# New Directions in Conservation Medicine

## Applied Cases of Ecological Health

Edited by A. Alonso Aguirre,
Richard S. Ostfeld,
and Peter Daszak

OXFORD
UNIVERSITY PRESS

# 5

# AN ECOSYSTEM SERVICE OF BIODIVERSITY

## The Protection of Human Health Against Infectious Disease

Felicia Keesing and Richard S. Ostfeld

In the face of unprecedented, rapid declines in global biodiversity, scientists have been investigating whether ecosystems with low biodiversity function differently than ecosystems with high biodiversity. If they do, the discovery of beneficial "ecosystem services" rendered by biodiversity has the potential to motivate conservation. Unfortunately, the kinds of ecosystem services typically investigated by scientists—ecosystem stability, resistance to invasion, productivity—often fail to capture the attention of most policymakers and the public (Biodiversity Project 2002; Ostfeld et al. 2009). Similarly, the types of biodiversity typically included in studies (e.g., wild plants or single-celled eukaryotes) are often not the types of biodiversity whose vulnerability motivates action. In this chapter, we describe an ecosystem service that has the potential to motivate conservation of biodiversity worldwide—the protection of human health by charismatic wild animals.

We will describe the role of biodiversity in the transmission of Lyme disease, a potentially debilitating condition that affects many tens of thousands of people every year in North America, Europe, and Asia. We will also describe how and why the patterns we see in Lyme disease are common to many disease systems, including not only other human diseases but also diseases of wildlife, domestic animals, and wild and cultivated plants.

## EPIDEMIOLOGY OF LYME DISEASE

About 30,000 people report confirmed cases of Lyme disease in the United States each year (CDC 2010), and an unknown number of others are also afflicted. In Europe and Asia, tens of thousands are infected each year, although reporting standards are less stringent (Lane et al. 1991; Barbour and Fish 1993; Lindgren and Jaenson 2006). In its early stages, Lyme disease is often recognized by a characteristic rash called *erythema migrans* (EM rash). Other characteristic early symptoms include headaches, fever, and pain in muscles and joints. At this stage, it can generally be treated effectively with antibiotics. However, if Lyme disease goes undetected or untreated at this early stage, it can become more severe, resulting in neurological symptoms including partial paralysis, endocarditis, and severe joint pain (Feder et al. 2007).

Lyme disease is caused by a bacterium, *Borrelia burgdorferi*, which is passed to humans through the bite of an infected ixodid tick. In the midwestern and eastern United States, the vector is the blacklegged tick, *Ixodes scapularis*. Other ixodid ticks serve as vectors in other areas, including *I. pacificus* in western North America and *I. ricinus* in Europe. Ixodid ticks have three post-egg life stages: larva, nymph, and adult. Each of these three stages takes a single blood meal from any of a wide variety of vertebrate hosts,

including humans, before dropping off and molting into the next stage, in the case of larvae and nymphs, or dropping off and reproducing, in the case of adults.

There are two points about the life cycle of the tick that heavily influence the ecology of the disease. The first is that the larvae hatch out of the eggs uninfected with the bacterium that causes Lyme disease, so the larvae are not dangerous to people (Patrican 1997). Ticks can become dangerous to people only if they pick up the infection during one of their blood meals. If they do, then they will retain this infection through their nymphal and adult stages. The second key point is that most cases of Lyme disease are caused by infected nymphal ticks (Barbour and Fish 1993). These infected nymphs picked up the bacterium during their larval meal. Therefore, if we want to understand how ticks become dangerous to people, we need to focus on the sequence of events in nature during which uninfected larvae become infected nymphs.

At our study sites, larvae seek hosts in late summer through early autumn. When a host closely approaches a host-seeking ("questing") larva, the tick can get on and attempt to find a location where it can feed on the host while avoiding being groomed off. If it avoids host grooming, it will take a blood meal, during which it may acquire the bacterium. When the meal is over, the larva disengages from the host and drops off onto the ground, molts into the nymphal stage about a month later, and then overwinters before seeking another blood meal (Fig. 5.1). Blacklegged ticks take their blood meals on a wide variety of vertebrate hosts, including mammals, birds, and reptiles. Does the kind of animal a larva feeds on affect its chances of making the transition from an uninfected larva to an infected nymph? In the past few years, we have been investigating that question through a series of experiments.

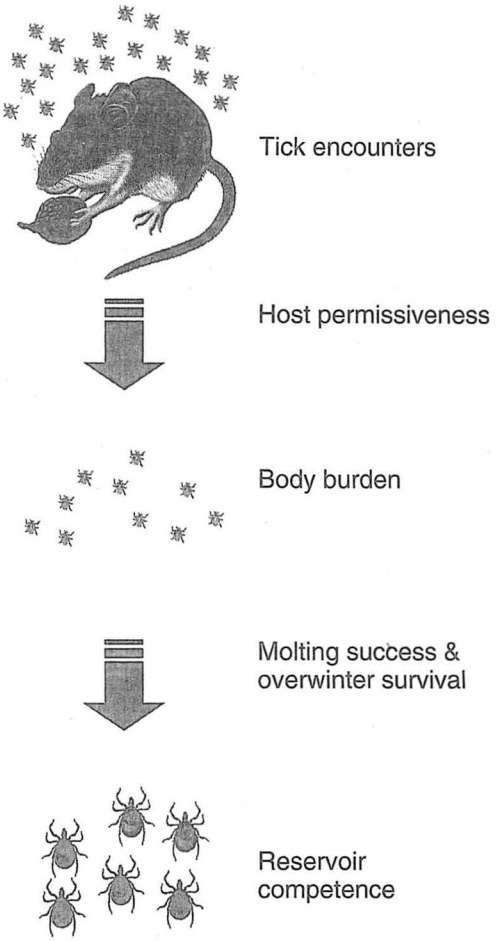


**Figure 5.1:**
Stages in the life cycle of blacklegged ticks (*Ixodes scapularis*) as they encounter and attempt to feed on a host (in this case a white-footed mouse), molt into the nymphal stage and overwinter, and either acquire the bacterium that causes Lyme disease or do not (reservoir competence). The fate of a tick through each transition is dependent on the identity of the host it encounters (see text).

## THE IMPORTANCE OF SPECIES IDENTITY

To ask whether larvae are more likely to feed successfully on some kinds of animals than others, we captured six common species of hosts for larvae at our study site in New York: white-footed mice (*Peromyscus leucopus*), eastern chipmunks (*Tamias striatus*), gray squirrels (*Sciurus carolinensis*), veeries (*Catharus fuscescens*), catbirds (*Dumatella carolinensis*), and opossums (*Didelphis virginiana*). These species were selected to provide a representative sample of hosts across a range of taxa and body sizes. We held individual hosts in cages until we were sure that they no longer carried any ticks they had acquired in the field, and then we carefully placed 100 larval ticks on each animal and let the ticks attempt to feed. We held the animals in special cages so that we could count any ticks that fell off the hosts, whether they had

fed successfully or not. Any ticks that we did not recover had been destroyed during host grooming; most were apparently swallowed. Our results clearly showed that larval ticks were better able to feed on some hosts than others (Keesing et al. 2009). At one extreme, about half of the ticks that were placed on mice were able to feed successfully, while at the other extreme, almost none of the ones placed on opossums were (Fig. 5.2).

In addition to knowing the *percentage* of ticks that feed successfully on each host species and the percentage that are killed in the attempt to feed, we also know how many larvae actually feed to repletion on each species of host when they range freely in natural habitats. This is because we capture free-ranging hosts during the season of larval activity and hold each animal sufficiently long for all naturally acquired ticks to fall off after a successful meal. Using these two pieces of information—the number of ticks that feed successfully from a given host species and the percentage of ticks attempting to feed that actually do so—we can estimate how many larvae *attempt* to feed on each species; by subtraction, we can determine how many are killed while trying. For example, the average mouse has about 25 larval ticks that feed successfully on it, but we know that only about 50% of the ones that try to feed manage to feed successfully. This allows us to estimate that about 50 larvae try to feed on each mouse, while only about half of these (25) manage to do so. In contrast, only about 3% of larvae that attempt to feed on an opossum feed successfully, and yet the average opossum has about 200 ticks that have fed to repletion. This allows us to estimate that the average opossum encounters about 5,000 ticks, of which the opossum consumes 97% during grooming before the ticks can feed (Keesing et al. 2009).

After feeding, larval ticks need to molt into nymphs and survive the winter before they can take their next meal. To find out whether the different kinds of hosts affect how well larvae molt and survive over the winter, we put fed larvae from different hosts into special tubes that we had filled with intact cores of forest soil. With the ticks inside, we covered the tubes with fine mesh cloth and then returned each tube to the forest floor for the winter. When we removed the tubes in the spring, the results were very clear. Fed larvae from mice, birds, and chipmunks had molted and survived the winter much better than fed larvae

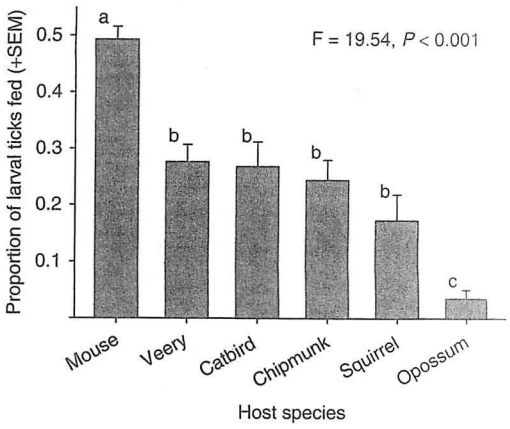


**Figure 5.2:**
The proportion of larval ticks that fed successfully (+s.e.m.) on six species that are common hosts for larval blacklegged ticks (*Ixodes scapularis*) in upstate New York. Hosts were captured in the field and held in the laboratory until ticks naturally feeding on them had fed to repletion and dropped off. Hosts were then reinfested with 100 larval ticks and monitored to determine the proportion of those ticks that fed successfully. Lowercase letters indicate results that were significantly different (one-way ANOVA; $p = 0.05$). Modified from Keesing et al. 2009.

from opossums and squirrels had (Brunner et al. 2011).

Finally, we can figure out how many larvae pick up the Lyme bacterium from each host species because we test nymphs from each host species to determine what proportion are carrying the infection. Over 90% of larval ticks that feed on white-footed mice pick up the bacterial infection from the mice, while only 50% of the ticks that feed on chipmunks do, and only 3% of the ticks that feed on opossums do (Fig. 5.3).

From these experiments, we can conclude that the most important factor determining the probability that an uninfected larval tick will become an infected nymph is what host species it feeds on. If a larva attempts to feed on a mouse, it is likely to have a successful meal, molt successfully and survive the winter, and pick up an infection that makes it potentially dangerous to humans. In contrast, if a larva tries to feed on an opossum, it is likely to get groomed off and killed. If it does manage to feed successfully, it is unlikely to molt and survive the winter; even if it does, it probably will not have picked up the Lyme bacterium anyway.

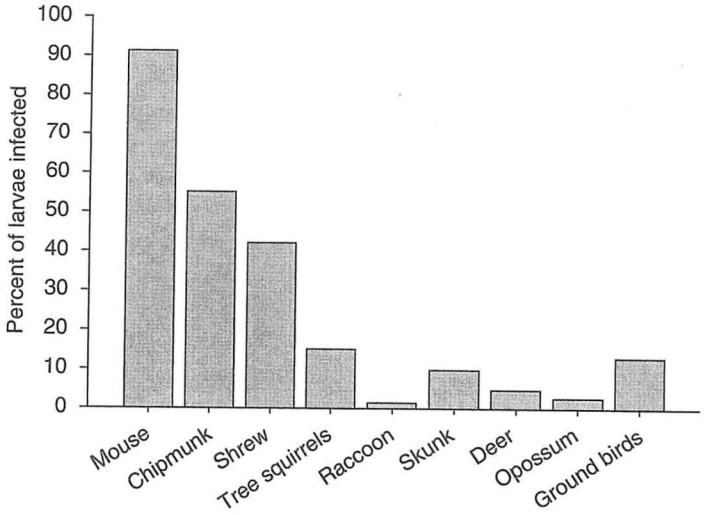


**Figure 5.3:**
The percentage of uninfected larval ticks that become infected after feeding on a particular host species. This is called the reservoir competence of the host species. Data from Keesing et al. 2009 and LoGiudice et al. 2003.

## THE ROLE OF DEER

We have discussed the importance of individual species in feeding and infecting ticks, but we have not yet discussed one host species that is frequently associated with discussions of Lyme disease: the white-tailed deer (*Odocoileus virginianus*). Many people assign deer the central role in determining Lyme disease risk because it has been considered the most important host for adult female ticks. Some researchers contend that adult females feed almost exclusively on deer during the fall. In the spring, these females lay eggs, producing the next generation of ticks that can become infected and thereby dangerous. As a consequence, the reasoning goes, if there are more deer, there will be more ticks. The origins of this dogma and its consequences have recently been thoroughly reviewed (Ostfeld 2011), so here we will only summarize the evidence that the story is not this simple.

Investigations of the role of deer in determining Lyme disease risk have typically taken one of two approaches. In the first approach, investigators reduce deer abundance by hunting or they exclude them with fencing. In the second approach, investigators determine if the abundance of ticks is correlated with the abundance of deer. Collectively, these experiments have yielded strikingly inconsistent results (Ostfeld 2011), in part because species other than deer also serve as hosts for adult ticks, particularly when deer are at low abundance. Keirans et al. (1996) documented that adult blacklegged ticks feed on at least 17 species of mammals, and therefore clearly are not specialists on white-tailed deer. Despite their broad range of hosts, no studies to date have compared the distribution of adult blacklegged ticks among various hosts within a community. The only study in which blacklegged tick populations were extirpated in response to the complete elimination of deer occurred on Monhegan Island, Maine, where no other hosts for adult ticks were present (Rand et al. 2003). In addition, as deer populations are reduced by hunting, the abundance of adult ticks on the remaining deer increases such that virtually equivalent numbers of adult ticks feed on the reduced deer population (Deblinger et al. 1993). We suspect that the ticks also aggregate on non-deer hosts when deer decline, although no studies to date have assessed this possibility.

As we develop a more sophisticated and subtle view of the role of deer in determining tick abundance, we also have to incorporate another crucial piece of evidence. In two decades of work by our group, we have found that the abundance of larval ticks does not

predict the abundance of nymphal ticks (Ostfeld et al. 2006; Fig. 5.4). In other words, even if the abundance of deer *were* related in a simple way to the abundance of larval ticks that hatch out of eggs, this relationship would not predict the abundance of the nymphal ticks that are actually dangerous to humans. Indeed, in some ways, deer are protective because they feed many larval ticks but infect almost none of them (LoGiudice et al. 2003). In this way, they are ensuring that a smaller proportion of ticks are infected than would be otherwise. We will discuss this issue in greater depth in the next section.

## THE IMPORTANCE OF THE COMMUNITY OF HOSTS

The results we have described so far demonstrate that the identity of the host species determines the probability that a larval tick will survive and become an infected nymph capable of transmitting infection to another host, including a human. The experiments described above tell us how many infected nymphs an individual of each of our representative species of hosts will produce. We have sought to use this information to predict how many infected nymphs will be produced by a particular community of vertebrate hosts for ticks. To make quantitative predictions, we need to estimate the population densities of each of these hosts. Years of extensive live-trapping efforts in the forests at our study site, combined with data from other studies, allow us to estimate the abundance of each species in the forest. In a one-hectare patch of intact forest, for example, there are about 30 mice, 15 chipmunks, one opossum, four catbirds, and a suite of other species (LoGiudice et al. 2008; Keesing et al. 2009). We can use this information, combined with the data from our laboratory experiments described above, to do some simple calculations. To figure out how many infected nymphal ticks there should be in a typical patch of woods, we simply add up the number that should be infected from each host species—in other words, the number infected by mice plus the number infected by chipmunks plus the number infected by raccoons, and so on for all host species in the community (Keesing et al. 2009). Determining the number infected by each host is also simple; at least once we have all the numbers. Each mouse feeds about 25 larvae successfully. Of these, about half molt and survive overwinter to become nymphs, and 92% of these have the Lyme bacterium from their mouse host. So for each mouse, there should be about 11 infected nymphs. In total, then, if there are 30 mice, then there will be over 300 nymphs infected by all of those mice. We can make the same calculation for each of the other hosts in the forest. When we do, we find that most of the infected ticks in an intact forest took their larval meals from mice (Fig. 5.5).

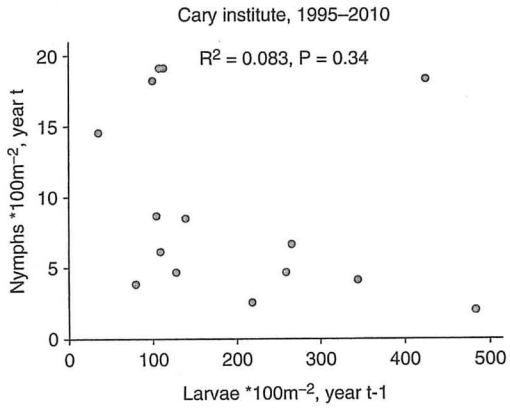


**Figure 5.4:**
The relationship between the number of larvae per hectare in one year and the number of nymphs the following year over 15 years of study at the Cary Institute in Millbrook, NY. The lack of a relationship demonstrates that something other than the number of larval ticks determines how many ticks molt and survive to become nymphs the following year. This contradicts the prevailing view that deer would be critical to Lyme disease risk if they determine the number of larvae that hatch the next year (see text).

One way to interpret this result is that mice are a critical host in the ecology of Lyme disease because most infected vectors got infected from them. Indeed, scientists are trying to figure out which hosts infect the most vectors for many diseases. One prominent example is the emerging disease West Nile virus (WNV) encephalitis, which is caused by a virus transmitted among hosts by mosquito vectors. In several studies of WNV, investigators have determined, through painstaking experimentation, which of the infected mosquitoes they capture got infected by which host species (Loss et al. 2009), as we have done for mice with Lyme disease. For WNV, American robins (*Turdus migratorius*) emerge as the host species that most infected mosquitoes have fed on, which has been interpreted as indicating that robins might be the

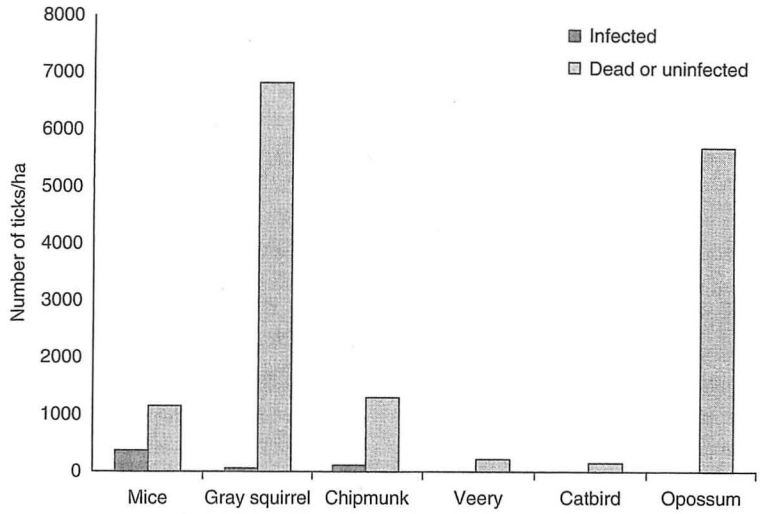


**Figure 5.5:**
The number of ticks per hectare predicted to be infected (black bars) or either killed or not infected (gray bars) after encountering one of six common hosts for ticks in northeastern U.S. forests. White-footed mice are responsible for infecting the greatest number of ticks, but other species play a much bigger role in either killing or feeding but not infecting ticks. Data from Keesing et al. 2009.

most important host species for this disease. If so, management to reduce WNV transmission could focus on reducing robin abundance. But our studies reveal that something more complicated might be going on: while the role of hosts in infecting other hosts is clearly important, the role of hosts in *preventing* infection could be just as important. Opossums and squirrels are responsible for killing, or for feeding but *not* infecting, many hundreds of ticks in the Lyme disease system (Fig. 5.5). Effective management of forest habitat to reduce Lyme disease risk, then, should focus just as much on maintaining opossum and squirrel populations as on reducing mouse populations.

Having quantified the role of each host in an intact forest community, we can now ask what would happen if each host species were to be lost from the forest. For example, how would Lyme disease risk change if there were no mice, or if there were no squirrels, in a patch of forest? We have begun to address these questions using computer simulations to remove hosts from a virtual community that initially consists of all the hosts for which we have the full complement of data described above. A fundamental issue in this computer exercise, however, is deciding whether the ticks that would have fed on the host species we remove end up feeding on the hosts that remain. If they do not—if the ticks that would have attempted to feed on a squirrel simply die in the absence of squirrels—then we would simply subtract the number of ticks feeding on squirrels from Figure 5.5. If, however, some or all of the ticks that would have fed on squirrels feed on the hosts that remain, the situation is somewhat more complicated. We have explored with our colleagues the consequences of these different scenarios for Lyme disease risk using a series of simulations.

In the simulation models, we remove each host species one at a time, and then we allow the ticks that would have fed on the removed host species to feed on the remaining hosts to varying degrees. If we remove hosts and their associated ticks simply die, then removing hosts always reduces Lyme disease risk (Fig. 5.6). However, if we allow their associated ticks to redistribute onto the hosts that remain, the picture changes considerably. When opossums are removed from our virtual forest community, for example, Lyme disease risk increases by approximately 35% if we allow just half of the ticks that would have fed on the opossums to find other hosts. Those other hosts are all more likely than opossums to allow the ticks to feed successfully, molt and overwinter, and sustain an infection with the Lyme bacterium. All of these factors contribute to the increase in risk with opossum removal.

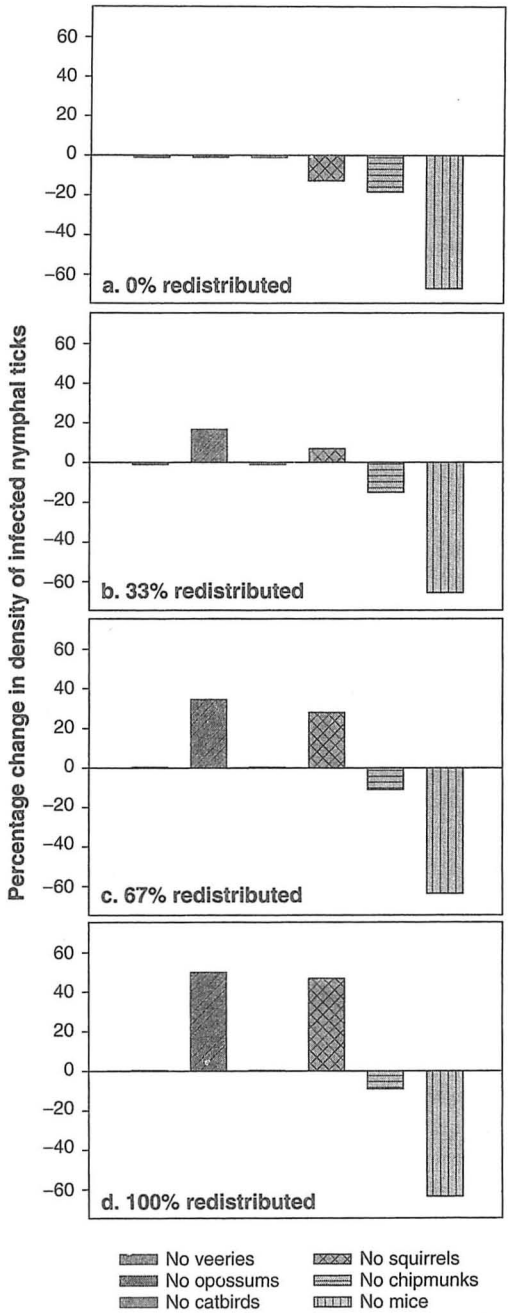


**Figure 5.6:**
The percentage change in the density of infected nymphal ticks as individual host species (see legend) were removed individually from the model. Ticks that would have fed on the removed host species were redistributed on the remaining hosts: (a) 0%; (b) 33%; (c) 67%; and (d) 100%. Figure modified from Keesing et al. 2009.

Given the different outcomes this model predicts from the removal of host species, it is critical to determine whether ticks redistribute onto other hosts and if so to what degree. This is a difficult question to test empirically, but field evidence does suggest that redistribution of ticks onto other hosts happens, and that it can be quite substantial. The best evidence comes from recent work by Brunner and Ostfeld (2008), who asked what factors affect the number of larval ticks on white-footed mice. After looking at many different factors across many different sites in many different years, they found that the best predictor of changes in the number of larval ticks on mice was the number of chipmunks in the forest at the same time. If there were lots of chipmunks around, there were few larval ticks on mice; if there were few chipmunks, there were many ticks on mice. This evidence strongly suggests that ticks redistribute from chipmunks to mice. A similar effect may occur for other hosts as well, but only further analyses and experiments can determine this with certainty.

In our previous use of the model, we removed one species at a time to observe how the loss of each individual species affected Lyme disease risk. However, conservation biologists have long known that, as forests are fragmented or degraded, some species are more likely to disappear than others. One prominent pattern is that medium-sized to large mammals often disappear from forest patches before small mammals do (Ostfeld and LoGiudice 2003). Others and we have also shown that as species disappear from forest patches, white-footed mice are always the last to go. Indeed, at our forested sites, mice are present at all sites, regardless of the number of other species present (LoGiudice et al. 2008).

We can use this information to ask what would happen to Lyme disease risk if species were lost in sequence—that is, with first one, then two, then three species disappearing, and so on. Using our data and that from other studies, we removed species from our model in a sequence that would be likely under common scenarios of biodiversity loss. The first species we removed was the veery, which is a forest-interior specialist and is sensitive to habitat disturbance. Then we removed opossums as well, followed one after another by squirrels, chipmunks, and finally catbirds. Mice were present in all runs of the model. The results of the model are clear. Lyme disease risk increases with every host removed if more than

about 10% of the ticks that would have fed on removed hosts are allowed to redistribute onto the hosts that remain (Keesing et al. 2009; Fig. 5.7). The identity of the hosts removed also matters. When the two bird species are removed, Lyme disease risk increases, but not substantially, whereas the removal of chipmunks increases risk a great deal. This occurs because some species have higher tick burdens, are more abundant, or are more likely to transmit the pathogen to feeding ticks than other species are, as we have described above.

This model, like all models, simplifies the interactions in this system. One potentially crucial simplification is that it assumes that the removal of one host species does not change the abundance of the other host species. This might not in fact be realistic. For example, if chipmunks disappear from a forest fragment, the density of the mice that remain might increase because chipmunks compete with mice for food and other resources (Ostfeld et al. 2006). Similarly, LoGiudice et al. (2008) found that northeastern U.S. forest fragments with more species of vertebrate predators had lower average densities of white-footed mice. Therefore, the loss of predatory species would be expected to release mice from regulation and thereby increase Lyme disease risk even further. Until more data are available on the direct and indirect effects of forest vertebrates on one another, we will not be able to add this important level of complexity to our models.

These modeling outputs help explain the results we obtained in a previous study (Allan et al. 2003). We compared the density of infected nymphal ticks in forest fragments that ranged in size from less than one hectare to about seven hectares. We predicted that in the smallest fragments, mice would be present and abundant; as a consequence, we expected the density of infected nymphal ticks would be high. In contrast, we predicted that mice would be less abundant and that many other species would be present in the larger fragments. As a consequence, we predicted that Lyme disease risk would be lower. The data from this comparative study confirmed our predictions. We are currently conducting a large-scale manipulation of host communities in a suite of forest fragments in upstate New York to see if fragments with fewer species have higher numbers of infected ticks.

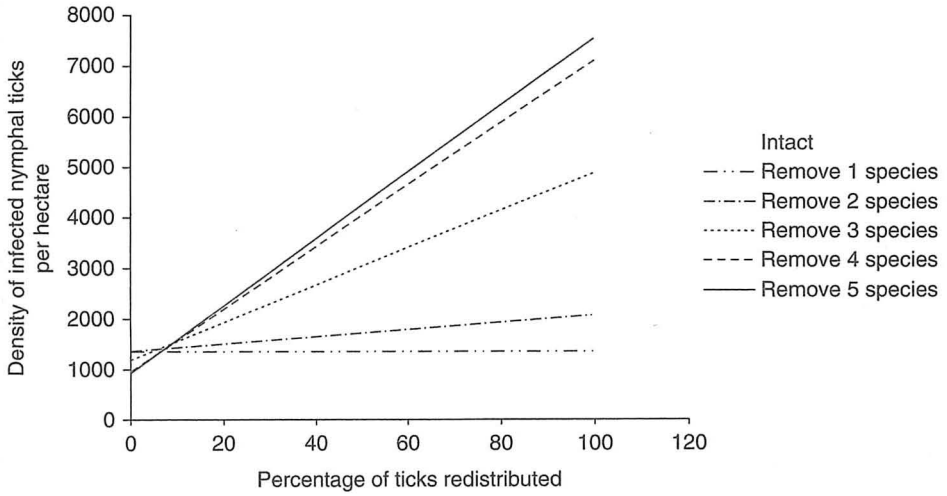


**Figure 5.7:**
The density of infected nymphal ticks (DIN) per hectare as host species were removed sequentially from our model, when the ticks that would have fed on missing hosts were redistributed among remaining hosts from 0% to 100%. Species were removed from the model in an order determined by empirical observations of the sequence of species loss in fragmented forest habitats. Veeries were removed first, and their removal did not result in differences from the density of infected ticks in "intact" forest (the two lines overlap). After veeries, opossums, squirrels, chipmunks, and then catbirds were removed, in that order; white-footed mice were present in all communities (see text). In habitats with two or more species lost, DIN was higher if ticks were redistributed on the remaining hosts, and greater rates of redistribution resulted in higher DIN values. Figure modified from Keesing et al. 2009.

## SEEKING GENERALITY

In the Lyme disease system, there are several distinct mechanisms by which the diversity of host species reduces Lyme disease risk (Keesing et al. 2006). First, in a diverse community, there are many species other than mice for ticks to feed on; in a low-diversity community, there will be mice and there might *only* be mice. Mice are important, as we have discussed, because they are abundant, they feed lots of ticks while killing few, and they are the host most likely to transmit the Lyme bacterium on to ticks. In contrast, larger species such as opossums are less likely to occur in low-diversity communities. The absence of opossums affects Lyme disease risk almost as much as the presence of mice does. This is because opossums are responsible for killing thousands of ticks that attempt to feed on them (see Fig. 5.5), which reduces risk substantially. Of the ones that do manage to feed, almost none become infected (Keesing et al. 2009). In low-diversity communities, those ticks that would have fed on opossums appear likely to feed on other hosts, including mice.

The pattern in the Lyme disease system is striking, but is it unique to Lyme disease? A growing number of studies suggests that it is not. In the past few years, researchers have found a similar pattern for a number of infectious diseases, including human diseases like hantavirus pulmonary syndrome (Suzán et al. 2009; Clay et al. 2009a; Dizney and Ruedas 2009) and West Nile virus (Ezenwa et al. 2006; Allan et al. 2009; Swaddle and Calos 2008), parasitic infections of amphibians (Johnson et al. 2008), and fungal infections of grasses (Mitchell et al. 2002; Roscher et al. 2007).

The role of diversity in affecting risk for hantavirus pulmonary syndrome provides a particularly interesting counterpoint to Lyme disease because hantaviruses are transmitted directly among their hosts, with no vector such as a tick involved. Hantaviruses are a group of negative-stranded RNA viruses that circulate primarily among wild rodents. The viruses are shed through excreta (e.g., urine, feces) and saliva; humans can be exposed if they breathe aerosolized excreta or get bitten by an infected rodent host. For people who get infected, the outcome is not good: case fatality rates are near 40% (CDC 2009).

The probability that a human will get exposed is a function of the density of infected rodent hosts (Yates et al. 2002), so recent studies have focused on what determines this key risk factor. In Oregon, for example, Dizney and Ruedas (2009) compared the proportion of infected rodents at a series of sites. Infection prevalence varied from 2% to 14% at their sites, and the only factor that explained this variation was the diversity of mammalian species. Clay et al. (2009a) found a similar pattern in Utah: sites with a high diversity of mammals had a low infection prevalence with the virus. Based on experimental work, it appears that this effect is because the deer mice (*Peromyscus maniculatus*) that serve as the primary hosts for the virus are less likely to encounter each other—and more likely to encounter individuals of other species—in more diverse communities (Clay et al. 2009b). As a consequence, transmission of the virus occurs at a lower rate in more diverse communities.

Suzán et al. (2009) provide a third example of the effects of host diversity on hantavirus risk. In this study, rodent communities in Panama were experimentally manipulated—species that are not hosts for the virus were removed from replicated experimental plots, while communities remained intact on control plots. The density of seropositive rodents was higher on the manipulated plots (Suzán et al. 2009) where diversity had been experimentally reduced. In hantavirus pulmonary syndrome and all of the other examples we mentioned above, host communities with higher diversity are correlated with lower rates of disease transmission (reviewed in Keesing et al. 2006, Johnson and Thieltges 2010; Keesing et al. 2010). There are counter-examples (Loss et al. 2009), but the pattern appears to occur more often than not. Why should diversity so frequently reduce disease transmission? The answer is perhaps best understood from another look at the Lyme disease system.

In the Lyme disease system, the mouse is an excellent host species for both ticks and spirochetes *and* a species reliably present in low-diversity communities. It is this correlation that drives the effects of diversity loss on disease in this system. One key question, then, is whether a similar correlation occurs in other disease systems and, if it does, what is the underlying biology. One hypothesis is that small-bodied, short-lived species that are particularly resilient to disturbance might allocate their immunological resources differently than longer-lived, larger-bodied species that are more

susceptible to disturbance. Another hypothesis is that ticks and spirochetes adapt to the hosts that they encounter most frequently. We have begun testing both hypotheses together. The apparent link between a host's ability to amplify pathogens and its resilience in the face of biodiversity loss (Ostfeld and Keesing 2000) suggests that low-diversity communities will often pose a strong risk of exposure to disease, which will be reduced in higher-diversity communities. If the pattern is indeed general, then protection against infectious diseases can legitimately be considered an ecosystem function that is enhanced by the protection of biodiversity.

## ACKNOWLEDGMENTS

The authors gratefully acknowledge financial support from the National Institutes of Health, the National Science Foundation, the U.S. Environmental Protection Agency, and the National Science Foundation–National Institutes of Health joint program in the ecology of infectious diseases. The work described here would not have been possible without the help of Shannon Duerr, Kelly Oggenfuss, Jesse Brunner, Kathleen LoGiudice, Mary Killilea, Ken Schmidt, Andrea Previtali, Anna Jolles, Marty Martin, Rhea Hanselmann, Laura Cheney, Charles Canham, Deanna Sloniker, and Holly Vuong.

## REFERENCES

Allan, B.F., F. Keesing, and R.S. Ostfeld. 2003. Effect of forest fragmentation on Lyme disease risk. Conserv Biol 17:267–272.

Allan, B.F., B. Langerhans, W.A. Ryberg, W.J. Landesman, N.W. Griffin, R.S. Katz, B.J. Oberle, M.R. Schutzenhofer, K.N. Smyth, A. de St. Maurice, L. Clark, K.R. Crooks, D.E. Hernandez, R.G. McLean, R.S. Ostfeld, and J.M. Chase. 2008. Ecological correlates of risk and incidence of West Nile virus in the United States. Oecologia 158:699–708.

Barbour, A.G., and D. Fish. 1993. The biological and social phenomenon of Lyme disease. Science 260:1610–1616.

Biodiversity Project. 2002. Americans and biodiversity: new perspectives for 2002. Belden Russonello and Stewart Research and Communications, Washington, DC. Available: http://www.biodiversityproject.org/docs/publicopinionresearch/americansandbiodiversitynewperspectivesfor2002.PDF

Brunner, J.L., and R.S. Ostfeld. 2008. Multiple causes of variable tick burdens on small-mammal hosts. Ecology 89:2259–2272.

Brunner, J.L., L. Cheney, F. Keesing, M. Killilea, K. Logiudice, A. Previtali, and R.S. Ostfeld. 2011. Molting success of *Ixodes scapularis* varies among individual blood meal hosts and species. J Med Entomol. 48:860–866.

Centers for Disease Control (CDC). 2009. Hantavirus pulmonary syndrome in five pediatric patients: four states, 2009. MMWR 58:1409–1412.

Centers for Disease Control (CDC). 2010. Reported cases of Lyme disease by year, United States, 1994-2008. URL: http://www.cdc.gov/ncidod/dvbid/lyme/ld_UpClimbLymeDis.htm accessed May 6, 2010.

Clay, C., Lehmer, E.M., St. Jeor, S., and Dearing, M.D. 2009a. Sin nombre virus and rodent species diversity: a test of the dilution and amplification hypotheses. PLoS One 4:e6467.

Clay, C.A., E.M. Lehmer, S. St. Jeor, and M.D. Dearing. 2009b. Testing mechanisms of the dilution effect: deer mice encounter rates, Sin nombre virus prevalence and species diversity. Ecohealth 6:250–259.

Deblinger, R.D., M.L. Wilson, D.W. Rimmer, and A. Spielman. 1993. Reduced abundance of immature *Ixodes dammini* (Acari: Ixodidae) following incremental removal of deer. J Med Entomol 30: 144–150.

Dizney, L.J., and L.A. Ruedas. 2009. Increased host species diversity and decreased prevalence of Sin nombre virus. Emerg Infect Dis 15:1012–1018.

Ezenwa, V.O., M.S. Godsey, R.J. King, and S.C. Guptill. 2006. Avian diversity and West Nile virus: testing associations between biodiversity and infectious disease risk. Proc R Soc B 273:109–117.

Feder, H.M., Jr., B.J.B. Johnson, S. O'Connell, E.D. Shapiro, A.C. Steere, G.P. Wormser, and the Ad Hoc International Lyme Disease Group. 2007. A critical appraisal of "chronic Lyme disease." N Engl J Med 357:1422–1431.

Johnson, P.T.J., and D.W. Thieltges. 2010. Diversity, decoys and the dilution effect: how ecological communities affect disease risk. J Exp Biol 213:961–970.

Johnson, P.T.J., P.J. Lund, R.B. Hartson, and T.P. Yoshino. 2009. Community diversity reduces *Schistosoma mansoni* transmission and human infection risk. Proc R Soc B 276:1657–1663.

Johnson, P.T.J., R.B. Hartson, D.J. Larson, and D.R. Sutherland. 2008. Linking biodiversity loss and disease emergence: amphibian community structure determines parasite transmission and pathology. Ecol Lett 11:1017–1026.

Keesing, F., L. Belden, P. Daszak, A. Dobson, D. Harvell, R.D. Holt, P. Hudson, A. Jolles, K. Jones, C. Mitchell, S. Myers, T. Bogich, and R. Ostfeld. 2010. Impacts of biodiversity on the emergence and transmission of infectious diseases. Nature 468:647–652.

Keesing, F., J. Brunner, S. Duerr, M. Killilea, K. LoGiudice, K. Schmidt, H. Vuong, and R.S. Ostfeld. 2009. Hosts as ecological traps for the vector of Lyme disease. Proc R Soc B 276:3911–3919.

Keesing, F., R.D. Holt, and R.S. Ostfeld. 2006. Effects of species diversity on disease risk. Ecol Lett 9:485–498.

Keirans, J. E., H. J. Hutcheson, L. A. Durden, and J. S. H. Klompen. 1996. *Ixodes (Ixodes) scapularis* (Acari: Ixodidae): Redescription of all active stages, distribution, hosts, geographical variation, and medical and veterinary importance. J Med Entomol 33:297–318.

Lane, R.S., J. Piesman, and W. Burgdorfer. 1991. Lyme borreliosis: relation of its causative agent to its vectors and hosts in North America and Europe. Ann Rev Entomol 36:587–609.

Lindgren, E., and T.G.T. Jaenson. 2006. Lyme borreliosis in Europe: influences of climate and climate change, epidemiology, ecology and adaptation measures. World Health Organization, Geneva, Switzerland.

LoGiudice, K., R.S. Ostfeld, K. Schmidt, and F. Keesing. 2003. The ecology of infectious disease: Effects of host diversity and community composition on Lyme disease risk. Proc Natl Acad Sci USA 100:567–571.

LoGiudice, K., S. Duerr, M. Newhouse, K.A. Schmidt, M.E. Killilea, and R.S. Ostfeld. 2008. Impact of community composition on Lyme disease risk. Ecology 89:2841–2849.

Loss, S.R., G.L. Hamer, E.D. Walker, M.O. Ruiz, T.L. Goldberg, U.D. Kitron, and J.D. Brawn. 2009. Avian host community structure and prevalence of West Nile virus in Chicago, Illinois. Oecologia 159:415–424.

Mitchell, C.E., D. Tilman, and J.V. Groth. 2002. Effects of grassland plant species diversity, abundance, and composition on foliar fungal disease. Ecology 83:1713–1726.

Ostfeld, R.S. 2011. Lyme disease: the ecology of a complex system. Oxford University Press, New York.

Ostfeld, R.S., M. Thomas, and F. Keesing. 2009. Biodiversity and ecosystem function: perspectives on disease. *In* Naeem, S., D. Bunker, A. Hector, M. Loreau, and C. Perrings, eds. Biodiversity and human impacts, pp. 209–216. Oxford University Press, New York.

Ostfeld, R.S., F. Keesing, and K. LoGiudice. 2006. Community ecology meets epidemiology: the case of Lyme disease. *In* Collinge, S., and C. Ray eds, Disease ecology: community structure and pathogen dynamics, pp. 28–40. Oxford Press, United Kingdom.

Ostfeld, R.S., and K. LoGiudice. 2003. Community disassembly, biodiversity loss, and the erosion of an ecosystem service. Ecology 84:1421–27.

Ostfeld, R.S., and F. Keesing. 2000. The function of biodiversity in the ecology of vector-borne zoonotic diseases. Can J Zool 78:2061–2078.

Patrican, L.A. 1997. Absence of Lyme disease spirochetes in larval progeny of naturally infected *Ixodes scapularis* (Acari: Ixodidae) fed on dogs. J Med Entomol 34:52–55.

Rand, P.W., C. Lubelczyk, G.R. Lavigne, S. Elias, M.S. Holman, E.H. Lacombe, and R.P. Smith. 2003. Deer density and the abundance of *Ixodes scapularis* (Acari: Ixodidae). J Med Entomol 40: 179–184.

Roscher, C., J. Schumacher, O. Foitzik, and E.D. Schulze. 2007. Resistance to rust fungi in *Lolium perenne* depends on within-species variation and performance of the host species in grasslands of different plant diversity. Oecologia 153:173–183.

Suzán, G., E. Marcéi, J.T. Giermakowski, J.N. Mills, G. Ceballos, R.S. Ostfeld, B. Armién, J.M. Pascale, and T.L. Yates. 2009. Experimental evidence for reduced rodent diversity causing increased Hantavirus prevalence. PLoS One 4:e5461.

Swaddle, J., and P. Calos. 2008. Increased avian diversity is associated with lower incidence of human West Nile infection: Observation of the dilution effect. PLoS One 3:e2488.

Yates, T.L., J.N. Mills, C.A. Parmenter, T.G. Ksiazek, R.R. Parmenter, J.R. Vande Castle, C.H. Calisher, S.T. Nichol, K.D. Abbott, J.C. Young, M.L. Morrison, B.J. Beaty, J.L. Dunnum, R.J. Baker, J. Salazar-Bravo, and C.J. Peters. 2002. The ecology and evolutionary history of an emergent disease: Hantavirus pulmonary syndrome. Bioscience, 52:989–998.