Corvalan et al. 2005, Harper & Hawksworth 1994).

Within each of the three levels comprising biodiversity (genotypes, species, communities), diversity can be characterized in three ways: (*a*) by the number of different entities (e.g., the number of species in a community, or species richness), (*b*) by the relative abundances of the different entities (e.g., the evenness by which species are represented in a community, or species evenness), and (*c*) by the specific identities of the different entities (e.g., the species composition of a community). Quantifying biodiversity is fairly straightforward for *a* and *b*, but more challenging for *c*. This challenge is sometimes addressed by grouping particular genes or species into functional or taxonomic units. In other cases, it is addressed by attempting to correlate species identity with a quantitative measure of biodiversity. For example, when species losses from a community occur in a more or less predictable sequence, then changes in community composition are correlated with changes in species richness, a quantitative metric. In some cases, the same change in a community can increase biodiversity at one level while decreasing it at another. For example, the addition of an exotic species to a community increases species richness by one species but decreases community diversity by homogenizing the donor and recipient communities.

Metrics of biodiversity can be used to characterize either the long-term, static characteristics of a biota or the dynamic changes that accompany ecological and anthropogenic changes.

Within any species, community, or metacommunity (a group of communities), native biodiversity is the result of biogeographic processes (e.g., speciation, community diversification) occurring over evolutionary time. In contrast, dynamic changes in biodiversity are dominated by anthropogenic processes acting locally and quickly. Overwhelmingly, these changes consist of biodiversity losses rather than gains. This review addresses the relationship between infectious diseases and both static biodiversity and dynamic changes in biodiversity. Because of the importance of applying our scientific understanding to the management of diseases, we focus largely on how dynamic changes in biodiversity affect pathogen transmission and disease risk.

GENETIC DIVERSITY WITHIN HOSTS

Recently, Lively (2010) provided a simple model of the establishment and spread of an infectious disease in a host species with different numbers of genotypes. This model assumed that each host genotype was susceptible to one of many pathogen genotypes and resistant to the rest, reflecting the matching alleles model of infection (Lively 2010). Lively focused on R_0, the number of secondary infections produced by the initial infection in a susceptible population. He found that the ability of an invading pathogen to establish in a host population, as measured by R_0, was inversely proportional to the number of genotypes in the host population. He also found that infections that are able to spread initially die out more rapidly when the host population is more genetically diverse. In a separate study, the severity of modeled livestock epidemics was also inversely proportional to host genetic diversity under the assumption of a single pathogen genotype and variation in the genetic resistance of host individuals to this pathogen (Springbett et al. 2003).

These theoretical explorations support empirical observations from a variety of natural and laboratory systems. Monocultures of genetically similar or identical plants are notoriously susceptible to disease spread, whereas genetic mixtures of the same plants are more resistant (Elton 1958, Mundt 2002). For example, experimentally varying the frequency of a susceptible genotype of wheat (*Triticum aestivum*) from 1.0 (low diversity) to 0.25 (high diversity) in a field experiment led to dramatically reduced prevalence of disease caused by striped rust, *Puccinia striiformis* (Mundt et al. 2011). On an even larger scale, a field experiment of enormous scope addressed the effects of planting diverse genotypes of rice (*Oryza sativa*) on the incidence of disease caused by rice blast (*Magnaporthe grisea*) in Yunnan Province, China (Zhu et al. 2000). Traditionally, rice farmers throughout Yunnan Province plant vast monocultures of single rice genotypes, and they often require extensive applications of fungicides to prevent blast epidemics. Glutinous rice is particularly susceptible to rice blast. By planting glutinous rice interspersed with other rice varieties in thousands of fields, farmers reduced fungal rice blast disease by 94% and increased glutinous rice yields by 89% compared with monocultures (Zhu et al. 2000) (**Figure 1**).

Dennehy et al. (2007) experimentally assessed the effects of bacterial (host) genetic diversity on attack rates by a pathogenic bacteriophage. Phage Φ6 attacks and kills its bacterial host, *Pseudomonas phaseolicola*, by attaching to pili (small protuberances the bacteria use to attach to plants on which they feed). When the bacteria withdraw their pili, attached phages enter the cell, replicate, and kill the bacterium. In addition to wild-type *P. phaseolicola* with these pili, two naturally occurring mutants also exist. One, called superpiliated, has many pili but never retracts them, so that it attracts phages but the phages cannot enter the bacterial cell. The other mutant, called neutral, has no pili and so Φ6 phages are unable to attach. Dennehy et al. subjected monocultures of the wild-type *Pseudomonas* to its Φ6 pathogen and then added each of the naturally occurring *Pseudomonas* mutant genotypes, increasing genotypic diversity. Compared to the wild-type monoculture, a mixed culture of 50% wild type and 50% neutral reduced the abundance of Φ6 phage almost

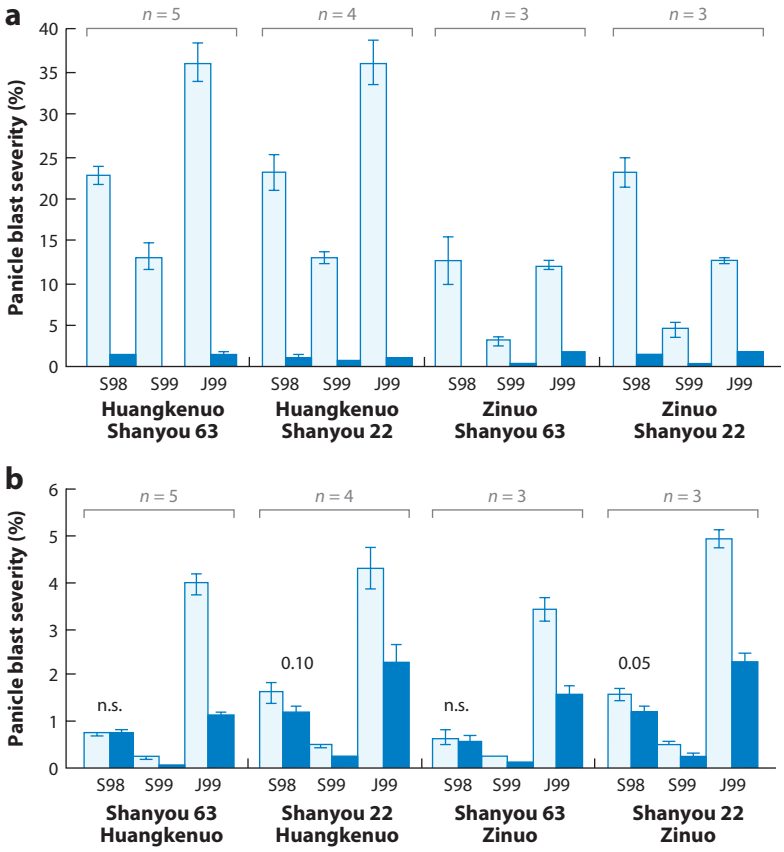

Figure 1

Severity of panicle rice blast disease (caused by *Magnaporthe grisea*) in monocultures (*light blue bars*) and polycultures (*dark blue bars*) of rice in China. (*a*) Susceptible, glutinous varieties of rice Huangkenuo and Zinuo; (*b*) more resistant, hybrid varieties Shanyuo 22 and Shanyuo 63. n = the number of plots included in the count for each bar. Error bars are 1 standard error. All differences between pairs of monoculture and polyculture bars are significant at $P < 0.01$ based on a one-tailed t-test, unless indicated by 0.05 (significant at $P < 0.05$), 0.10 (significant at $P < 0.10$), or n.s., (not significant at $P = 0.10$). Reproduced with permission from Zhu et al. (2000).

tenfold. When they presented the phage with a mixture of 50% wild type and 50% superpiliated *P. phaseolicola*, the phages declined in abundance by about 700-fold.

Similar experiments performed with animals give similar results. Using outdoor mesocosms, Altermatt & Ebert (2008) exposed populations of *Daphnia magna* water fleas to *Octosporea bayeri* microsporidian parasites. *Daphnia* populations were established by allowing clonal reproduction of genotypes taken from natural lakes and seeding experimental mesocosms with low (1 genotype) and high (10 genotypes) genetic diversity. Hosts in these mesocosms were exposed to parasite populations with different numbers of genotypes. Parasite prevalence (proportion of hosts infected) was consistently higher in low- than in high-diversity host populations; this result held irrespective of parasite genetic variation.

Several mechanisms appear capable of causing observed inverse relationships between host genetic diversity and disease severity or spread (Keesing et al. 2006). The data from all of the examples

above are consistent with the encounter reduction mechanism of Keesing et al. in which host diversity (genetic diversity, in these cases) reduces rates of encounter between susceptible hosts and pathogens. For striped rust and rice blast, less susceptible genotypes appear to intercept dispersing fungal pathogens that might otherwise contact susceptible individuals. Superpiliated *P. phaseolicola* bacteria absorb but do not contribute phages, reducing phage encounters with wild-type hosts. Similarly, less susceptible *Daphnia* genotypes apparently act as dead-end hosts when they filter from the water column parasites that might otherwise infect susceptible genotypes. Apparently, encounter reduction can occur in systems in which genetic variation is spatially structured, as for plants in crop fields, and in which it is not, as for *Daphnia* in the water column.

Another mechanism by which genetic diversity might reduce pathogen transmission consists of the regulation of the population density of susceptible hosts by other competing genotypes [susceptible host regulation sensu Keesing et al. (2006)]. In the *Daphnia* study (Altermatt & Ebert 2008), this mechanism was rejected by the observation that genetically diverse host populations did not contain lower densities of susceptible hosts. In the bacterium-phage example, regulation of wild-type bacteria by competition with the neutral genotype appeared to reduce phage abundance (Dennehy et al. 2007). No evidence for susceptible host regulation has been detected in the plant-fungus studies described above, but an additional mechanism, which might be called resistance enhancement, might operate in the rice blast system. Zhu et al. (2000) postulated that the diverse mixtures of rice genotypes supported a diverse assemblage of fungal pathogens, none of which became very abundant. Each of these pathogens appeared to vaccinate rice plants and increase their resistance to multiple pathogens. Mechanisms underlying decreased disease prevalence with increasing genetic diversity require more attention.

In some of the examples, the reduction in pathogen transmission accompanying increased genetic diversity arose from specific traits of the genotypes used in field or lab experiments. For instance, in the experiments on fungal pathogens of plants, the monoculture consisted of a susceptible genotype and the polyculture included less susceptible ones. In other cases, however, reduced disease under increased genetic diversity occurred without regard to the specific genotypes used. Genetic diversity per se was responsible for reduced disease in the models of Lively (2010) and Springbett et al. (2003) and in the *Daphnia* experiments of Altermatt & Ebert (2008). In these cases, when faced with a genetically diverse group of pathogens, any host monoculture was more susceptible than any host polyculture.

SPECIES DIVERSITY AMONG HOSTS

In a sense, the effect of species diversity on pathogen transmission is simply an extension of the effect of genetic diversity within species. Just as with different host genotypes, different host species are expected to vary in their susceptibility to, and ability to support replication of, specific pathogens. But differences between species are expected to be larger than those within a species.

Both theoretical and empirical treatments of the effects of changes in species diversity on disease dynamics have tended to explore dynamics in a single-host system and then ask how disease dynamics change when species are added. An early example is transmission of the malaria parasite (*Plasmodium* spp.) by mosquitoes to humans. Investigators proposed that the presence of wild or domestic animals that did not support *Plasmodium* might divert blood-seeking mosquito vectors away from potential human hosts, an idea that has been called zooprophylaxis (Service 1991, World Health Organization 1982). This concept, following an earlier treatment by Brumpt (1944–45), implies two specific conditions: (*a*) that the added host does not amplify the pathogen and (*b*) that the added host reduces disease risk by diverting the vector from biting humans. Later, Matuschka & Spielman (1992) noticed parallels between malaria zooprophylaxis and another vector-borne

disease, Lyme disease. Here the vector is an *Ixodes* tick and the pathogen is a spirochete, *Borrelia burgdorferi*. Ticks acquire pathogens readily by feeding on certain species of small mammals, but they acquire pathogens much less efficiently when feeding on other species of host, including some songbirds, ungulates, and carnivores (LoGiudice et al. 2003, Matuschka et al. 1993, Richter & Matuschka 2006, Richter et al. 2000). When these latter hosts, which are considered incompetent reservoirs for the Lyme pathogen, are present in the host community, they can potentially divert tick meals away from the competent reservoirs and reduce tick infection prevalence. Norman et al. (1999) used the term dilution effect to refer to the potential for increases in host diversity to drive another tick-borne pathogen, Louping ill virus, to extinction. They modeled the Louping ill system with both a reservoir-competent host (red grouse, *Lagopus lagopus scoticus*) and a reservoir-incompetent host (mountain hares, *Lepus timidus*); diversity was increased by increasing the relative abundance of the latter. Hence, their model did not manipulate species richness, but rather the evenness of the two hosts. As the ratio of incompetent to competent reservoirs increased from a low level, more tick bites were received by the incompetent host, reducing virus transmission until it was eliminated from the system.

Initial development of the concept that increased diversity decreases disease risk, under the aegis of either the term zooprophylaxis or dilution effect, was mechanistic and specific to a particular disease system. To generalize the concept and distinguish the phenomenon from the underlying mechanisms, Keesing et al. (2006) redefined the term dilution effect to refer to the inverse relationship between diversity and disease risk. They then characterized a set of potential mechanisms that can cause the relationship. Considerable recent research on the dilution effect (hereafter DE) has taken one of two general approaches. One approach asks whether a specific manipulation of host species diversity produces a DE—i.e., can it occur? The second asks, is the DE frequently observed in nature—i.e., does it occur?

Can the Dilution Effect Occur?

Addressing this question involves manipulating host species diversity either in laboratory experiments or in mathematical models and then measuring indicators of pathogen transmission or disease risk. Dobson (2004) and Rudolf & Antonovics (2005) used epidemiological models to explore the conditions under which increases in host diversity dilute, versus amplify, pathogen transmission. Both studies considered disease systems in which rates of pathogen transmission are proportional to the frequency of infected individuals in the host population (frequency-dependent transmission), or alternatively to the density of infected individuals in the host population (density-dependent transmission). Frequency-dependent transmission is thought to characterize most vector-borne diseases because a vector's biting rate (and thus its opportunities to become infected) is assumed to be determined by intrinsic physiological or behavioral features of the vector rather than by host density. Consequently, the probability of the vector becoming infected is determined by the frequency of infection in the host. Frequency dependence also pertains to sexually transmitted diseases. Density-dependent transmission is thought to characterize systems with free-living infective stages, aerial plumes of pathogens, or direct transmission in an unstructured (randomly mixing) host population. When transmission is frequency-dependent, increases in biodiversity suppress pathogen transmission, and this DE occurs regardless of the identities or changes in abundances of individual species (Dobson 2004, Rudolf & Antonovics 2005). When transmission is density dependent, increases in biodiversity tend to amplify pathogen transmission when the added species simply increase the total abundance of all hosts in the system, that is, when there are no compensatory reductions in host abundance with increased species richness. A DE occurs in systems with density-dependent transmission when compensatory

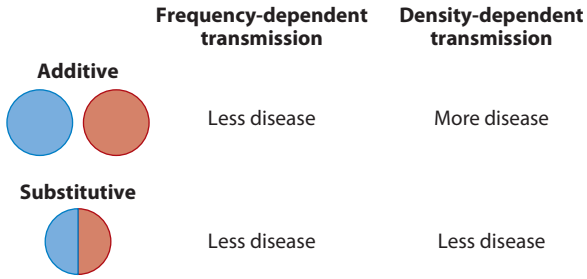

Figure 2

Effect of transmission mode on disease levels in a target (*blue*) population following the addition of a second (*red*) species, i.e., an increase in diversity. The bottom right-hand outcome panel represents density-dependent dilution, and outcomes in the two left-hand outcome panels represent frequency-dependent dilution. Reproduced with permission from Rudolf & Antonovics (2005).

reductions in abundance accompany the addition of new host species (Rudolf & Antonovics 2005) (**Figure 2**).

In addition to these general models, specific models of particular disease systems have been built to ask whether a DE can occur. In an epidemic model developed for hantavirus pulmonary syndrome, with a deer mouse host and a competing rodent nonhost, Peixoto & Abramson (2006) found that competition from the nonhost reduced prevalence of hantavirus infection in the mouse host and could, when competition was intense, drive the pathogen locally extinct. A detailed analytical model of Lyme disease showed that a DE occurred when abundances of inefficient reservoir hosts exceeded those of efficient reservoirs, and could also occur at any combined abundances of competent and incompetent reservoirs as long as tick abundance increases nonmonotonically with total host abundance (Rosa & Pugliese 2007). In a highly mechanistic simulation model of Lyme disease, a DE occurred under three conditions: (*a*) when high diversity reduced density of the main reservoir host, the white-footed mouse (*Peromyscus leucopus*) by any form of competition—direct, indirect or apparent; (*b*) when the nonmouse hosts in the community fed proportionally more nymphal than larval ticks compared to *P. leucopus*; and/or (*c*) when tick mortality was higher on nonmouse than mouse hosts (Ogden & Tsao 2009). When these conditions are not met, high diversity can amplify the number of infected ticks, and hence disease risk. Little direct evidence can be brought to bear on the first condition, although circumstantial evidence is supportive (Nupp & Swihart 2000). Supporting evidence for the second condition is provided by Ogden & Tsao's observation that in 12 of 18 studies nonmice had higher nymph:larva ratios than mice. The third condition is strongly supported by the dramatically higher mortality rates of larval ticks on nonmouse than mouse hosts observed by Keesing et al. (2009, 2010).

Manipulating host diversity in field experiments has also led to insights about whether the DE can occur. For example, Mitchell et al. (2002) varied the diversity of prairie plants from 1 to 24 species per plot and monitored the severity of disease caused by foliar fungal pathogens on all host plants. Plant species were selected by random draw, so species composition varied randomly in all field plots and did not confound variation in species richness. For 11 fungal pathogens, severity of disease decreased significantly with increasing plant species richness, whereas for only one pathogen did disease increase with increasing host richness. In about half of the pathogens showing a DE, reduced disease severity was associated with reduced host density, providing examples of susceptible host regulation (Keesing et al. 2006). Roscher et al. (2007) also studied disease severity in field plots planted with variable numbers of herbaceous plant species (from 0 to 59 additional species). In this study, the focal diseases were caused by crown rust (*Puccinia coronatum*) and stem

rust (*P. gramminis*), and the focal host plant was perennial ryegrass (*Lolium perenne*). Although different cultivars of ryegrass varied in their susceptibility to both pathogens, for all cultivars disease severity and infection prevalence declined dramatically with plant species richness. Although initial ryegrass density was constant in all treatments, both densities and individual plant sizes decreased with increasing diversity. Therefore, both these field experiments with plants strongly suggest that, even if pathogen transmission is density dependent, a DE occurs when increased diversity causes compensatory declines in host abundance or biomass, supporting a main conclusion of the Rudolf & Antonovics (2005) model. In contrast to these results that support the model, Borer et al. (2010) found that plant species richness did not predict prevalence of aphid-transmitted barley-cereal yellow dwarf virus in experimental plant communities. Instead, virus prevalence was predicted by local variation in percent cover of perennial grasses and phosphorus enrichment.

Experiments varying animal host diversity have demonstrated a DE for diseases of amphibians and humans. Johnson et al. (2008) examined infestation of American toads [*Anaxyrus* (= *Bufo*) *americanus*] with the trematode parasite *Ribeiroia ondatrae*, which causes limb malformations and increases mortality. They raised toads alone, in conspecific pairs (increased density), and in heterospecific pairs with either a treefrog [*Pseudacris* (= *Hyla*) *versicolor*] or the frog *Rana clamitans* or both. Adding a treefrog significantly reduced trematode burden in toads, and this effect of increased diversity was independent of either toad or total amphibian density. Adding *R. clamitans*, however, did not reduce trematode burden in toads. Using a similar experimental design, Searle et al. (2011) varied species richness of amphibians and total amphibian density and measured infection of a particularly susceptible species, the western toad (*Anaxyrus boreas*) with the fungal pathogen *Batrachochytrium dendrobatidis* (Bd), which is causing amphibian declines worldwide. Nontoad species added to manipulate species diversity were treefrogs (*Pseudacris regilla*) and the frog *Rana cascadae*. Increased host species richness consistently reduced Bd infection prevalence and infection severity both in toads alone and in all species combined (**Figure 3**). In contrast with the *Ribeiroia* study, both nontoad species reduced Bd infection, and the effect of adding *Rana* was somewhat stronger than that of adding *Pseudacris*.

To test for a DE in human schistosomiasis, Johnson et al. (2009) created monocultures of the snail *Biomphalaria glabrata*, which is an important intermediate host for *Schistosoma mansoni*. They also created polycultures containing *B. glabrata* and naturally co-occurring snail species. They added identical concentrations of *S. mansoni* miracidia to containers with either *B. glabrata* snails alone, *B. glabrata* with *Helisoma trivolvis* or *Lymnaea stagnalis* snails, or both (neither of these snail species supports replication by *S. mansoni* miracidia) and monitored cercarial release rates, which are strong predictors of human risk. In containers with two or three species of snail (*Biomphalaria* plus one or both of the other snails), both the proportion of snails infected and the cercarial release rates were strongly reduced. *Biomphalaria* snails raised alone released, on average, between two and five times as many schistosome cercariae as did the snails raised together with one or two other species. Several other experimental investigations of a DE in helminth parasites are reviewed by Johnson & Thieltges (2010) and Keesing et al. (2010).

From these modeling and experimental studies we can conclude that (*a*) a DE can occur under a wide range of conditions, including frequency- and density-dependent transmission of the pathogen, in pathogens with simple or complex life cycles, in terrestrial and aquatic systems, and in plants and animals; (*b*) in some cases, reduced pathogen transmission with increased diversity depends on the specific identity of the species added to the system, but in other cases the DE occurs irrespective of species identity; and (*c*) a DE can occur in host communities confronted with both single and multiple pathogens.

The potential for the DE to occur under a variety of conditions does not demonstrate that it does occur regularly in nature. A DE is not expected to occur, and indeed, an amplification

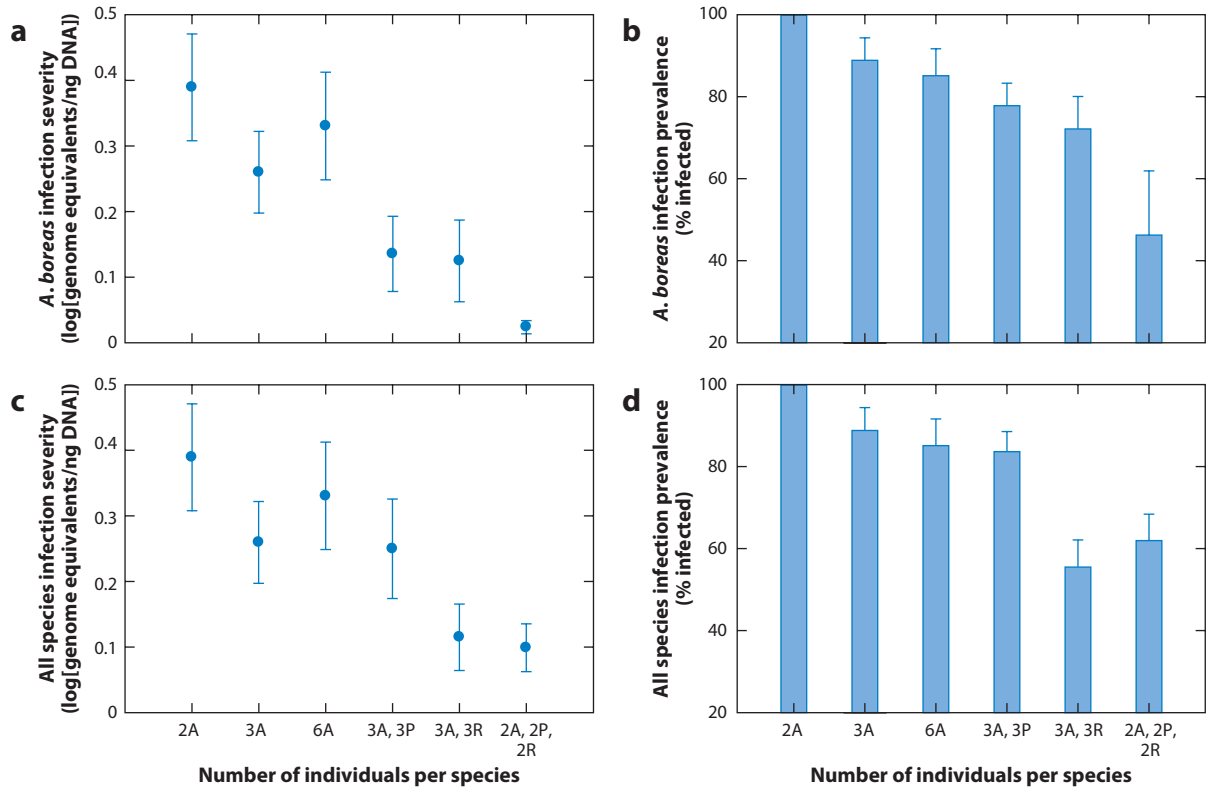

Figure 3

Average infection severity and prevalence of *Batrachochytrium dendrobatidis* (Bd) with varying host density and species richness. Treatments labeled on the horizontal axis represent the number of individuals of each species, with "A" for *Anaxyrus boreas*, "P" for *Pseudacris regilla*, and "R" for *Rana cascadae*. (*a*,*c*) Points show the average Bd infection severity (log + 1-transformed; ± standard error) for *A. boreas* (*a*) and for all species present (*c*). (*b*,*d*) Bars show the mean percentage (+standard error) of *A. boreas* testing positive for infection (*b*) and the percentage infection for all species (*d*). Reproduced with permission from Searle et al. (2011).

effect (Keesing et al. 2006) can occur when (*a*) the species added to foster diversity increases are the most competent reservoirs for the pathogen (Ostfeld & Keesing 2000, Schmidt & Ostfeld 2001) or (*b*) pathogen transmission is density dependent and more diverse host communities show no compensatory reductions in abundance of reservoir-competent hosts (Dobson 2004, Rudolf & Antonovics 2005). In addition, (*c*) if the pathogen is vector borne, host diversity might be relatively unimportant if the vector is a strict host specialist (i.e., changes in host diversity do not influence vector feeding patterns) and compensatory reductions in the most competent reservoir(s) do not accompany increased diversity (Loss et al. 2009, Ogden & Tsao 2009, Ostfeld & Keesing 2000, Schmidt & Ostfeld 2001).

Does the Dilution Effect Occur in Nature?: Plants and Aquatic Organisms

Correlative studies assessing the relationship between diversity and disease risk are accumulating, some of which use statistical approaches to infer, if not demonstrate, causality. Perhaps the most comprehensive individual field study to date concerns infection of woody plants by the causative agent of sudden oak death (SOD), *Phytophthora ramorum*, in central coastal California. Haas

et al. (2011) analyzed plant communities and pathogen prevalence in 280 500-m^2 plots within a 79,356-ha study area over two years. They used Bayesian hierarchical modeling to assess the effects of host species diversity (richness and Shannon diversity) on pathogen prevalence in local plant communities, with models accounting for an abundance of plots with no pathogen (zero inflated models) and for spatial autocorrelation at a variety of scales. All of their Bayesian models indicated a negative relationship between species diversity (both richness and Shannon diversity) and pathogen incidence. This strong DE remained after statistically accounting for local density of the most competent host plants [bay laurel (*Umbellularia californica*) and tanoak (*Notholithocarpus densiflorus*)]. Detection of a DE was consistent with prior experimental studies on diseases of herbaceous plants (Knops et al. 1999, Mitchell et al. 2002).

Hall et al. (2009) examined the prevalence of fungal (*Metschnikowia bicuspidate*) infection in *Daphnia* communities in a series of lakes in Michigan, USA, that varied in host diversity. Some lakes were virtual monocultures of *Daphnia dentifera*, which is readily infected by the pathogen, whereas other lakes were more diverse, with *D. dentifera* comprising between about 25% and 80% of the *Daphnia* community. The relative host index, defined as the population density of *D. dentifera* divided by the summed densities of the three other *Daphnia* species, in a lake measured before fungal epidemics was a significant predictor of the size of the epidemic. Lower diversity communities were more dominated by *D. dentifera* and had larger epidemics.

In other freshwater systems, the introduction of an exotic species has been associated with strong declines in disease within native hosts. Introductions of a non-native freshwater snail (*L. stagnalis*) and non-native brown trout (*Salmo trutta*) reduced prevalence of infection of native snails with trematode parasites (Kopp & Jokela 2007) and of native fishes with several helminth parasites (Kelly et al. 2009a), respectively. Although these species introductions increased species richness by one species, it is important to note that they reduced community diversity by homogenizing the native and adoptive communities. In addition, in some cases, the addition of non-native species with their associated pathogens to susceptible host communities can increase pathogen transmission in the native community (Gurnell et al. 2006, Tompkins et al. 2003).

Does the Dilution Effect Occur in Nature?: Nonvector-Borne Zoonoses

Correlative studies of several zoonotic disease systems that lack vectors demonstrate the frequent occurrence of the DE in nature. Perhaps the most widely studied of these are the hantaviruses (family Bunyaviridae), common rodent-associated viruses widespread in Europe, Asia, North America, and South America. Virus can be transmitted among individual small mammals during fighting and other contacts, and humans can be exposed if they inhale airborne particles of small-mammal excreta that contain virus particles. Risk of human exposure is a function of both the population density and infection prevalence of the rodent reservoir (Yates et al. 2002). Each type (species) of hantavirus tends to be associated with only one species, or a group of closely related species, of reservoir host, although spillover to other species is possible. The list of rodent species that act as key reservoir hosts worldwide includes the Norway rat (*Rattus norvegicus*), black rat (*R. rattus*), bank vole (*Myodes glareolus*), deer mouse (*Peromyscus maniculatus*), white-footed mouse (*P. leucopus*), hispid cotton rat (*Sigmodon hispidus*), rice rat (*Oryzomys palustris*), and small vesper mouse (*Calomys laucha*). It is noteworthy that each of these species is a habitat generalist, geographically widespread, locally highly abundant, and resilient to anthropogenic disturbance. Consequently, these reservoir species tend to occur and even thrive in low-diversity small-mammal communities, potentially leading to higher transmission risk when biodiversity is low.

Studying Laguna Negra hantavirus in the Paraguayan Chaco, Yahnke et al. (2001) analyzed small mammal communities and virus distributions in four habitat types over 15 months. The most

abundant and widespread mammal they trapped, *C. laucha*, was the only demonstrated host for the virus. Infection prevalence in host populations was positively correlated with the proportion of *C. laucha* in the rodent community, with highest prevalence found in sites where >30% of the rodent fauna consisted of *C. laucha*, but was not correlated with host density per se. Piudo et al. (2011) assessed the causes of variation in infection prevalence of Andes hantavirus in its reservoir host, *Oligoryzomys longicaudatus*, in both peridomestic and forest habitats of Patagonia. They found that *O. longicaudatus* was the numerically dominant small-mammal species in peridomestic habitats where small-mammal diversity was low but not in sylvan habitats where diversity was higher. They found that the number of infected *O. longicaudatus* was negatively correlated with small-mammal diversity during the same month and in the prior two months; however, they did not find a significant correlation between mammal diversity and the proportion of reservoir hosts infected. A similar result was obtained by Ruedas et al. (2004) studying Choclo and Calabazo hantaviruses in 9 sites in Panama's Azuero Peninsula, where the rodent reservoirs are *O. fulvescens* and *Zygodontomys brevicauda*. These researchers compared small-mammal communities at sites where human hantavirus disease was detected (case sites) with the fauna at a reference site with no human disease; case sites had significantly lower diversity (Shannon index) than reference sites. In a later live-trapping study in the same region, Suzan et al. (2009) permanently removed all small-mammal species except the community dominants *O. fulvescens* and *Z. brevicauda* on 16 sites, which created an experimental reduction of species diversity that mimicked natural patterns (Ruedas et al. 2004; Suzan et al. 2008a,b). On the remaining 8 sites—the control sites—the investigators marked and released all animals captured, but did not manipulate abundances. In the 16 removal plots, population densities of the two reservoir species were significantly increased relative to their densities on the control plots, indicating that high small-mammal diversity suppresses abundance of reservoir hosts. More strikingly, the removal of nonreservoir species was associated with a dramatic increase in the proportion of the reservoir populations that were infected with hantavirus, from 8% to 12% on control plots to about 35% on removal plots (**Figure 4**). Studying a European hantavirus (Puumala virus) in 14 sites in northern Belgium, Tersago et al. (2008) found that

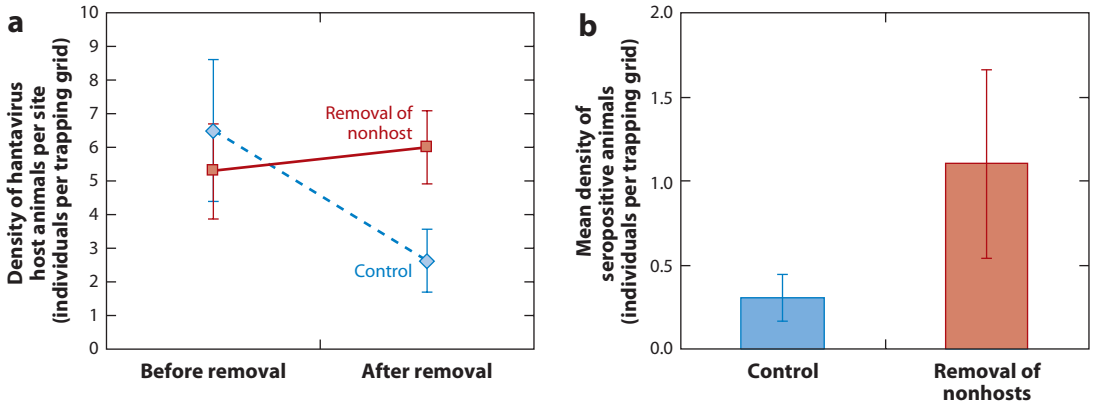

Figure 4

Effects of experimental removal of hantavirus reservoir species, *Oligoryzomys fulvescens* and *Zygodontomys brevicauda* on density of these hosts (*a*) and density of seropositive hosts (*b*). Shown in panel *a* are means (+ standard error) from field plots before and after nonhost species had been removed (*solid line*) and from unmanipulated controls (*dashed line*). Hosts on control plots underwent a strong seasonal decline in abundance, whereas those on plots where nonhosts were experimentally removed did not. Shown in panel *b* are means (+ standard error) of seropositive (currently or previously infected) animals on plots from which nonhosts had been removed and on control plots. Reproduced with permission from Keesing et al. (2010) based on data from Suzan et al. (2009).

hantavirus infection prevalence in *M. glareolus* reservoirs was strongly, negatively correlated with the relative abundance of a nonreservoir host, the wood mouse (*Apodemus sylvaticus*), which was the only other common rodent at these sites.

Several recent studies have assessed the relationship between mammalian diversity and hantavirus risk in North American Sin Nombre virus, for which the deer mouse *P. maniculatus* is the primary reservoir host. Dizney & Ruedas (2009) captured about 5,000 individuals of 21 species of small- and medium-sized mammals in five sites around Portland, OR, USA, and found that all sites that maintained moderate to high mammalian diversity were characterized by low (~2%) hantavirus infection prevalence in deer mice, whereas the one site with low mammalian diversity had 14% infection prevalence, a result that was highly statistically significant. In Montana, Carver et al. (2011) analyzed 15 years of live-trapping data on three field plots on which deer mice were always present but voles (nonreservoirs) were only occasionally trapped. They found that the presence of voles was associated, on average, with a 54% to 64% reduction in infection prevalence of deer mice. Deer mouse infection prevalence did not vary with vole population density; the mere presence of voles, even in low numbers, apparently was sufficient to suppress mouse infection rates. On the Channel Islands of southern California, Orrock et al. (2011) found that the species diversity of predators on small mammals (carnivores and raptors) was strongly negatively correlated with hantavirus infection prevalence in deer mice.

Attention has turned to the mechanisms that might underlie the negative correlation between mammalian biodiversity and hantavirus transmission. The Dizney & Ruedas (2009) study did not find that higher mammalian diversity was correlated with lower abundance of deer mouse reservoirs, nor that hantavirus infection prevalence was positively correlated with deer mouse abundance. They therefore conclude that, rather than regulating populations of reservoir hosts, high diversity reduced encounters among deer mice that could result in virus transmission. Studying Sin Nombre virus dynamics in Utah, Clay et al. (2009a,b) and Lehmer et al. (2008) uncovered a somewhat more complex set of factors influencing infection prevalence in deer mice. Clay et al. found a negative correlation between nocturnal mammal diversity and infection prevalence of deer mice with Sin Nombre virus across 16 field sites, supporting the occurrence of a DE. Although they found that both the population density of deer mice and the average survival (persistence) of individual mice were lower where diversity was higher, infection prevalence was negatively correlated only with deer mouse survival and not with deer mouse density (Clay et al. 2009c; Lehmer et al. 2008). By monitoring encounter rates between mice in foraging plots, Clay et al. (2009b) found that contacts between deer mice were less frequent in areas with high mammalian diversity. The weight of evidence for the Sin Nombre hantavirus system in western North America suggests that high diversity of mammals causes deer mice to increase their frequency of encounters with heterospecifics at the cost of encounters with conspecifics. Heterospecific encounters typically do not result in hantavirus transmission, whereas hantavirus transmission rates correlate positively with the frequency of intraspecific encounters (Dearing & Dizney 2010). In addition to reduced biodiversity per se, several studies suggest that land conversion to agriculture and cattle ranching (Goodin et al. 2006; Yan et al. 2007; Zhang et al. 2009a,b), human habitation (Kuenzi et al. 2001, Langlois et al. 2001), and habitat fragmentation (Mackelprang et al. 2001; Suzan et al. 2008a,b) can increase hantavirus infection prevalence in reservoir hosts (Dearing & Dizney 2010).

The DE has also been observed in other zoonoses that lack vectors. Derne et al. (2011) examined the relationship between mammalian species richness and per capita incidence of leptospirosis—the most common bacterial zoonosis worldwide—on the world's island nations. Rats (*R. rattus* and *R. norvegicus*) are the most competent reservoirs for this pathogen and occur throughout the world's islands mostly as a result of dispersal on ships. Human cases of leptospirosis (cases per 100,000 per year) across island nations were significantly, negatively correlated with mammalian

species richness. The DE in leptospirosis persisted after statistically accounting for variation in land mass among islands.

In contrast to the experimental demonstration of a DE in North American chytridiomycosis discussed above (Searle et al. 2011), a field study on two common, widely distributed frogs in Costa Rica and Australia (Rain frog, *Craugastor fitzingeri*, and Stony Creek frog, *Litoria lesueuri*, respectively) found support for an amplification effect (Becker & Zamudio 2011). For both species, higher occurrence or prevalence of Bd at a site was correlated with both lower levels of habitat destruction and higher amphibian species richness. Becker & Zamudio postulated that habitat destruction creates less favorable abiotic conditions for Bd, and also that amphibian species that amplify the pathogen might be more likely to occur in species-rich communities. The qualitative differences between the experimental lab study (Searle et al. 2011) and nonexperimental field study (Becker & Zamudio 2011) might result from differences in the characteristics of both the focal species chosen and the nonfocal species providing variation in host biodiversity.

Does the Dilution Effect Occur in Nature?: Vector-Borne Zoonoses

The involvement of an arthropod vector in pathogen transmission adds at least two additional mechanisms by which species diversity can influence risk. High diversity can potentially influence the abundance of the vector, by increasing or decreasing total feeding opportunities or vector survival, and it can influence encounter rates between the vector and the most competent reservoir host (Keesing et al. 2006). The DE has been evaluated extensively in Lyme disease, a tick-borne bacterial zoonosis, and West Nile fever, a mosquito-borne viral zoonosis.

The hard (Ixodid) ticks are vectors of many human, livestock, and wildlife pathogens worldwide. Risk of human exposure to tick-borne pathogens is a function of both the population density of ticks and their infection prevalence (Ostfeld 2011). Each active life stage—larva, nymph, and adult—typically requires a single blood meal from a host before dropping off the host, undergoing diapause, and molting into the next stage, or reproducing and dying. Ticks can acquire an infection with the causative agent, *Borrelia burgdorferi*, only by feeding on a reservoir host; that is, they acquire the bacteria horizontally rather than vertically. Ticks are weakly motile and require a host to approach closely in order to embark and attempt a blood meal. The tick species responsible for transmitting most zoonotic pathogens are strong host generalists, typically feeding from dozens of different host species.

Because of the reliance of ticks on access to vertebrate hosts and high mortality when they fail to find a host, tick abundance is widely thought to be correlated with that of hosts. Models of tick-borne zoonoses therefore often predict that disease risk is positively correlated with host diversity, i.e., an amplification effect (e.g., Dobson 2004), as long as high diversity leads to high total abundance of hosts (i.e., hosts are additive). However, when positive correlations between tick abundance and host abundance are detected, the correlation is specific to one species of host. For example, some studies have found positive correlations between an abundance of white-tailed deer (*Odocoileus virginianus*) and that of ticks (e.g., Deblinger et al. 1993, Rand et al. 2004, Stafford et al. 2003; but see Ostfeld 2011), and others have detected positive correlations between the abundance of white-footed mice (*P. leucopus*) and that of ticks (Ostfeld et al. 2006). Deer and mice are important hosts for the adult and immature stages, respectively, of the blacklegged tick, *Ixodes scapularis*. To our knowledge, no studies have assessed the relationship between total host abundance and tick abundance. Consequently, whether tick-borne disease is accurately portrayed with density-dependent rather than frequency-dependent transmission models is unknown.

A DE is expected to operate in the Lyme disease system if increases in the species diversity of host communities (*a*) tend to add species that are relatively poor reservoirs for the bacterial agent

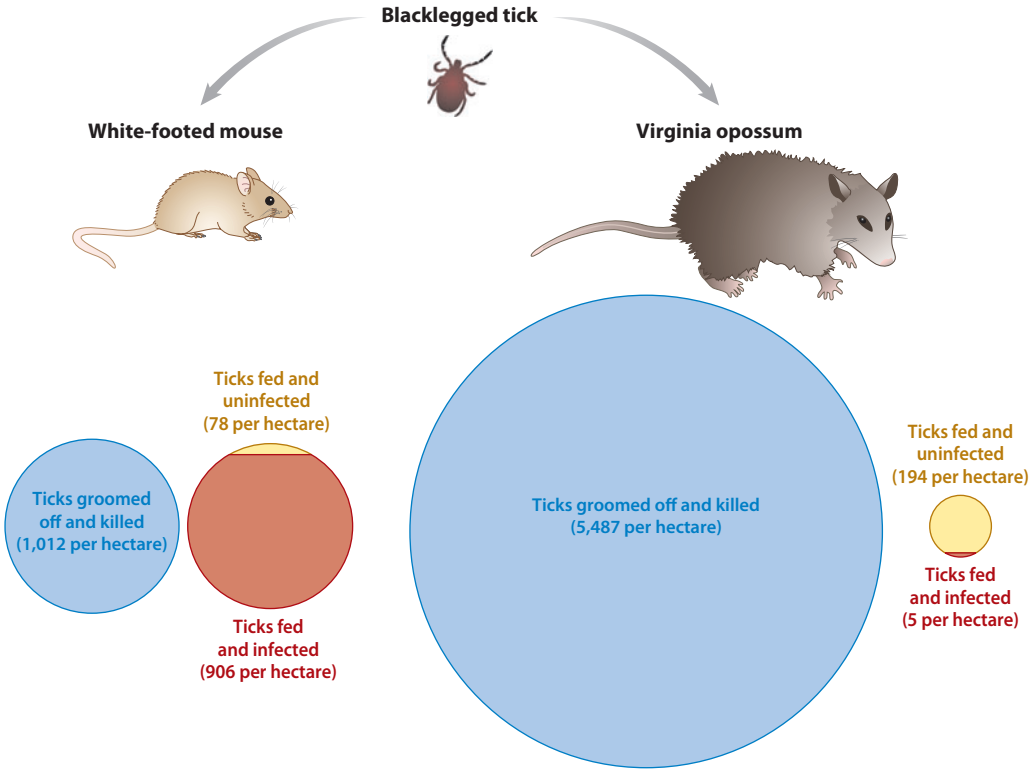

Figure 5

Roles of host species in the transmission of Lyme disease in the northeastern United States. Lyme disease is transmitted to humans by the bite of an infected blacklegged tick (*Ixodes scapularis*). Immature ticks can acquire the infection if they feed on an infected host and can become infectious to humans if they subsequently survive to the next life stage. White-footed mice are abundant in northeastern forests and feed many ticks. Ticks that attempt to feed on Virginia opossums are likely to be groomed off and killed. Red and yellow circles show the mean number of ticks per hectare fed by mice or opossums; yellow shading shows the proportion of ticks infected after feeding. Blue circles show the mean number of ticks per hectare groomed off and killed. Ticks that feed on mice are highly likely to become infected with the bacterium that causes Lyme disease, whereas those that feed on opossums are not. Reprinted with permission from Keesing et al. (2010).

and/or poor hosts for the tick vector, (*b*) regulate population densities of the most competent reservoir hosts, (*c*) regulate densities of the highest quality hosts for the tick vector, or (*d*) deflect tick meals away from the most competent pathogen reservoir and/or the highest quality tick host.

Extensive field and laboratory studies in the northeastern United States have documented that white-footed mice are the most competent reservoir for *B. burgdorferi* (Donahue et al. 1987, Lane et al. 1991, LoGiudice et al. 2003, Mather et al. 1989), with eastern chipmunks (*Tamias striatus*) and short-tailed shrews (*Blarina brevicauda*) being secondarily competent reservoirs and most other vertebrate species having low reservoir competence (Brisson et al. 2008, LoGiudice et al. 2003). Of four commonly parasitized mammals and two birds, white-footed mice were by far the most permissive host for blacklegged ticks, with tick survival rates dramatically higher on mice than on any other host (Brunner et al. 2011, Keesing et al. 2009) (**Figure 5**). Although the impact of mammalian biodiversity in regulating mouse populations is poorly studied, some evidence suggests that mouse density is reduced where species richness or abundance of nonmouse species is higher (LoGiudice et al. 2008; Nupp & Swihart 1998, 2000). A long-term study of the determinants of

tick burdens on white-footed mice revealed that an increased abundance of chipmunks was the strongest factor reducing numbers of larval ticks on mice (Brunner & Ostfeld 2008). These data suggest that, at least for this pair of host species, increasing availability of nonmouse hosts strongly deflects tick meals away from mice.

Several studies in the eastern United States demonstrate that white-footed mice are among the most widespread vertebrate species within heterogeneous, fragmented landscapes (Nupp & Swihart 2000, Rosenblatt et al. 1999). White-footed mice were the only species to occupy all forest patches sampled for vertebrate occupancy in Connecticut, Indiana, New Jersey, and New York (LoGiudice et al. 2008, Nupp & Swihart 2000, Swihart et al. 2003b). These studies also show that eastern chipmunks were nearly ubiquitous. In Indiana, habitat occupancy was positively correlated with diet and niche breadth, providing the basis for the nested, rather than random, pattern of species occupancy (Swihart et al. 2003a,b). Therefore, low-diversity communities are highly likely to contain white-footed mice and eastern chipmunks.

Models parameterized with data on host attributes relevant to tick survival and infection indicate that, as species are added to low-diversity communities (mice only), both tick infection prevalence and population density of infected ticks decline (Keesing & Ostfeld 2012; Keesing et al. 2009; LoGiudice et al. 2003, 2008; Ostfeld & LoGiudice 2003; Schmidt & Ostfeld 2001). These studies all treat habitat occupancy to be nested, such that the sequence of species additions as diversity increases is nonrandom, reflecting empirical observations (Ostfeld 2011). Whenever habitat occupancy patterns are nested, species diversity and species composition are correlated. In a study testing these models with field data, LoGiudice et al. (2008) found that the prevalence of infection of nymphal ticks with Lyme spirochetes in a forest patch was negatively correlated with species richness, but that the relationship was weak. Including information on the specific identities of the species added as diversity increased dramatically strengthened their power to predict nymphal infection prevalence both across space and through time.

Species area curves observed for vertebrate hosts for ticks, combined with the nested occupancy patterns (LoGiudice et al. 2008, Rosenblatt et al. 1999, Swihart et al. 2003b), suggest that larger forest patches should contain tick populations that are less abundant, have lower infection prevalence, or both. Allan et al. (2003) found strong negative correlations between forest fragment size and both tick (nymph) density and infection prevalence in New York State. Brownstein et al. (2005) found that more highly fragmented landscapes around Lyme, CT, had higher densities of infected blacklegged ticks. Jackson et al. (2006a,b) found that landscapes in Maryland characterized by high percentages of edge between forest and herbaceous habitat, a measure of fragmentation, tended to have high incidences of Lyme disease in human residents. In contrast, Wilder & Meikle (2004) found that a lower proportion of mice in small forest fragments rather than large fragments in Ohio were infested with blacklegged ticks. And, despite a higher density of infected ticks in their fragmented sites in Connecticut, Brownstein et al. (2005) found lower incidence rates in human populations within these sites, suggesting that in some cases high ecological risk does not predict high disease incidence (Ostfeld 2011).

West Nile virus is a flavivirus (relative of the yellow fever virus) amplified in certain species of birds and transmitted among wildlife hosts by mosquitoes, predominantly *Culex* and *Aedes*. The virus was restricted to parts of Africa, Asia, and Europe until 1999 when it was inadvertently introduced into the New York City area, from which it has dispersed throughout much of North America, where it remains a serious health threat to both people and native avifauna (Allan et al. 2009; Kilpatrick et al. 2006a; LaDeau et al. 2007, 2008).

Like the Lyme disease spirochete, West Nile virus relies on horizontal (host to vector to host) transmission rather than on vertical (transovarial) transmission across generations of mosquitoes. Therefore, the prevalence of infection in the vector depends on which hosts are bitten and how

likely those hosts are to transmit the pathogen to the feeding mosquito. Mosquitoes in the *Culex pipiens* complex often feed disproportionately on birds, and American robins in particular seem to be favored (Apperson et al. 2004; Hamer et al. 2011; Kilpatrick et al. 2006a,c). Nevertheless, within West Nile endemic zones, ample evidence indicates that infection is widespread among birds, mammals, and some reptiles (LaDeau et al. 2007, 2008; Marra et al. 2004), and birds other than robins often are disproportionately represented in blood-meal analyses (Loss et al. 2009), confirming that, despite their feeding preferences, these mosquitoes readily bite many different species of hosts (Kilpatrick et al. 2007, Komar et al. 2003, LaDeau et al. 2008, Marra et al. 2004). The different blood-meal hosts for mosquitoes vary dramatically in their ability to support replication by the pathogen, the length of time they remain infected, and their probability of transmitting virus to feeding mosquitoes (Kilpatrick et al. 2006b, Komar et al. 2003). Although studies at different North American localities often implicate different bird species as reservoirs, in general American robins, house sparrows, common grackles, American crows, blue jays, and house finches are the most competent reservoirs for West Nile virus. Many other passerines (songbirds), nonpasserine birds, mammals, and reptiles, either fail to permit virus infection or amplification, producing very low viremias, or they permit a high viremia but for only a very brief period, rendering them inefficient reservoirs.

Ezenwa et al. (2006) postulated that, because nonpasserine birds were generally incapable of producing high viremias, the presence of a high diversity of these bird species should cause mosquitoes to feed predominantly on poor reservoir hosts, reducing transmission rates of West Nile virus from host to vector. In their Louisiana, USA, study sites, they found that the proportion of mosquitoes infected with West Nile virus was significantly negatively correlated with species richness of nonpasserines. No correlation existed for passerines. Population density of infected *Culex* mosquitoes was also negatively correlated with nonpasserine diversity, suggesting that these birds might be injuring or killing mosquitoes that attempt to feed (Day & Edman 1984, Edman & Kale 1971, Edman et al. 1972). In addition, examining county-specific data throughout Louisiana, Ezenwa et al. found that the per capita incidence of West Nile disease in humans was negatively correlated with species richness of nonpasserines in that county.

Three later studies also detected a DE in West Nile virus, although in all these studies, virus prevalence was negatively correlated with passerine, rather than nonpasserine, diversity. Swaddle & Calos (2008) selected 65 adjacent pairs of counties in the eastern United States, with each pair consisting of one county with and an adjacent county without human cases of West Nile encephalitis. They tested the hypothesis that the West Nile–negative county in each pair would contain higher bird species diversity, as measured by the Breeding Bird Survey data from the United States Geological Survey. They found that the pairs of counties with the largest difference in bird diversity also had the largest difference in prevalence of West Nile encephalitis, with higher bird diversity being correlated with lower disease in humans.

Allan et al. (2009) examined human incidence of West Nile disease and bird diversity (Shannon Index, calculated from the Breeding Bird Survey) from 742 US counties within 38 states during three years (2002, 2003, and 2004) of rapid, cross-country spread. They calculated the total community competence of birds by multiplying the abundance of each species by its reservoir competence and summing the species-specific totals. Community competence provides an estimate of the likelihood that a particular bird community will produce infected mosquitoes. They found that bird assemblages with the highest community competence were also those with the lowest species diversity, whereas high-diversity communities tended to include poorer reservoirs. Consequently, as with observations on Lyme disease, host species most resilient to forces causing biodiversity loss tend to be the most competent reservoirs for the pathogen (see also Keesing et al. 2010). By comparing different models for explaining the variation in West

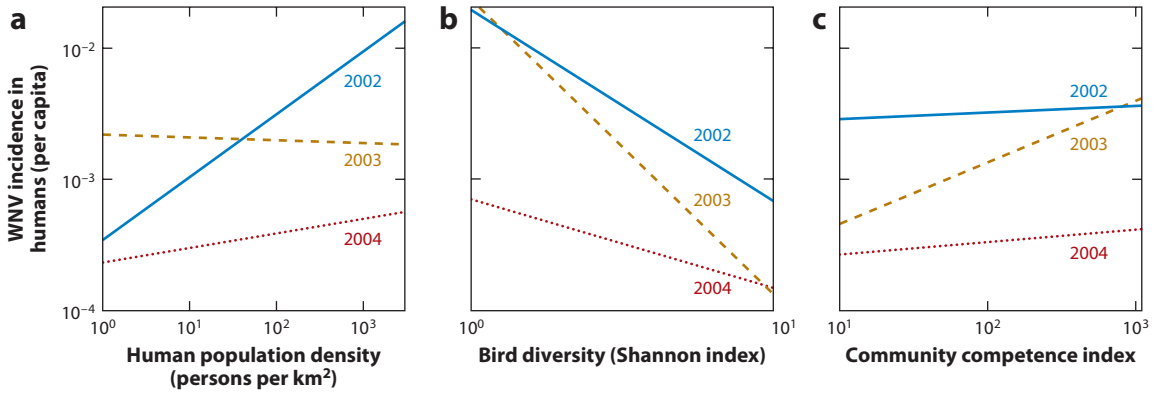

Figure 6

Relationship of human per capita incidence of West Nile virus (WNV) illness in the US counties with (*a*) human population density, (*b*) bird diversity (Shannon index), and (*c*) community competence index in 2002 (*solid line*), 2003 (*dashed line*) and 2004 (*dotted line*) as shown by multiple regression conducted separately for each year. Slopes reflect partial regression coefficients after statistically controlling for the other factors in the model. After controlling for spatial autocorrelation, relationships in panel *b* remained statistically significant, whereas many of the other relationships did not. Reprinted with permission from Allan et al. (2009).

Nile disease among counties, Allan et al. found that bird diversity was the strongest and most consistent factor—counties with low avian diversity had, on average, much higher rates of West Nile disease than did those with high diversity (**Figure 6**).

Koenig et al. (2010) examined the role of bird diversity in population declines of American crows during the initial five-year sweep of West Nile virus across the United States. Crows can experience rapid mortality after infection, resulting in severe population declines as West Nile virus invades new areas (LaDeau et al. 2007); therefore, crow population declines are a reasonable proxy for transmission rates within wildlife communities. Koenig et al. quantified the severity of crow declines using the Breeding Bird Survey data for individual survey routes conducted before and after invasion by the virus. They tested the ability of several factors to explain the severity of crow declines, including the year West Nile virus was first detected in the state, population density of crows, bird diversity (Shannon index), urbanization (estimated by human population density), total number of individual birds, mean rainfall, mean maximum temperature, and spatial autocorrelation. The causal variables best supported by the data were bird diversity (crows were more likely to decline where bird diversity was low), urbanization (crow declines were more likely in more urbanized areas), and crow density (declines were more likely where initial crow density was high).

Hamer et al. (2011) examined the relationship between bird diversity and West Nile virus infection in *Culex pipiens* mosquitoes in Chicago, IL. They assessed mosquito abundance and infection prevalence, total bird diversity (richness and Shannon index), and the diversity of the birds from which the mosquitoes fed based on molecular diagnostic tests of blood in captured mosquitoes. These data allowed them to test the hypothesis that selective feeding by the mosquitoes was strong enough to weaken the effect of the diversity of available bird hosts. Hamer et al. estimated each bird species' contribution to the pool of infected mosquitoes by calculating host-specific "force of infection" (the squared fraction of total blood meals taken from a host species times that species' reservoir competence), which also allowed them to calculate "community force of infection" by summing across all host species present at a site. Although they found strong apparent host preferences overall, these preferences differed among sites, suggesting that preferences

are not fixed but might vary with local host availability. Diversity of birds available and diversity of birds represented in the blood-fed mosquitoes were not correlated. Despite apparently strong host preferences by mosquitoes, the best-supported model invoked an interaction between bird diversity and the community force of infection. The majority of infected mosquitoes had fed on American robins, house sparrows, and house finches, species that tend to reach high abundance in low-diversity communities (Allan et al. 2009). A plausible interpretation of these results is that selective feeding by mosquito vectors causes a multiplicative effect with diversity, whereby bird species with high reservoir competence are both preferred by mosquitoes and more likely to be abundant in low-diversity communities.

One recent study found no support for a DE in West Nile virus dynamics. In 2005 and 2006, Loss et al. (2009) sampled mosquito and bird communities in 13 sites within the Chicago metropolitan area to assess the relationship between bird diversity and the proportion of *Culex* mosquitoes infected with the virus. Avian species richness in a site was not a significant predictor of mosquito infection prevalence. Loss et al. argued that a DE did not occur because the most competent reservoirs were not disproportionately well represented in species-poor communities. Their data supported only a weak, positive relationship between reservoir competence of a bird host and its relative abundance (ubiquity) across sites in this urban environment ($r = 0.11$).

COMMUNITY DIVERSITY

The possible effects of diversity of community types on the dynamics of infectious diseases have received scant attention. The invasion of a community by nonindigenous species reduces community-level diversity by homogenizing donor and recipient communities. When communities are invaded by nonindigenous species that are infected with pathogens, these pathogens often spill over into the indigenous species and increase disease risk, incidence, and mortality (Parrish et al. 2008, Vandegrift et al. 2010). Even when nonindigenous species invade and do not import their pathogens, they can often become competent reservoirs for pathogens in the indigenous community and increase disease risk via spillback (Kelly et al. 2009b, O'Brien et al. 2011, Poulin et al. 2011). In other cases, nonindigenous species invading without their pathogens can reduce disease risk in indigenous hosts (reviewed above) by absorbing but not releasing pathogens. Recent reviews of these processes in both freshwater and terrestrial wildlife communities suggest that how reductions in community diversity via invasion by nonindigenous species affect pathogen transmission depends on (*a*) the ability of the invading species to support proliferation of pathogens native to the habitats it invades, (*b*) whether the nonindigenous species bring their pathogens into these habitats, and (*c*) the extent to which the nonindigenous species regulate the abundance of indigenous reservoir hosts (Johnson & Thieltges 2010; Poulin et al. 2011; Tompkins et al. 2003, 2011).

GLOBAL-SCALE PATTERNS OF DIVERSITY AND HUMAN INFECTIOUS DISEASES

Although high host diversity often reduces pathogen transmission for existing diseases, some researchers have postulated that high host diversity might increase the probability of disease emergence by providing a large source of potential zoonotic pathogens. Both vertebrate and parasite diversity tend to be higher at low rather than high latitudes (Guernier et al. 2004, Pianka 1966), leading to the hypothesis that emergence rates of human infectious diseases will be positively correlated with vertebrate diversity and negatively correlated with latitude (Dunn et al. 2010). Evidence pertaining to this hypothesis is equivocal. Using structural equation modeling, Dunn

et al. concluded that bird and mammal species richness drives richness of human pathogens, which in turn drives the prevalence of 22 diseases in their database.

In contrast, Jones et al. (2008) compiled a data set consisting of 335 infectious diseases of humans that emerged after 1940 and found as follows:

> The highest concentration of EID [emerging infectious disease] events per million square kilometers of land was found between 30 and 60° north and between 30 and 40° south, with the main hotspots in the northeastern United States, western Europe, Japan and southeastern Australia.
>
> (Jones et al. 2008, p. 991)

To account statistically for the possibility that the geographic pattern of EIDs could be biased by geographic variation in the abundance or activity of scientists likely to detect and report these diseases, Jones et al. included as an independent variable the frequency of each country listed as the address for each author in all papers published in the *Journal of Infectious Diseases* since 1973. Using this added variable, Jones et al. found that the emergences of zoonotic pathogens from wildlife and of vector-borne pathogens were not significantly associated with latitude, but that emergence events of zoonotic pathogens from wildlife hosts were significantly, positively correlated with wildlife species richness. However, this correlation was quite weak, with wildlife species richness explaining only between 0.8% and 1.3% of the spatial variation in emergence. In contrast, human population density, a primary driver of biodiversity loss, was positively correlated with disease emergence, explaining 54% of the spatial variation in EIDs. Consequently, whether high host diversity is an important risk factor for the emergence of zoonotic diseases from wildlife remains an open question.

CONCLUDING COMMENTS

Neither the potential for the DE to occur nor its actual occurrence in a variety of natural and constructed systems is controversial, as the studies reviewed above indicate. For many but not all disease systems, host diversity explains much of the variation in disease risk. What remains unresolved is the degree to which the DE is general. A recent review of the consequences of biodiversity loss (Cardinale et al. 2012) found that 80% of statistical tests of associations between biodiversity and disease transmission showed a statistically significant negative relationship (DE), whereas 12% showed a significant positive relationship (amplification effect), and 8% were not significant (**Table 1**). These results provisionally indicate that the dilution effect is indeed widespread in a diversity of disease systems.

A DE is expected to occur when the following conditions are met: (*a*) hosts differ in their quality as hosts for a pathogen and/or its vector; (*b*) the taxa most likely to remain when diversity

Table 1 Number of statistical tests of the relationship between diversity and disease transmission in which the association was significantly ($P < 0.05$) negative (dilution), positive (amplification), or not significant (neither)[a]

Taxon (N)	Dilution	Amplification	Neither
Plants (107)	91	16	0
Animals (45)	30	2	13
Total (152)	**121**	**18**	**13**

[a]Data taken from Cardinale et al. (2012).

is lost tend to support greater abundance of the pathogen or vector, whereas those most likely to be added as diversity increases tend to be poorer hosts; and (*c*) the taxa most likely to be added as diversity increases reduce either encounter rates between high-quality hosts and pathogens or abundance of high-quality hosts. The generality of the first condition is abundantly demonstrated by the literature reviewed above. Although some support exists for the second and third conditions (Johnson & Thieltges 2010, Keesing et al. 2010, Ostfeld & Keesing 2000, Pongsiri et al. 2009), their generality remains to be evaluated comprehensively. The second condition can be further subdivided into the following two patterns: (*i*) communities have nested patterns of species composition across gradients in diversity—i.e., as species diversity varies among communities, some species tend to be ubiquitous and others are more likely to be absent when diversity is lower; and (*ii*) a positive correlation exists between resilience (defined here as the tendency to remain when diversity is lost) and host quality. Some supporting evidence for these subconditions exists for plants (Cronin et al. 2010), amphibians (Johnson et al. 2012), and rodents (Previtali et al. 2012). Furthermore, it has been postulated that certain life-history traits might underlie both resilience to anthropogenic forces that reduce biodiversity and permissiveness to pathogens and vectors. Specifically, species with a fast pace of life (short lifespan, early and rapid reproduction, high dispersal ability) might often adopt pathogen defense strategies that are innate (as opposed to induced), energetically inexpensive, and potentially less effective against some pathogens (Cronin et al. 2010; Johnson et al. 2012; Martin 2009; Martin et al. 2007, 2008; Palacios et al. 2011; Previtali et al. 2012).

Even where a DE might occur, it is expected to be weakened by strong specialization by either the pathogen or the vector on one species of host. Under these conditions, variation in host diversity will not cause similar variation in the distribution of pathogens or vectors among those hosts. Such an effect is thought to underlie the lack of a DE in West Nile virus in Chicago, IL (Loss et al. 2009). But it is important to note that the degree to which pathogens and vectors specialize is difficult to assess. For vectors, host specialization is typically assessed by analyzing the distribution of blood meals across a community of potential hosts (for mosquitoes) or by counting ectoparasites attached to hosts (e.g., ticks). But such analyses consider only those vector bites that were successful (i.e., resulted in a blood meal) and neglect the potential for hosts to kill or injure vectors attempting a blood meal (Edman & Kale 1971, Edman et al. 1972, Keesing et al. 2009). Blood-meal analyses therefore might not represent either feeding preferences or the effects of various host species on vector populations. Similarly, a DE is expected to be absent, weak, or complex where no single host is sufficient for pathogen maintenance and transmission. For instance, for a vector with a complex life cycle requiring multiple hosts, a low-diversity community might not provide sufficient host diversity for vector or pathogen persistence. One might expect a unimodal relationship between diversity and disease risk for such systems, whereby intermediate levels of diversity maximize pathogen transmission, below which an amplification effect occurs and above which a DE occurs (Ostfeld & Keesing 2000, Van Buskirk & Ostfeld 1995).

The possibility remains that high host diversity generally reduces the transmission and risk of existing diseases while it increases the probability of new diseases emerging. However, any positive correlation between wildlife diversity and the probability of emergence appears to be weak, explaining only ~1% of the variation in emergence. Nevertheless, it will be important to distinguish strategies for focusing our surveillance of potential emergence events from those for mitigating human-caused increases in risk of existing diseases. For anticipated emergence events, surveillance possibly should be concentrated in biogeographic areas where diversity of potential pathogens is known or expected to be high. But for many existing diseases, mitigation strategies should be considered in situations where human activities decrease host diversity.

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