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Diversity, decoys and the dilution effect: how ecological communities affect disease risk

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Summary

Growing interest in ecology has recently focused on the hypothesis that community diversity can mediate infection levels and disease ('dilution effect'). In turn, biodiversity loss – a widespread consequence of environmental change – can indirectly promote increases in disease, including those of medical and veterinary importance. While this work has focused primarily on correlational studies involving vector-borne microparasite diseases (e.g. Lyme disease, West Nile virus), we argue that parasites with complex life cycles (e.g. helminths, protists, myxosporeans and many fungi) offer an excellent additional model in which to experimentally address mechanistic questions underlying the dilution effect. Here, we unite recent ecological research on the dilution effect in microparasites with decades of parasitological research on the decoy effect in macroparasites to explore key questions surrounding the relationship between community structure and disease. We find consistent evidence that community diversity significantly alters parasite transmission and pathology under laboratory as well as natural conditions. Empirical examples and simple transmission models highlight the diversity of mechanisms through which such changes occur, typically involving predators, parasite decoys, low competency hosts or other parasites. However, the degree of transmission reduction varies among diluting species, parasite stage, and across spatial scales, challenging efforts to make quantitative, taxon-specific predictions about disease. Taken together, this synthesis highlights the broad link between community structure and disease while underscoring the importance of mitigating ongoing changes in biological communities owing to species introductions and extirpations.

Key words: emerging disease, community ecology, global change, disease ecology, parasite, invasive species, biodiversity.

Introduction

'Outbreaks most often happen on cultivated or planted land – that is, in habitats and communities very much simplified by man.'

(C. S. Elton, 1957; p. 147)

Throughout parts of Africa, many rural societies engage in a long-established epidemiological practice: cattle are strategically placed near human dwellings to distract malaria-carrying mosquitoes away from people. In other disease-plagued regions, similar roles have been suggested for rabbits in reducing sand fly-borne leishmaniasis, cats and dogs in reducing mosquito-borne encephalitis, and lizards in reducing tick-borne Lyme disease (Hess and Hayes, 1970; Lane et al., 2006; Chelbi et al., 2008). 'Zooprophylaxis', literally the use of animals to protect people from infection, has been recognized for over a century and depends on the principle that livestock are 'dead end' hosts for many vector-borne infections that cause human disease (e.g. WHO, 1982; Service, 1991; Dobson et al., 2006). It also underscores the importance of interactions within ecological communities, including those among human hosts, vectors, pathogens and non-host species in controlling disease transmission.

Stemming from this principle and in response to the rapid losses of many populations and even entire species of organisms associated with the global biodiversity crisis, growing interest has recently focused on the intersection between biodiversity loss and disease emergence (Mitchell et al., 2002; Begon, 2008; Allan et al., 2009; Ostfeld, 2009). The 'dilution effect' hypothesis suggests that the net effects of biodiversity (including host and non-host species) reduce the risk of certain diseases in ecological communities (Keesing et al., 2006). Given accelerated rates of population extirpations and species' extinctions associated with human activity, the idea that maintaining (or enhancing) biodiversity could promote human and wildlife health has generated considerable interest. The origins of the idea trace back nearly a century and can be linked to the epidemiological practice of zooprophylaxis and the agricultural practice of crop rotation (Elton, 1958; Service, 1991).

On the basis of recent work with Lyme disease in the USA, Rick Ostfeld and colleagues formalized the dilution effect hypothesis to help explain why infection risk varied inversely with vertebrate host diversity (Ostfeld and Keesing, 2000a; Ostfeld and Keesing, 2000b; Schmidt and Ostfeld, 2001; LoGuidice et al., 2003). Integration of field surveys, experimental infections and simulation modeling led the authors to suggest that more species-rich communities supported a greater fraction of low competency hosts, such that tick vectors derived more blood meals from hosts that were unlikely to maintain adequate infections of the bacterium *Borrelia burgdorferi*, the causative agent of Lyme disease. This led to an increase in 'wasted' transmission events and a reduction in infected ticks relative to more species-poor communities. Negative correlations between diversity and disease have also been reported for West Nile virus in birds, hantavirus in rodents, *Bartonella* in wood mice, tick-borne encephalitis in rodents, and

louping ill in sheep (see Keesing et al., 2006; Perkins et al., 2006; Swaddle and Calos, 2008; Allan et al., 2009; Dizney and Ruedas, 2009; Suzán et al., 2009).

Complex life cycle parasites and the dilution effect

Thus far, most evaluations of the dilution effect have focused on vector-borne microparasites, limiting our understanding of when and for what other types of disease systems we might expect a dilution effect to occur. Moreover, despite the growing number of empirical examples supporting a negative relationship between community diversity and disease risk, the correlative nature of many such studies has left the underlying mechanisms uncertain (but see Suzán et al., 2009), which may have important implications for disease management and mitigation. For example, in the absence of experimental manipulations, it may be impossible to determine whether changes in infection patterns in diverse communities are due to changes in host density (e.g. from interspecific competition) or are the direct result of changes in diversity ('pure' diversity effect) (Mitchell et al., 2002).

We advance that, alongside vector-borne pathogens, diseases involving complex life cycle parasites are likely to exhibit strong responses to changes in community diversity and composition. Complex life cycle parasites are those that move sequentially among different host species in order to complete their life cycles. Examples include many trematodes, cestodes, nematodes, acanthocephalans, chytridiomycetes, oomycetes and myxosporeans. Collectively, these parasites are responsible for a wide range of human, livestock and wildlife diseases, including schistosomiasis in humans, fascioliasis in cattle, giardiasis in humans, toxoplasmosis in sea otters, whirling disease in salmonids, cysticercosis in pigs, and nematodiasis in livestock. Because of their dependency on short-lived, free-living infectious stages such as eggs, larvae, oncospheres, corracidia, miracidia and cercariae (Fig. 1), these parasites are strongly influenced by the biological community. Changes in community structure and biodiversity can increase the risk that infectious stages fail to reach a suitable host owing to the effects of predation, attempted infections of poor or unsuitable hosts, mechanical interference or toxic compounds. As a result, we suggest that the

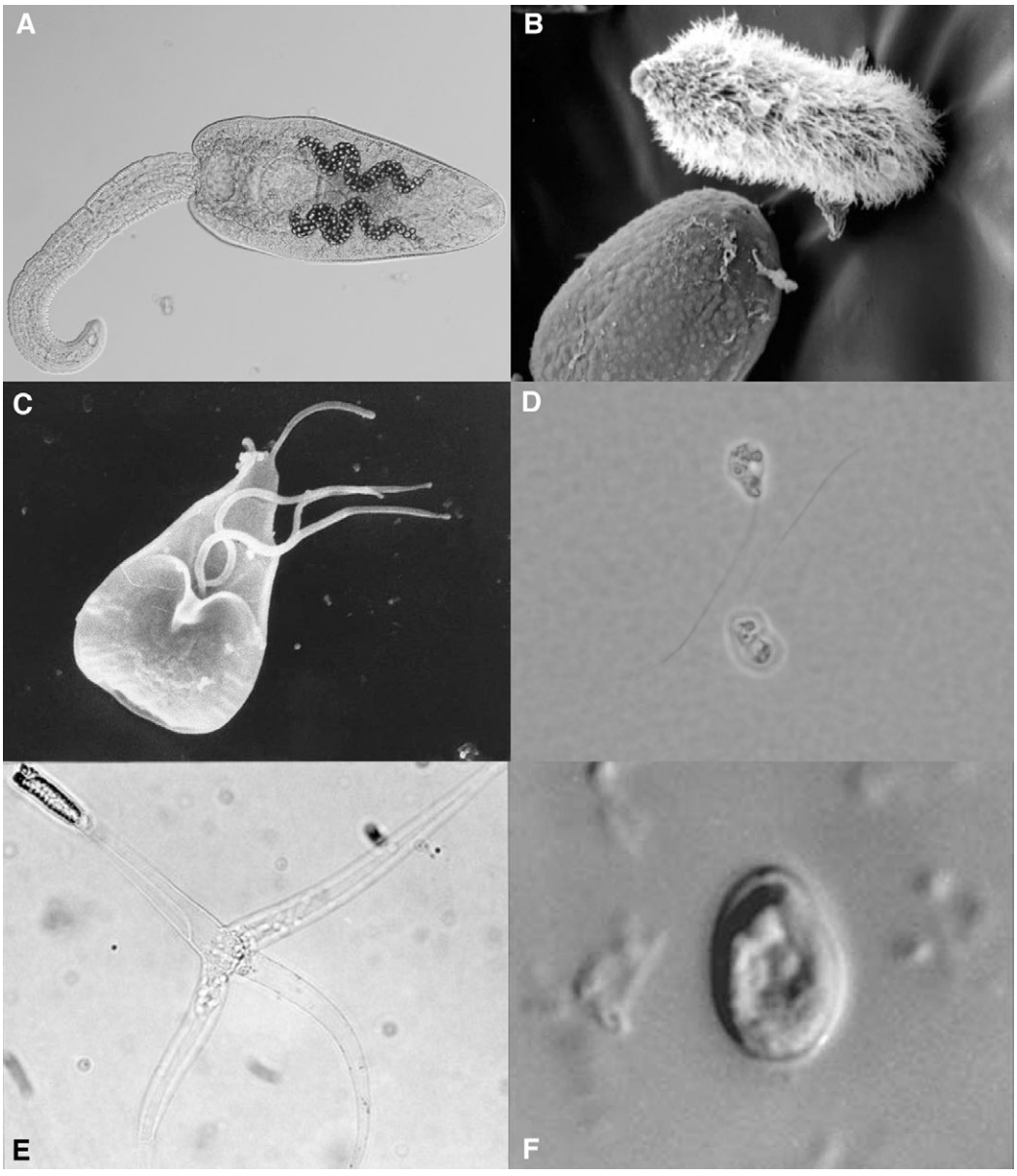

Fig. 1. Representative free-living stages of different complex life cycle parasites. (A) Cercariae of the trematode *Ribeiroia ondatrae*; (B) egg (left) and hatched miracidium (right) of trematode *Schistosoma margrebowiei*; (C) trophozoite of the diplomonad protist *Giarida lamblia*; (D) zoospore of chytridiomycete *Polycaryum laeve*; (E) triactinomyxon stage of the myxosporean *Myxobolus cerebralis*; (F) oocyst of the apicomplexan protist *Cryptosporidium muris*. Reproduced with permission (A, Pieter Johnson; B, Padraic G. Fallon; C, CDC/Janice Carr; D, Joyce Longcore; E, USGS; and F, CDC).

dilution effect will significantly affect the transmission of complex life cycle parasites. Because these free-living infectious stages are more amenable to experimental manipulation than many vector-borne infections, studies with complex life cycle parasites can explicitly examine the mechanistic relationships driving the diversity–disease relationship.

The goal of the current paper is to broadly explore the relationship between diversity and disease by extending the dilution effect beyond vector-borne microparasites. Specifically, we focus on complex life cycle parasites with free-living infectious stages, especially the macroparasites. Although largely ignored in contemporary discussions, macroparasitological research on the relationship between community structure and parasite transmission is extensive (for a review, see Thieltges et al., 2008b). Thus, one of our priorities is to unite the disparate and independently evolving disciplines of parasitology and disease ecology to explore how they mutually enhance our understanding of the diversity–disease relationship. In the sections that follow, we draw upon this information to: (1) identify the ecological mechanisms linking community structure and parasite transmission with a focus on experimental research; (2) evaluate what makes a 'good' diluting host or community; (3) explore how the relationship between diversity and disease varies with spatial scale, parasite life history stage and taxa; and (4) assess the net effects of community diversity on host fitness. Finally, based upon the emerging synthesis of information from varying disease systems, we suggest general criteria for predicting when dilution effects are likely to occur and explore how patterns of infection are likely to change with ongoing species extirpations and invasions.

Mechanisms linking diversity and disease

Keesing and colleagues (Keesing et al., 2006) reviewed the dilution effect hypothesis and outlined five hypothetical mechanisms through which changes in species richness could influence infection risk: reductions in encounters between host and parasite, reductions in transmission (following an encounter), increased host recovery from infection, increased mortality in infected hosts, and decreased density of susceptible hosts. The authors developed these mechanisms through careful examination of the parameters in standard infectious disease models, beginning with a directly transmitted microparasite and extending this approach to a vector-borne infection. Most of the empirical examples reviewed by the authors involve encounter reduction and susceptible host (or vector) regulation. Thus, changes in community richness tend to either reduce the availability of susceptible hosts (e.g. through interspecific competition) or reduce the likelihood that an infected host/vector encounters a susceptible host, independent of host density. Whether other mechanisms are less likely to cause a dilution effect or are simply understudied remains conjectural. Given that many of these mechanisms are difficult to differentiate from field data alone, it is also possible that field-observed correlations between species richness and disease risk represent the product of multiple, concurrently operating mechanisms.

How do these mechanisms apply to parasites that use free-living infectious stages to move among different host species? Keesing and colleagues (Keesing et al., 2006) did not include macroparasites or other pathogens dependent on free-living infectious stages in their review (although they acknowledged that these parasites may have their own unique mechanisms for the dilution effect). Within this group, transmission depends upon the success of free-living parasites in navigating through the environment to find and infect a suitable host and can be modeled as follows (modified from Dobson and Hudson, 1992):

$$\frac{\mathrm{d}W}{\mathrm{d}t} = \lambda P - \delta W - \beta W H \ ,$$

in which free-living parasite stages (W) are released from infected hosts of species P and seek out susceptible hosts of species H. The success of free-living infectious stages can be broken down into the production of infectious stages (λ) by infected hosts (P), survival of free-living stages (δ), the probability of an infectious stage encountering a susceptible host (product of W and H), and the

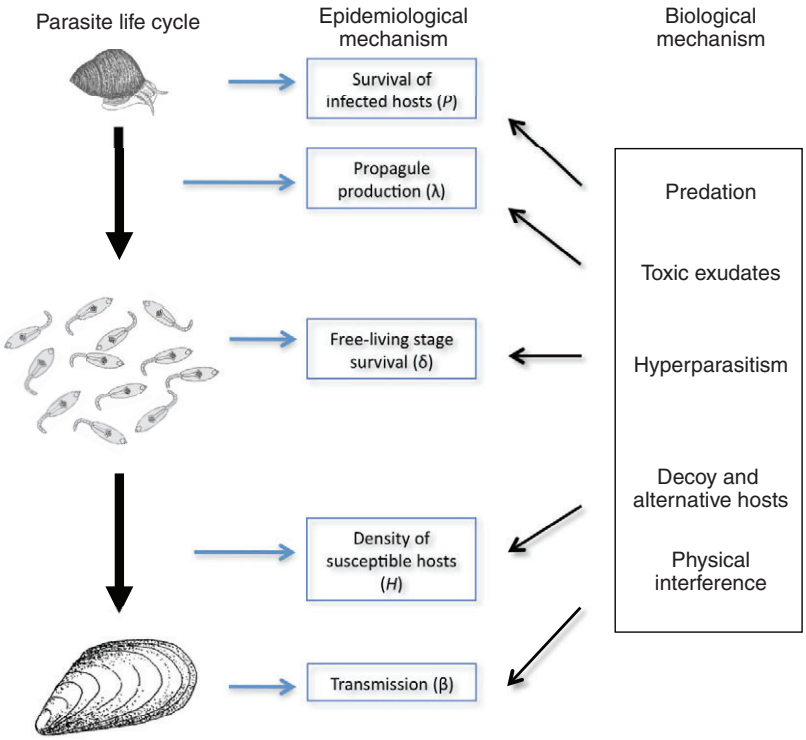

Fig. 2. Mechanisms through which community diversity can influence the transmission of complex life cycle parasites.

likelihood of transmission given an encounter (β). These mechanisms broadly mirror those outlined by Keesing and colleagues (Keesing et al., 2006), including encounter reduction (increase in δ), transmission reduction (reduction in β), susceptible host regulation (reduction in *H*), infected host mortality (reduction in *P*), but with some modifications (Fig. 2). For example, changes in the number of infective propagules ('propagule production', reduction in λ) produced by infected hosts have no immediate parallel to the disease systems included by Keesing and colleagues (Keesing et al., 2006). Considering that the number of infective propagules produced by an infected host can vary over several orders of magnitude (e.g. the number of cercariae released by an infected snail), changes in propagule production can be more significant than changes in the number of infected hosts.

Because of the relative ease with which free-living infectious stages can be manipulated and the extensive literature on host diversity and macroparasites, we draw upon experimental evidence to explore each of these mechanisms. We highlight selected case studies here and refer the reader to Thieltges et al. (Thieltges et al., 2008b) for a more comprehensive review of empirical examples. In previous studies with macroparasites, the effects of species diversity on infection risk were differentiated by the biological mechanisms through which species altered infection in the focal host (e.g. predation), rather than by the model parameter or variable affected. Thieltges and colleagues (Thieltges et al., 2008b) recognized roles for predation, physical disturbance, toxic exudates, decoy and alternative hosts, and hyperparasitism. We maintain that convention here but place additional emphasis on identifying which infection parameters are influenced in the process. We focus on mechanisms directly involving changes in diversity ('pure' diversity effects rather than indirect changes involving host density), as susceptible host regulation and infected host mortality are already well-established mechanisms to control infection.

Decoy and alternative hosts

The macroparasite literature includes numerous examples of organisms that 'distract' free-living parasites away from suitable hosts, leading to wasted transmission events. These can be broadly divided into cases involving completely unsuitable hosts (decoy effect) and those involving low competency hosts (alternative hosts) (although we freely acknowledge that, for some disease systems, differentiating between these categories will be challenging). Addition of such species to the community can cause several of the outlined dilution mechanisms, including encounter reduction, in which fewer parasites find a suitable host, transmission reduction, in which fewer parasites succeed in infecting an encountered host, and propagule reduction, in which suitable hosts, once infected, produce fewer infectious stages than those from less diverse communities (Fig. 2).

Some of the most thoroughly studied examples of decoys and low competency hosts involve trematodes, including parasites in the genus *Schistosoma* (blood flukes), which alternate between select species of freshwater snails (intermediate hosts) and vertebrate hosts (definitive hosts) using free-swimming stages (cercariae and miracidia, respectively). In humans, these parasites cause urinary and intestinal schistosomiasis, which currently afflict 200 million people in parts of Africa, Asia, the Middle East and South America (Steinmann et al., 2006). Field and laboratory experiments have revealed that increases in community diversity can interfere with parasite transmission both from humans to snails and from snails to humans. Laracuente and colleagues (Laracuente et al., 1979) found that the addition of any of four non-host snails reduced the success of *Schistosoma* miracidia by 25–99%. This resulted both from parasites penetrating unsuitable hosts (an example of encounter reduction) and from parasite exhaustion or physical damage during interactions with non-hosts, such that parasites were less successful when attempting to infect a suitable host (transmission reduction) (e.g. Chernin and Perlstein, 1969; Combes and Mone, 1987). Johnson and colleagues (Johnson et al., 2009) also showed that host snails exposed to miracidia alongside non-host species subsequently produced 60–80% fewer *Schistosoma mansoni* cercariae, which are the infectious stage to humans, illustrating the additional mechanism of propagule reduction (see also Frandsen and Christensen, 1977).

Low competency hosts (as opposed to decoy hosts) are susceptible to infection but may alter patterns of transmission by reducing transmission to downstream hosts or by reducing infection in a more sensitive host. For example, non-native oysters (*Crassostrea gigas*) in the European Wadden Sea can become infected with native trematodes but, unlike native mollusks, are not consumed by the appropriate bird definitive hosts and thus act as 'dead ends' for the parasite (Krakau et al., 2006). In studies with the trematode *Ribeiroia ondatrae* and larval amphibian hosts, Johnson and Hartson (Johnson and Hartson, 2009) found that while both larval gray treefrogs and larval American toads were hosts for *Ribeiroia*, treefrogs supported far fewer metacercariae. When the two species were raised together in experiments, the presence of treefrogs reduced the total success of *Ribeiroia* cercariae by up to 64%, leaving fewer parasites available for transmission to definitive bird hosts. Toads raised alongside treefrogs also supported 37% fewer parasites than toads raised with conspecifics, suggesting roles for both encounter reduction (diverting parasites away from highly susceptible toads) and transmission reduction (elimination of colonizing parasites within the less susceptible treefrogs) (Johnson et al., 2008).

Predators and hyperparasites

Predators consume a wide variety of free-living parasite forms, including the miracidia and cercariae of trematodes, the eggs, coracidia and onchospheres of cestodes, the zoospores of chytridiomycetes, the trophozoites of protists, and the eggs of nematodes and acanthocephalans (Johnson et al., in press). This includes active predation by visual predators as well as more indiscriminate predation by filter feeders, carnivorous plants, anemones and hydras (Thieltges et al., 2008b). The consequences of predation for parasite transmission can be considerable. Achinelly and colleagues (Achinelly et al., 2003) reported that copepod predation on juvenile nematodes reduced their abundance by 70–100%, leading to as a much as a 50% infection reduction in the subsequent host (larvae of the mosquito *Aedes aegypti*). Pellegrino and colleagues (Pellegrino et al., 1966) found that addition of guppies to field cages dramatically reduced the success of free-living schistosome cercariae in finding mouse definitive hosts, reducing infection burdens from 29.1 to 3.8 worms per mouse. Similarly, many marine organisms (e.g. crabs, shrimps, barnacles, anemones and grazing snails) actively or passively consume cercariae of trematodes, often causing substantial reductions in infection of downstream hosts (Thieltges et al., 2008a; Prinz et al., 2009). Nor are such examples limited to helminths. Kagami and colleagues (Kagami et al., 2004) found that *Daphnia* consume chytrid zoospores parasitizing diatoms, with potentially important implications for epidemics in phytoplankton. In streams and rivers, communities of oligochaete worms can influence transmission of the myxosporean parasite, *Myxobolus cerebralis*, the causative agent of whirling disease in salmonids. Certain cryptic species of *Tubifex* ingest the myxospores but are resistant to infection,

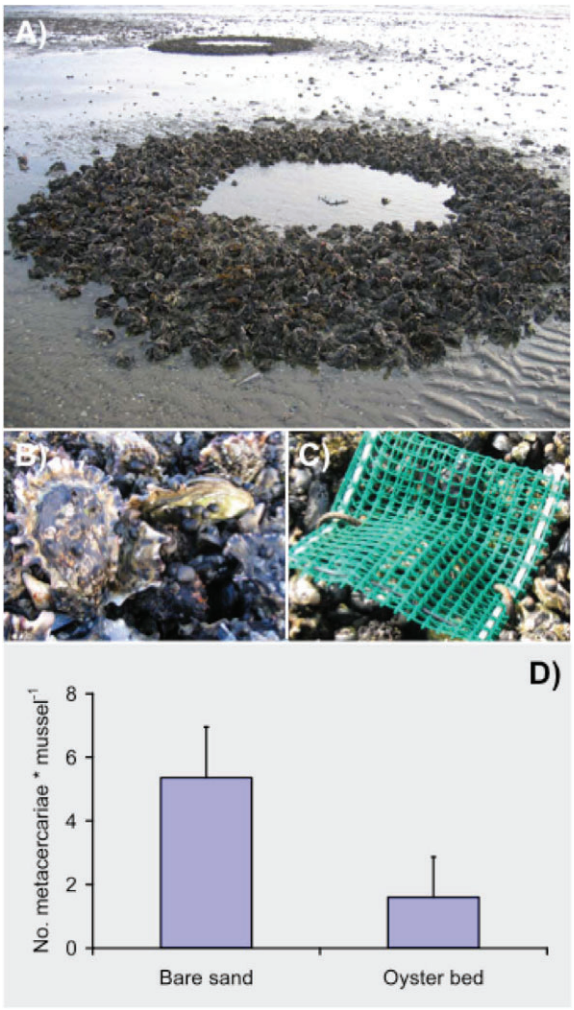

Fig. 3. Field experiment on the effect of Pacific oysters (*Crassostrea gigas*) on transmission of trematode cercariae (*Himasthla elongata*) to blue mussel (*Mytilus edulis*) target hosts. (A) Experimental oysters rings (outer ring 4 m diameter, inner ring 2 m diameter) on a tidal flat in the northern Wadden Sea, Germany. (B) Close-up of oysters. (C) Bags with experimental target mussels deployed on the rings. (D) Results of experiments showing a reduction of infection levels (number of metacercariae) in mussels by oysters after 2.5 months exposure (from Thieltges et al., 2009). Reproduced with permission (A, Judith Kochmann; B and C, David Thieltges).

and the relative dominance of these worms in the oligochaete community correlates negatively with the disease impact in fishes (Beauchamp et al., 2005) (but see Elwell et al., 2009).

Parasites are also at risk from other parasites. Juvenile plant-root nematodes, for example, can be infected and killed by bacteria (parasite mortality) (Sayre and Wergin, 1979). Similarly, trematode rediae and cercariae become infected with microsporidian parasites (Knapp et al., 1972; Canning et al., 1983); infected cercariae exhibit physical degeneration and are less successful in infecting new hosts relative to uninfected cercariae (transmission reduction). Antagonism between different trematode species is also common within snail hosts. Multi-species coinfections within snail hosts are significantly less common than expected by chance, and controlled experiments indicate that some trematodes will consume or outcompete other species as a function of parasite size, type of development (rediae *vs* sporocysts), and priority of establishment (Kuris and Lafferty, 1994).

Physical and chemical interference

The physical presence of other species can also alter a parasite's encounter rate with target hosts. This can occur due to physical changes in the environment, for example when plants or algae reduce the success of free-swimming parasites, or when forage plants with differing moisture retention properties alter the desiccation risk of nematode eggs and juveniles (Christensen, 1980; Niezen et al., 1998; Prinz et al., 2009). It also occurs when non-host species influence the behavior or activity of a focal host and its likelihood of parasite encounter. Thieltges and colleagues (Thieltges et al., 2008a) suggested that repeated disturbance of cockle hosts by non-host organisms caused cockles to retract their siphons and reduce their filtration rate, thereby lowering their exposure to infective parasites. Other non-host species can produce compounds that are toxic to free-living parasite stages, further contributing to parasite mortality and the degree of encounter reduction. Planarians excrete substances that are highly lethal to trematode miracidia and cercariae, leading to 43–79% reductions in infection (Christensen, 1980). Some bacteria (e.g. *Bacillus sphaericus* and *B. thuringiensis*) produce a toxin that kills nematode eggs in a dose-dependent manner (Bone et al., 1987; Bottjer et al., 1985). Similar patterns have been reported for an alga (*Caulerpa taxifolia*) and adult toads (Christensen, 1980; Bartoli and Boudouresque, 1997).

Diversity effects in natural communities

Collectively, highlighted examples from laboratory experiments provide convincing evidence that increases in diversity can reduce infection levels in target hosts, but are such effects relevant under more realistic conditions? Most parasites with free-living infectious stages produce tremendous numbers of infective propagules to help overcome the challenges inherent in finding a suitable host, calling into question the significance of a dilution effect in nature. Nevertheless, the few experimental and correlative studies available strongly suggest that diversity influences parasite transmission in naturally occurring systems. Many of these studies involve dilution effects on free-living trematode stages resulting from predation, decoy hosts or toxic exudates. Thieltges and colleagues (Thieltges et al., 2009), for example, used experimental oyster rings to investigate the effect of Pacific oysters (*C. gigas*) on the transmission of trematode infective stages (cercariae) to their target mussel hosts (*Mytilus edulis*) on tidal flats in Europe (Fig. 3). Over the course of 2.5 months, mussels deployed on experimental oyster rings acquired 70% fewer parasites than mussels on bare sand, as predicted from the results of corresponding laboratory experiments in which oysters sharply reduced parasite transmission to mussels. Oysters filter cercariae from the water column, leading to encounter reduction between parasite and host (Thieltges et al., 2009). Additional evidence for dilution effects in the field comes from applied studies on parasitism in livestock. For example, nematophagous fungi kill larval nematode stages on pasture land, such that foals and pigs grazing on treated pasture acquire fewer parasites than those on untreated plots, suggesting a 'green' practice for controlling nematodes in livestock (Larsen et al., 1996; Waller and Thamsborg, 2004). In the context of human diseases, the experimental addition of diluting snails, fishes, shrimps and tadpoles to outdoor pond systems reduces or even blocks schistosome infection in target snails, thereby reducing human disease risk (Fig. 4) (Upatham and Sturrock, 1973; Laracuente et al., 1979). All these studies suggest that dilution effects are widespread under natural conditions but more field studies are needed to evaluate the relevance for other host–parasite systems.

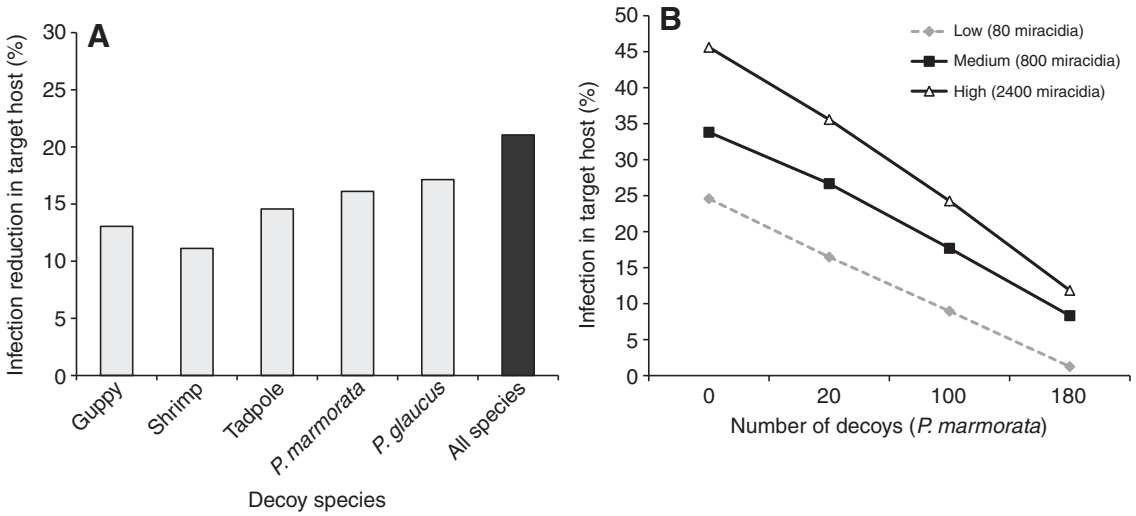

Fig. 4. (A) Effect of dilution hosts individually and collectively on transmission of *Schistosoma mansoni* miracidia to target snail hosts (*Biomphalaria glabrata*). All dilution hosts were effective in reducing transmission (relative to controls), but their combined effects were less than additive (red bar). Treatments included 40 *B. glabrata*, 20 miracidia of *S. mansoni*, and 'medium' densities of each dilution species. (B) Effects of number of decoy hosts (individuals of snail *Physa marmorata*) and of number of parasite miracidia (low, medium and high) on transmission of *S. mansoni* to target hosts. Either increases in decoy hosts or decreases in parasite dosage lead to lower levels of infection in target hosts. Data from Upatham and Sturrock (Upatham and Sturrock, 1973).

Understanding the dilution effect in complex communities

Most experimental studies to date have tested the effect of a single added species on parasite transmission. However, hosts are embedded in a matrix of surrounding organisms, all of which may influence parasite transmission and disease risk. How do dilution effects operate in more complex communities?

The simplest assumption is that additional species will result in further reductions of parasite transmission to a given target host, resulting in a monotonic decrease in parasite loads with increasing diversity. However, experimental studies suggest that the dilution capacity of individual species varies widely, and some studies report a lack of additivity with the addition of multiple dilution hosts (Fig. 4A) (Upatham and Sturrock, 1973; Johnson et al., 2009). Some organisms tested experimentally have no effect whereas others can almost completely block transmission (Thieltges et al., 2008b). Thus far, preliminary comparisons do not support the idea that some biological mechanisms (e.g. predators) have a stronger effect than others (e.g. decoys) (Thieltges et al., 2008b). Rather, in a particular host–parasite system, certain species exhibit stronger dilution capacities than others, regardless of their dilution mode or biomass. In mesocosm experiments, for example, neither filter-feeding cockles and barnacles nor filamentous algae interfered with the transmission of cercariae to juvenile stalk-eyed mud crabs (*Macrophthalmus hirtipes*), whereas anemones (*Anthopleura aureoradiata*) caused a >4-fold reduction in parasites acquired by crabs (Hopper et al., 2008). Similarly, in experiments with trematodes and larval amphibians, the presence of gray treefrog tadpoles – but not those of green frogs (*Rana clamitans*) – significantly reduced trematode infections in co-occurring toads (Johnson et al., 2008). This suggests that the strength of dilution effects in a given system will depend on the identity and specific traits of diluting organisms rather than on simple measures of species richness (LoGuidice et al., 2008).

The strength of any dilution effect also depends on the relative abundance of dilution hosts relative to focal hosts. Parasite load in target hosts usually decreases with the number of diluting organisms (Fig. 4B). For example, the combined dilution effect of a community of diluters (mixed assemblage of guppies, shrimps, tadpoles and snails) on schistosome infections in snail hosts (*Biomphalaria glabrata*) increased with the total density of non-hosts (Upatham and Sturrock, 1973). This indicates that studies have to consider both the role of species traits (e.g. species identity) as well as the density of the diluting organisms (e.g. species evenness) (Fig. 5). This creates challenges when comparing the diluting capacities of different species. While density effects can be controlled for in

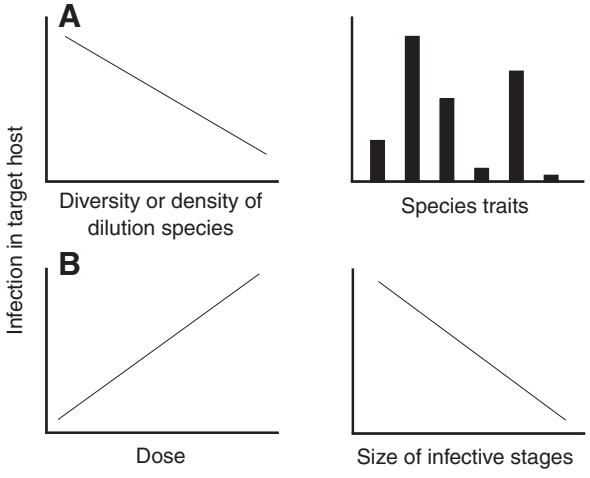

Fig. 5. Conceptual depiction of how properties of the diluting organisms or of infective stages influence the strength of the dilution effect. (A) Effects of diversity, density and species traits of diluting species on parasite loads in target hosts. The dilution effect increases with diversity and density of dilution host but depends on the specific dilution properties of the species. (B) Effects of dose and size of infective stages on parasite load in target hosts. The dilution effect decreases with dose and increases with the size of infective stages.

morphologically and physiologically similar organisms (e.g. tadpoles or snails of different species), comparing diluters with very different morphologies and diluting mechanisms is more difficult. For example, how do you compare the dilution capacity of 10 bivalve decoys with 10 crab predators? Direct comparisons of dilution capacities require careful thought when designing experiments.

Susceptibility to dilution effects will also be influenced by properties of the free-living infectious stage, including its size, longevity in the environment and host specificity (Fig. 5). For example, the risk of trematode cercariae being consumed by larval fish predators strongly depends on their size, with larger cercariae consumed at higher rates than small ones as a function of their visibility to predators (Kaplan et al., 2009). Similarly, parasite stages that are either extremely short-lived (<24 h) or highly host specific will be particularly vulnerable to dilution effects. Thus, many dilution examples involve trematode miracidia, which generally survive for ~12 h and have high host specificity for their molluscan intermediate hosts. This further suggests that, even within a single parasite's life cycle, diversity will have different effects at various stages of transmission. Increases in snail diversity, for example, will likely reduce trematode transmission to target hosts, whereas changes in vertebrate diversity may have few effects on transmission to definitive hosts, for which trematodes exhibit much lower host specificity. Finally, as predicted from transmission models, the success of a parasite in finding a host will depend on the number of free-living stages produced, their longevity, and the number or proportion of susceptible hosts in the environment. In particular, high concentrations of infectious stages can 'swamp out' a dilution effect, leading to high infections in target hosts even in the presence of dilution host(s). For example, the community of dilution hosts in the example referenced above (miracidia of *Schistosoma mansoni* infecting the snail *B. glabrata*) exhibited a much weaker dilution effect at high doses of infective stages (Fig. 4) (Upatham and Sturrock, 1973). Integrated field- and modeling-based approaches are necessary to understand this dose dependency of the dilution effect and how it varies in response to changes in infectious stages, target hosts and dilution hosts.

How does the relationship between diversity and disease vary across space?

A more complete understanding of the dilution effect also requires exploration of how the diversity–disease relationship varies with spatial scale (Ostfeld and Keesing, 2000b; Allan et al., 2009). Studies of biodiversity, for example, typically examine diversity and local (α), inter-site (β), and regional (γ) spatial scales. Which scale is appropriate when studying the dilution effect? And what are the relative contributions of host, non-host and parasite diversity in driving dilution effects? *A priori*, we might expect that local scales of diversity will be the most important in determining infection dynamics and the relevance of a dilution effect. However, defining local diversity will depend on the home-range of different hosts and vectors and the spatial scale at which they interact (landscape epidemiology) (see Ostfeld et al., 2005). For example, the movement of short-lived trematode miracidia is often extremely local, frequently leading to significant spatial heterogeneity in snail infections, even within a single wetland ecosystem (Smith, 2001). In contrast, tick vectors are comparatively long lived and can travel widely with their vertebrate hosts, effectively increasing the spatial scale of transmission.

Changes in host and parasite diversity across scales will also shape infection levels in target hosts. Because many parasites are relatively host specific (Poulin and Keeney, 2008) and do not share all hosts in a given community, greater numbers of host species generally support a wider diversity of parasites (Fig. 5). This relationship has been found at various spatial scales (Watters, 1992; Hechinger and Lafferty, 2005). At the continental scale, both hosts and parasites generally show higher species richness toward the equator, which is also where the greatest diversity of human diseases occurs (Fig. 6) (Rohde, 1992; Guernier et al., 2004; Hillebrand, 2004; Jones et al., 2008).

How do these larger scale patterns of host and parasite diversity influence the dilution effect? Comparative studies along latitudinal or diversity gradients have yet to be undertaken, but we can generate several intriguing predictions based on theory. First, the net effects of diversity in reducing infection ought to be greatest in tropical (lower latitude) regions owing to the wider diversity of potential dilution organisms in local ecosystems (Fig. 6). Hence, while higher host diversity may result in a higher diversity of infectious pathogens, infection levels with particular parasites may nevertheless be relatively low compared with regions at higher latitudes due to dilution effects. This trend could be magnified if parasites have antagonistic interactions with one another, such that interactions within hosts (or within the environment) reduce the survival or pathology of one or more parasites. For example, Harris and colleagues (Harris et al., 2009) found that interactions between pathogenic and non-pathogenic microbes on amphibian skin communities could help regulate disease. Second, the loss of species from temperate areas where local diversity is lower could cause proportionately greater increases in disease risk because of the smaller number of dilution hosts in the system (Fig. 6) (Ostfeld and Keesing, 2000b; Dobson et al., 2006). Modeling and empirical efforts suggest that the consequences of species loss will be greatest

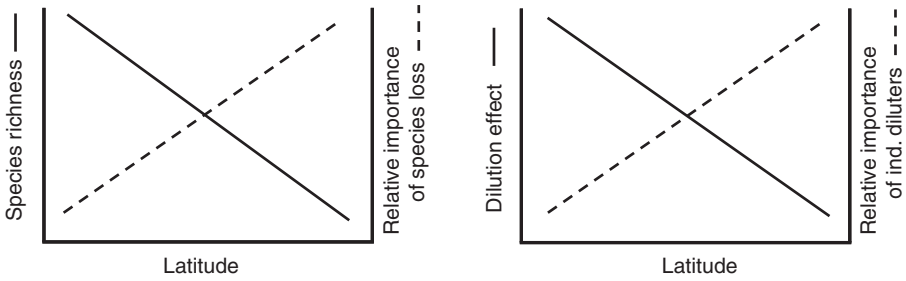

Fig. 6. Effects of latitude on the dilution effect. In general, species richness decreases with latitude (left graph, solid line), suggesting strongest dilution effects at low latitudes (right graph, solid line). Based on this, the relative importance of species loss (left graph, dashed line) and of individual diluters (right graph, dashed line) can be expected to increase with latitude, i.e. they will be most important at species-poor low latitudes.

in low diversity communities (Schmidt and Ostfeld, 2001; Dizney and Ruedas, 2009). While the idea of a latitudinal gradient in dilution strength is intriguing, such large-scale effects may be overridden by interactions between hosts and parasites at smaller spatial scales (e.g. within the local host space) and by shifts in habitat or the types of host–parasite systems that occur across such gradients. Experimental and observational studies along host and diluter diversity gradients and on different spatial scales will be necessary to disentangle the various effects.

Apparent facilitation and the net effects of diversity

Increases in diversity may often lead to decreases in infection, but they can also generate increased costs from interspecific competition or predation. The net effect of higher diversity will often depend on how pathogenic the infection is relative to the costs involved in competition and predation. In the previous example involving larval amphibians and trematodes, toad larvae raised alongside gray treefrogs took longer to metamorphose and were smaller at metamorphosis than toads raised with conspecifics, illustrating interspecific competitive effects. However, toads raised with treefrogs also exhibited significant reductions in infection and in parasite-induced pathology, including higher survival and fewer limb malformations, suggesting that the benefits from reduced parasitism outweighed the costs of competition. This phenomenon has been termed 'apparent facilitation' (Johnson et al., 2008).

In snails, trematode infections frequently cause reproductive castration; thus, the relative fitness of patently infected snails falls to zero. Non-host snails, which often compete for similar food resources with host snails, can cause decreases in the fraction of parasites that successfully infect target hosts, conferring an indirect benefit in the form of higher reproduction (Johnson et al., 2009). The transition from monospecific (target host only) to heterospecific communities (with decoy snails) caused a 30–50% reduction in focal host infections by *S. mansoni* and a 100% increase in per capita egg production (Johnson et al., 2009), further illustrating the importance of apparent facilitation. Interestingly, however, such increases in snail fecundity could lead to long-term increases in the target host population, which may in turn enhance parasitism by increasing the availability of susceptible hosts. The same issue arises when considering our original example of zooprophylaxis. The use of non-human decoys (e.g. livestock) to divert feeding mosquitoes away from humans may reduce vector-borne infections in the short term, but the increase in successful blood meals has the potential to cause long-term increases in mosquito populations and thereby increase the risk of subsequent human exposure (Saul, 2003; Dobson et al., 2006).

Conclusions

Our review extends the dilution effect beyond vector-borne microparasites, which have thus far been the primary focus of investigations. Based on a review of recent and historical literature, we argue that dilution effects are widespread for many complex life cycle parasites, including those of medical, veterinary and conservation importance. Because of the relative ease of manipulating the free-living stages of these parasites, experimental work in the field and laboratory has led to clear demonstrations of many of the postulated mechanisms underlying the diversity–disease relationship. Importantly, this has included pure diversity mechanisms (rather than simple changes in host density) such as encounter reduction and transmission reduction. Research with complex life cycle parasites has also revealed new mechanisms linking changes in community structure and infection (e.g. propagule reduction) and highlighted a broader range of direct and indirect examples of existing mechanisms. For example, within 'encounter reduction', we identify mortality of free-living stages, mortality of intra-host stages, and changes in host behavior/distribution as possible forms of this mechanism. Collectively, dilution effects in complex life cycle parasites include roles for a wide range of host and non-host species within the community, including active predators, filter feeders, non-host decoys, alternative hosts, toxin-producers, plants and bioturbaters.

Despite this extension of the dilution effect to a broader range of parasites, we do not suggest that increases in species richness will always decrease disease risk; indeed, in some cases diversity will cause an increase in infection risk (amplification hosts) (Begon, 2008) and species losses will exclude a parasite by eliminating a necessary host. Thus, the challenge lies in identifying when and for what types of host–parasite interactions we are likely to find evidence of a negative relationship between diversity and disease. By integrating the information presented here for complex life cycle parasites with existing information on the dilution effect in vector-borne pathogens, we advance the following criteria for when dilution effects are likely to occur (modified from Ostfeld and Keesing, 2000b):

(1) Parasites infect multiple host species within a community, either alternatively with the same stage of infection or sequentially involving different forms of infection. This list includes but is not limited to indirect life cycle parasites that use vectors or free-living infectious propagules for transmission. Theoretical studies have suggested that the dilution effect will be greatest for pathogens in which within-species transmission is greater than between-species transmission and for which transmission is frequency dependent rather than density dependent (e.g. Dobson, 2004; Keesing et al., 2006). However, the relevance of such predictions when extending the dilution effect to a broader range of parasites has not been explored.

(2) Species within the community, including alternative hosts, non-hosts and other parasites, directly or indirectly affect parasite transmission into a focal host and resulting disease risk.

(3) Low diversity communities are dominated by highly competent host species in which transmission is maximized. Ostfeld and Keesing (Ostfeld and Keesing, 2000b) found empirical support for this pattern for several zoonotic diseases and argued that, based on evolutionary pressures on parasites to adapt to locally abundant and regionally common hosts, this may be common (see Keesing et al., 2006).

(4) More diverse communities include a greater fraction of species that interfere with parasite transmission through a suite of potential mechanisms, thereby reducing disease risk in a focal host.

These criteria remain hypothetical as the necessary comparative work among different parasites and across gradients of community structures have yet to be undertaken. It is also important to recognize that changes in biodiversity are but components of environmental change; shifts in the physical environment, including temperature, humidity and disturbance regime, can all have direct effects on parasites, either positive or negative. We further recognize that patterns of species richness, host abundance and parasite infection are dynamic variables even within a single ecosystem, and that community assembly and disassembly may follow differing pathways. Nevertheless, these criteria offer an initial foundation to help guide subsequent studies toward a more predictive framework.

Where to go from here

We are only beginning to understand the importance of diversity in complex disease systems. There is a pressing need for experimental

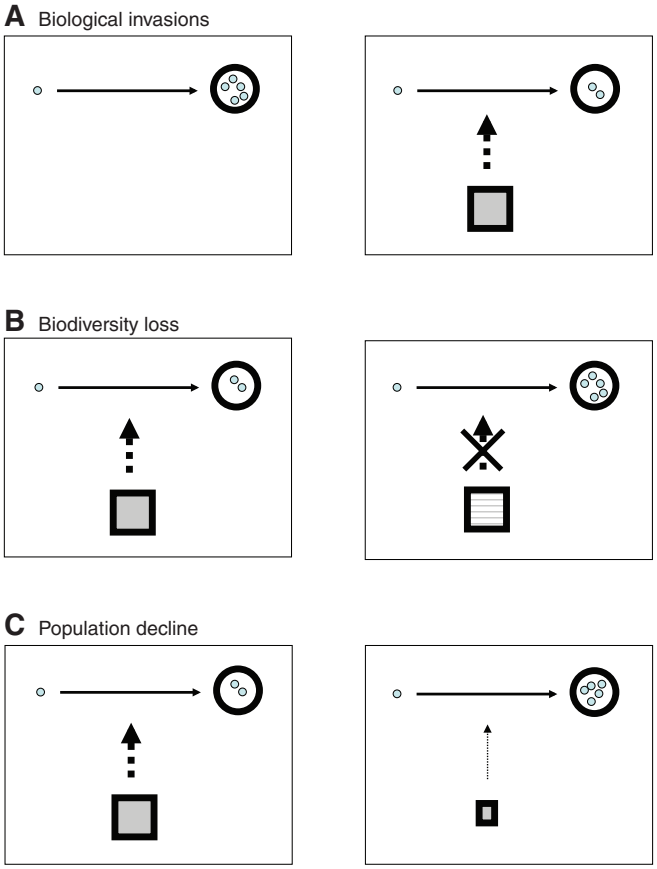

Fig. 7. Changes in the dilution effect in a changing world: (A) the introduction of species with diluting capacities may reduce infections in native hosts; (B) in contrast, the loss of key diluting species may lead to an increase in infections in target species; and (C) population declines of diluting species may reduce dilution effects, resulting in increased infection of target hosts. Small circles denote parasites (free-living stages or within hosts); large circles denote hosts; and boxes denote diluters. The size of arrows and boxes symbolize interaction strength or population sizes, respectively.

studies that carefully manipulate the diversity and density of diluting organisms to identify key diluters for given parasite–host systems. It will be further rewarding to examine the dose dependency of many dilution effects to characterize relationships among parasite dose, community diversity and disease pathology, with careful attention to the occurrence of thresholds and other non-linearities. Experiments should increasingly focus on investigating how multi-species communities influence infection and disease risk as most studies to date have compared only monospecific and heterospecific settings. Initial experiments will best be carried out under controlled laboratory conditions but additional field observations and experiments will be necessary to validate dilution mechanisms and patterns in natural systems (e.g. Suzán et al., 2009). A promising alternative to adding diluters involves removal experiments, in which select species or groups of species are experimentally removed from natural systems. These experiments should follow the approach of research on the relationship between biodiversity and ecosystem function (e.g. Loreau et al., 2001; Cardinale et al., 2006). In addition to small-scale experimental approaches, studies on latitudinal gradients and other large-scale patterns in the strength of dilution effects will be valuable. These can use sampling and experimental campaigns along existing gradients or utilize 'natural experiments', in which species are added (species introductions) or removed (species extinctions) from natural systems on larger spatial scales. Finally, we still know comparatively little about the role of parasite diversity in contributing to dilution effects and the resultant pathology. Given that most hosts support an entire community of parasites, interactions among parasites could have important effects on patterns of infection and pathology (e.g. Belden and Harris, 2007). Decreases in parasite diversity alongside host diversity could weaken competitive interactions among parasites, thereby enhancing the success of generalist species. Interactions such as these may create non-linear responses between disease and diversity and preclude quantitative, species-specific predictions about the responses of particular diseases to biodiversity loss.

The future of diversity and disease: invasions and extinctions

Given the importance of dilution effects for many parasite–host systems, the rapid decline of many populations and species coupled with an increase in species invasions can be expected to have ramifications for disease dynamics (Fig. 7). These effects may serve to enhance or reduce endemic disease. For example, invading species may introduce dilution effects formerly absent in the invaded system. In New Zealand, invasive non-host snails (*Lymnaea stagnalis*) reduced trematode infections in the native freshwater snail (*Potamopygus antipodarum*) by eating the parasite's eggs (Kopp and Jokela, 2007). Similarly, invading Pacific oysters (*C. gigas*) in the European Wadden Sea reduced infection levels in native blue mussels (*M. edulis*) by filtering out and digesting infective stages (Thieltges et al., 2009). Loss of species from a system may also affect disease dynamics, for example by releasing dilution pressure on infective parasite stages and increasing infections in target hosts. For instance, Ostfeld and Holt (Ostfeld and Holt, 2004) argued that the loss of mesopredators, many of which prey on rodents, leads to increased rodent-borne zoonotic diseases. We are not aware of comparable examples involving a pathogen with free-living stages, but the widespread importance of dilution effects for complex life cycle disease systems makes this effect likely, particularly when a key diluting species is lost or diminished. To date, such effects have received scant scientific interest but the ubiquity of dilution effects discussed above suggests that species invasions and losses – as well as population changes – will have consequences for disease dynamics in many natural systems, underscoring the need for more experimental studies on changes in dilution effects in response to current and forecasted shifts in community structure.

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