

West Nile Virus Revisited: Consequences for North American Ecology

SHANNON L. LADEAU, PETER P. MARRA, A. MARM KILPATRICK, AND CATHERINE A. CALDER

It has been nine years since West Nile virus (WNV) emerged in New York, and its initial impacts on avian hosts and humans are evident across North America. The direct effects of WNV on avian hosts include documented population declines, but other, indirect ecological consequences of these changed bird communities, such as changes in seed dispersal, insect abundances, and scavenging services, are probable and demand attention. Furthermore, climate (seasonal precipitation and temperature) and land use are likely to influence the intensity and frequency of disease outbreaks, and research is needed to improve mechanistic understanding of these interacting forces. This article reviews the growing body of research describing the ecology of WNV and highlights critical knowledge gaps that must be addressed if we hope to manage disease risk, implement conservation strategies, and make forecasts in the presence of both climate change and WNV—or the next emergent pathogen.

Keywords: West Nile virus, disease ecology, birds, mosquitoes, hierarchical analyses

A century ago, Hawaiian forests looked and sounded very different than they do today. Many endemic bird species made these forests home, feeding on insects and fruits, dispersing seeds, and broadcasting their spectacular songs across the valleys. Today, relatively few native bird species survive in low-elevation forests on the Hawaiian Islands. The emergence of avian pox (*Poxvirus avium*) and avian malaria (*Plasmodium relictum*) in the early 19th century exacerbated ongoing population declines caused by habitat loss and introduced predators, which resulted in the decimation of 75% of Hawaii's native bird species and in profound changes to ecosystem services (van Riper et al. 1986, Jacobi and Atkinson 1995). Island communities are especially susceptible to catastrophic declines following pathogen invasions because their populations are smaller, less genetically diverse, and isolated from mainland populations. However, the past decade has seen a growing appreciation of how disease can affect mainland populations as well. Increased globalization and ongoing climate changes facilitate shifts in the geographic distribution of known pathogens and the emergence of previously unrecognized agents across island and continental communities (Daszak et al. 2000). Examples of these shifts include the expansion of arbovirus (arthropod-borne virus) vector ranges (Woolhouse and Gowtage-Sequeira 2005), the emergence of highly pathogenic H5N1 influenza (Kilpatrick et al. 2006a), fungal infection and global amphibian declines (Norris 2007), forest tree pathogens (Lovett

et al. 2006), and the arrival of the West Nile virus (WNV) in North America (Lanciotti et al. 1999, Marra et al. 2004). Identifying, tracking, and managing the impacts of emergent pathogens in both human populations and ecological communities are not only current research goals but also a societal necessity.

WNV (genus *Flavivirus*) was first detected in the Western Hemisphere in 1999, when it caused 62 reported human infections (7 fatalities) and marked mortality of American crows (*Corvus brachyrhynchos*) in the New York City vicinity (Lanciotti et al. 1999). Today, nine years after the introduction of WNV, outbreaks recur annually across North America and we are just now beginning to identify the ecological consequences of this pathogen's emergence in the Western Hemisphere. The observed, dramatic changes in the populations of avian host species are only the initial signal of

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WNV's ecological impact, though the taxonomic breadth and spatial synchrony of declines resemble population responses seen previously in vulnerable island avifauna. In this article, we review what has been learned about the ecology of WNV in North America and highlight persistent gaps that limit our ability to forecast epidemics and interpret ecological impacts. Prominent among these knowledge gaps is the importance of climate and human-mediated landscapes in determining patterns of disease intensity in time and space (figure 1).

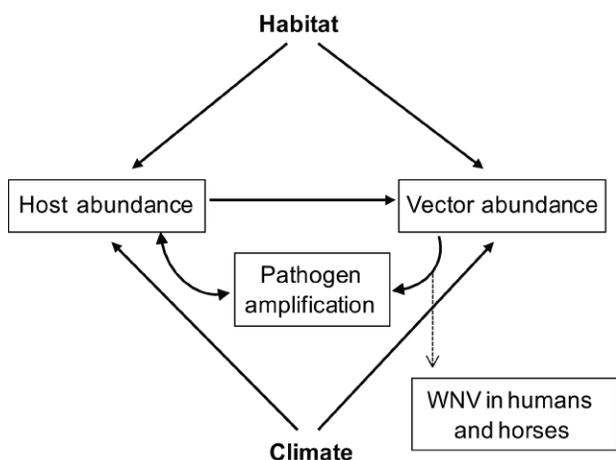


Figure 1. West Nile virus ecology. Arrows signify the direction of influence. Habitat and climate affect both host and vector populations independently. Pathogen amplification (and incidental infections in humans) relies on the abundance of and contact rates between host and vector organisms.

Pathogen invasion

The 1999 discovery of WNV in New York was unexpected, but the intensity and persistence of pathogen amplification and disease that spread across the United States were even more surprising: WNV not only survived northern winters but also dispersed from New York south to Florida and west to California, leaving behind millions of dead birds and recurrent human epidemics each year. By contrast, in the Eastern Hemisphere, WNV has historically been viewed as one of the less virulent arboviruses. WNV was initially isolated in Uganda in 1937, where it was associated with mild to moderate febrile disease in humans (Smithburn et al. 1940). From its discovery until the mid-1990s, records indicate only sporadic disease outbreaks in Africa, the Middle East, and eastern Europe (Hubalek and Halouzka 1999). One of the largest human epidemics before 1999 occurred in South Africa in 1974, but no human or unusual avian mortalities were reported at that time (McIntosh et al. 1976). During the past two decades WNV has been increasingly associated with severe human illness and epizootics in horses across the Mediterranean Basin, including outbreaks in Romania (1996), Russia (1999), France (2000), and Israel (2000) (Zeller and Schuffenecker 2004). The increase in WNV-associated disease may be related to greater virulence in some strains of the virus, including the strain that

arrived in New York City (Brault et al. 2004). Although we may never really know how the virus was first introduced to the Western Hemisphere, the New York strain that emerged was genetically similar to a strain that circulated in Israel in 1998 (Lanciotti et al. 1999).

The emergence of WNV in New York has now led to pathogen invasion in all 48 contiguous states, as well as in the Caribbean, Mexico, Central America, South America, and most provinces of Canada (see reviews by Komar and Clark 2006, Kilpatrick et al. 2007). The rapid and extensive spread has most likely occurred through a combination of dispersing residents (mosquito or bird) and long-distance spread with migrating birds and human help (e.g., mosquito or bird movement by plane, train, or automobile). An experimental infection study demonstrated that at least two migratory bird species can maintain migratory activity while viremic (Owen et al. 2006).

Human, horse, and wild bird infections have been prevalent in Canada and the United States since 2001. Reports from countries south of the US-Mexico border are few but include a human case in northern Mexico in 2004 (Ramos and Falcón Lezama 2004) and horse mortalities in El Salvador between 2001 and 2003 (Cruz et al. 2005) and Argentina in 2006 (Morales et al. 2006). Although there are many endemic pathogens that demand attention in Neotropical and tropical countries (e.g., malaria and dengue), Mexico and other countries now sporadically test for and identify WNV infection in horses and wild birds (Komar and Clark 2006). WNV transmission is undoubtedly occurring throughout the Western Hemisphere, so the absence of documented mortality events must reflect differences in surveillance intensity, in the host or vector communities, or in the virus itself. Acquired immunity or evolved resistance from exposure to other circulating flaviviruses may protect birds, as well as humans and horses, from severe WNV disease (e.g., Fang and Reisen 2006). A combination of all of these hypotheses, or something else entirely, may explain why WNV transmission in the tropics does not result in the WNV epidemics or epizootics experienced in North America over the past nine years.

Arthropod vectors

WNV is an arbovirus and is maintained in the environment through transmission between arthropod vectors (mosquitoes) and competent amplifying hosts (figure 1). Amplifying hosts appear to be predominantly birds but could also include any animal that can produce sufficient virus concentration in the blood (viremia) to infect mosquitoes if bitten (see "Avian hosts," below). By contrast, humans and horses are considered "dead-end" hosts because they do not produce a high enough viremia to reinfect a biting mosquito.

Sixty-two different species of mosquitoes have tested positive for WNV infection in the United States (CDC 2007a). This does not imply, however, that all or even many of these species are important in WNV transmission: vectors must both feed on host species and become infectious (when virus infection disseminates to the salivary glands; e.g., Turell et al.

2001). Mosquitoes from the genus *Culex* have been identified as the predominant enzootic (bird-to-bird) vector across North America (Turell et al. 2005) and the Eastern Hemisphere (Hubalek and Halouzka 1999). *Culex* mosquitoes frequently feed on birds, though many *Culex* species will also take a percentage of bloodmeals from other animals, including humans (Apperson et al. 2004, Kilpatrick et al. 2005, Molaei et al. 2006, Savage et al. 2007). The propensity of *Culex* species to feed from both birds and mammals makes them a particularly effective bridge vector between bird and human infections, though other mosquito species may also occasionally transmit WNV infection beyond the endemic bird cycle (Apperson et al. 2004, Kilpatrick et al. 2005, Turell et al. 2005, Molaei and Andreadis 2006). WNV may also be transmitted by ingestion if infected vertebrate prey or mosquitoes are consumed and through direct transmission between birds that share a cage (Komar et al. 2003). It is unclear how important these modes of transmission are in the wild.

Researchers need to further evaluate the causes of temporal and spatial heterogeneity in vector abundance and community composition, and their effects on disease dynamics. We also need to continue to identify early seasonal predictors of annual epizootics and human epidemics (e.g., mosquito abundance, winter pathogen survival).

Avian hosts

Scientists have learned a great deal about which bird species may act as hosts for WNV amplification. More than 300 species of dead birds with WNV infections have been reported to the Centers for Disease Control and Prevention (CDC), and the majority of studies that search for WNV exposure (antibodies or infection) among potential hosts in the wild find it (e.g., in Passerines [Beveroth et al. 2006, Gibbs et al. 2006], raptors [Nemeth et al. 2006], and even small mammals [Root et al. 2007]). As with evidence of infection in mosquitoes, however, most of these species are unlikely to be important hosts for WNV amplification.

A species can be a competent amplifying host only if (a) the pathogen is able to multiply to concentrations within the host that are high enough so that a mosquito vector could become infectious if it feeds on the host's blood, and (b) mosquitoes actually feed on the host in the wild. More than 50 different vertebrate species have been tested for WNV competence under laboratory conditions (see the review in Kilpatrick et al. 2007). The most competent amplifying hosts in these studies are avian and include five families from two orders. Blue jay (*Cyanocitta cristata*), western scrub-jay (*Aphelocoma californica*), American crow, common grackle (*Quiscalus quiscula*), house finch (*Carpodacus mexicanus*), house sparrow (*Passer domesticus*), ring-billed gull (*Larus delawarensis*), black-billed magpie (*Pica hudsonia*), American robin (*Turdus migratorius*), and song sparrow (*Melospiza melodia*) were the 10 most competent species (listed from high to low) in published experimental infection studies (Kilpatrick et al. 2007). Infection with WNV would lead to 20% to 48% of mosquitoes biting these bird species to become

infectious in each of the five days after infection (Kilpatrick et al. 2007). Experimental infections have also demonstrated that American alligators (*Alligator mississippiensis*) and eastern chipmunks (*Tamias striatus*) can produce viremias that could potentially infect mosquitoes but would lead to fewer than 10% of biting mosquitoes transmitting WNV, and no blood meals from these species have been discovered in mosquito feeding studies (Klenk et al. 2004, Kilpatrick et al. 2007, Platt et al. 2007). Sixteen other vertebrates showed little or no potential as WNV-amplifying hosts (e.g., rock pigeon [*Columba livia*], wood thrush [*Hylocichla mustelina*], green iguana [*Iguana iguana*], and American bullfrog [*Rana catesbeiana*] [Kilpatrick et al. 2007]).

Predicting which bird species are important for WNV amplification in the wild requires an understanding of the species that WNV vectors feed on in nature. Several studies have shown that vectors do not feed evenly from all bird species and that mosquitoes actually feed preferentially on some species in the local avian community (Kilpatrick et al. 2006b). Although the American robin was only the ninth (of 53 species tested) most competent host in laboratory infection experiments (Kilpatrick et al. 2007), high levels of mosquito feeding indicate that this species may be the most important amplifying host in the eastern United States (Kilpatrick et al. 2006b, Molaei and Andreadis 2006, Savage et al. 2007). In a related analysis, Kilpatrick and colleagues (2006c) demonstrated that in urban and residential areas, *Culex pipiens* mosquitoes shift their feeding to humans when American robins dispersed from urbanized habitats in late summer, which may contribute to the severe human epidemics of WNV in North America.

Seroprevalence studies in wild vertebrates have also added to our understanding of which species may be important hosts for maintaining and dispersing WNV in the wild (Beveroth et al. 2006, Gibbs et al. 2006, Ezenwa et al. 2007). However, while seroprevalence studies may distinguish general patterns of relative exposure to WNV, results can be difficult to interpret and are biased because of varied mortality rates among species. For example, American crows have relatively low WNV seroprevalence in the wild (Wilcox et al. 2007), though this is very likely due to high mortality rather than low exposure (Komar et al. 2003).

We need to evaluate further the importance of different vertebrate species for amplifying and dampening local WNV transmission, and explore how changes in host population abundances or avian community diversity influence disease outbreaks (enzootics or epidemics in humans).

Spatial and temporal drivers of WNV amplification

WNV amplification relies on at least three interacting populations: pathogen, host, and vector (figure 1). Each of these populations may respond independently to spatial and temporal drivers (e.g., precipitation, temperature, land cover) during the process of pathogen amplification in the environment. Deconvolution of these distinct and interacting

influences is difficult, but is critical for understanding spatial and temporal heterogeneity in disease outbreaks.

Current hypotheses explaining spatiotemporal patterns in WNV outbreaks in North America suggest that climate and land use play prominent roles in driving WNV dynamics. If extreme droughts or heat waves do favor pathogen amplification, then weather forecasts could help preempt outbreaks through timely public warnings and supplemental mosquito abatement programs. Alternatively, if something inherent in the North American landscape (e.g., extensive suburban sewer network or agricultural matrix) facilitates WNV amplification, then interventions may need to be more complicated. In this section we review what is known about where and when WNV outbreaks have occurred and highlight important gaps in current understanding that must be addressed before we can advocate either of these hypotheses.

It is useful to begin with where WNV epidemics have *not* occurred. Of the 48 continental states, Maine is both the most northern and the only state without reported human disease (CDC 2008). Although WNV transmission has been identified in northern New England, there have been few

human infections and no significant impacts on American crow populations in this region overall (figure 2). New England's cold winters or short, cool summers may reduce productivity of both vector and virus. Laboratory studies demonstrate that WNV replication in *Culex* vectors is strongly influenced by ambient temperature (Dohm et al. 2002), although very high temperatures can decrease mosquito survival (Reisen et al. 2006). Replication of WNV in *Culex tarsalis* was accelerated when mosquitoes were held at warmer temperatures (22 to 30 degrees Celsius), resulting in reduced time between initial mosquito exposure and viral transmission (Reisen et al. 2006). A study by Gibbs and colleagues (2006) also found lower WNV seroprevalence in birds sampled in cooler mountainous regions of Georgia versus nearby warmer, low-elevation sites.

Mosquito eggs and larvae need water to develop, and any changes in precipitation regimes that affect soil moisture and standing water could influence vector abundance. However, as with temperature, the relationship between precipitation and pathogen transmission is neither simple nor linear (Shaman et al. 2005, Koenraadt and Harrington 2008). *Culex*

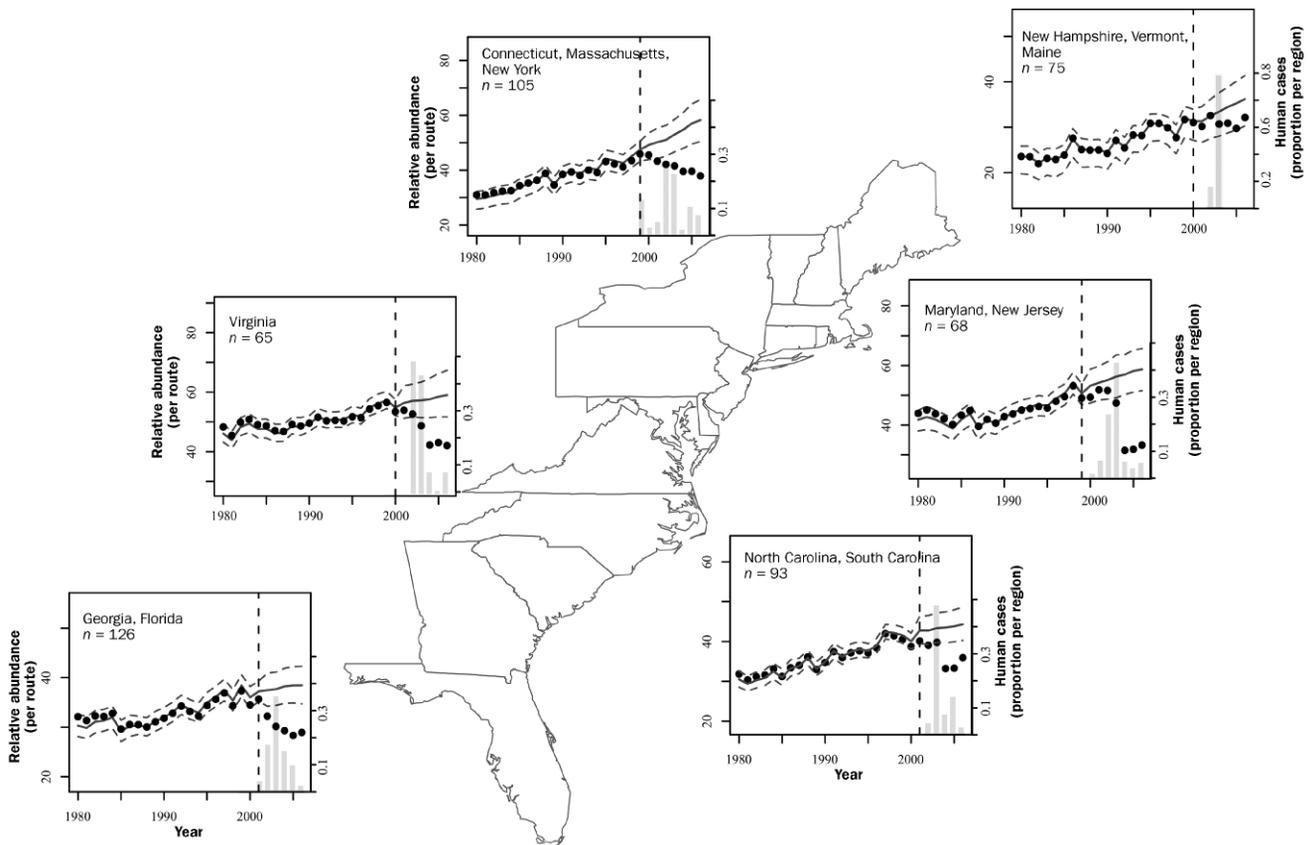


Figure 2. Observed (circles) and expected (solid line) abundances for American crow populations along the East Coast. Left axes record the mean abundance per Breeding Bird Survey route (n = number of routes used per region). States included in each plot are shown in the upper left. Dashed lines denote 95% credible intervals around expected abundances. The model used to calculate expected abundance is described in the section “Host mortality.” Vertical dashed lines denote the first year of West Nile virus incidence (avian or human) in each region. Bar plots and right axes show the relative incidence of human cases reported to the Centers for Disease Control (as a proportion of total cases in region). Maximum single-year human cases per region are as follows: CT, MA, NY = 122; NH, VT, ME = 6; MD, NJ = 107; VA = 29; NC, SC = 30; GA, FL = 144.

species tend to breed in shallow, stagnant water pools that could be compromised by either heavy precipitation or prolonged drought. Thus, the timing between rain events may be especially important in determining vector abundances (Shaman et al. 2005, Koenraadt and Harrington 2008). Unfortunately, the scale at which we generally measure droughts may not capture the scale of precipitation events that is important to mosquitoes.

Precipitation and ambient temperature very likely play an important role in controlling vector populations and pathogen transmission, but linking processes occurring at mosquito-relevant scales with dynamics at spatiotemporal scales important to pathogen or bird populations remains a critical roadblock to managing arbovirus outbreaks or forecasting changes in disease intensity. Human incidence of WNV infections peaked synchronously with avian population declines in 2003 across the eastern seaboard (figure 2) and in Colorado (LaDeau et al. 2007), although the most severe summer droughts this decade in both regions were recorded in 2002 (US Drought Monitor, www.drought.unl.edu/dm/monitor.html) and 2003 was relatively wet in the Northeast. Additionally, although 2005 and 2007 were relatively wet summers in Colorado, the lowest statewide human WNV incidence since the pathogen emerged occurred in 2005, and the second highest incidence rate was recorded in 2007.

In addition to climatic influences, observed patterns of WNV intensity are spatially heterogeneous within a region (Gibbs et al. 2006, Ruiz et al. 2006, Ezenwa et al. 2007). Early studies of WNV dynamics in the Eastern Hemisphere described a relationship between transmission activity and human populations or irrigated farmland (Hayes 2001). Likewise, estimated declines of American crow following WNV emergence in Chicago (Ward et al. 2006) and in the northeastern United States (figure 3) have also been located near high-density human population centers. Studies that evaluated human risk of WNV exposure within cities have suggested that living close to vegetation cover within a city may constitute an elevated infection risk (Ruiz et al. 2006). One hypothesis for these patterns is that WNV vectors breed in the shallow water pools and container environments in human-mediated landscapes, and that pathogen transmission flourishes when fragmentation forces vectors and hosts to share smaller patches of habitat. This pattern could also help explain the low WNV incidence in northern New England, where urbanization is generally lower than in the mid-Atlantic, although this relationship is certainly more complex than a linear relationship with urbanization. Given even this limited understanding of WNV dynamics, it is clear that the increased frequency of extreme weather events predicted by the Intergovernmental Panel on Climate Change (2007) and continued rates of urbanization will present critical challenges to managing epidemics of WNV in the future.

We still need to improve understanding of how climate, extreme weather events, and land use affect each of the three critical populations across both time and space (avian hosts, mosquito vectors, and pathogen). There is an ongoing need

to generate data to improve mechanistic models to forecast fine- and regional-scale growth in vector populations and guide targeted mosquito abatement programs.

Comparison with other North American arboviruses

The unique combination of host and vector communities, low host immunity, and the North American landscape (e.g., suburban and agricultural network) has supported WNV amplification in a way not evident in the Eastern Hemisphere (or in Central and South America). However, WNV is not the only arbovirus (or even flavivirus) circulating in the United States. In fact, St. Louis encephalitis (SLE, genus *Flavivirus*), western equine encephalitis (WEE, genus *Alphavirus*) and eastern equine encephalitis (EEE, genus *Alphavirus*) all depend on a mosquito-bird-mosquito transmission cycle similar to that of WNV. Only 220 EEE and 639 WEE human cases have been reported in 40 years, and 4669 cases of SLE were reported between 1964 and 2007, versus more than 27,000 cases of WNV since 1999 (CDC 2008). The CDC estimates that less than 1% of humans infected with SLE develop disease, whereas closer to 20% of WNV infections develop to illness. Birds rarely suffer mortality following SLE infection (Reisen et al. 2005), though some species may die following EEE infection (Komar et al. 1999).

A key difference among these arboviruses may be the size and diversity of vector and host communities involved in pathogen amplification and transmission. For example, whereas multiple mosquito vectors from habitats closely associated with human populations have been implicated in WNV transmission, the pathogen that causes EEE has just one primary vector (*Culiseta melanura*), which breeds in freshwater

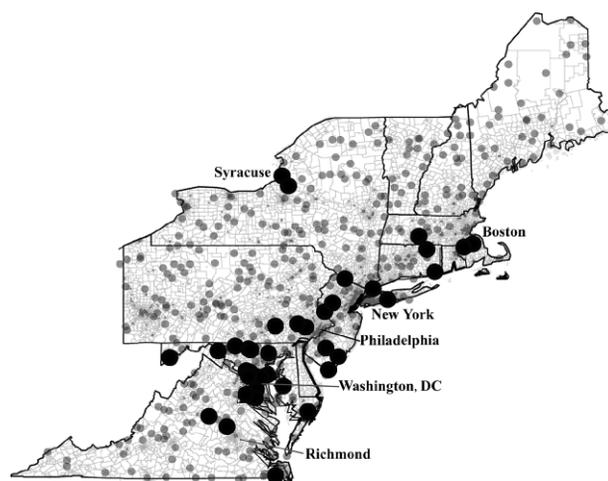


Figure 3. Breeding Bird Survey (BBS) routes (small, light circles) are plotted against a background of US Census Bureau tracts (US Census Bureau 2000), where denser lines identify high-density human centers. Large circles are BBS routes where American crow populations were significantly lower than expected in two or more years after West Nile virus emergence (observed abundance < 95% credible intervals).

swamps (CDC 2006). Differences in the ecology of SLE and WNV systems are less apparent, but differential amplification may be due to higher WNV host viremias (Reisen et al. 2005) or to coevolution of the SLE vector and host species in North America.

Research in this area could improve mechanistic understanding of the interactions among the epizootic and enzootic host and vector communities in WNV and SLE systems, and the importance of multiple vectors versus the identity of the vector (e.g., *Culex* species) in determining the intensity and frequency of arboviral outbreaks.

Host mortality

Although WNV dependence on a bird-mosquito transmission cycle has been recognized for decades, WNV-related mortality in avian populations was not considered an important indicator of viral activity until 1998, after dead domestic geese (*Anser* spp.) and migrating white storks (*Ciconia ciconia*) were diagnosed with WNV infection in Israel (Malkinson et al. 2002). Likewise, the most marked signal of West Nile amplification in North America is avian mortality.

The experimental infection studies introduced in the section "Avian hosts" documented considerable variation in survival (0% to 100%) among avian species (Komar et al. 2003). For example, all infected American crows died, blue jays and common grackle died in some trials, and all mourning doves (*Zenaidura macroura*) survived (Komar et al. 2003, Reisen et al. 2005). However, disease-related mortality rates in laboratory settings can be difficult to interpret because of factors such as the stress of captivity, free access to food and water, and the absence of predators. Furthermore, wildlife susceptibility to disease in nature is exacerbated by compounding stressors associated with habitat loss, human impacts, and weather events, making actual survival in the wild more stochastic than laboratory-based experimentation could predict. Still, the results from controlled challenge experiments provide a framework for comparing species-specific susceptibility with infection, and may reflect differential vulnerability to WNV in the wild.

Tens of thousands of dead birds found across North America test positive for WNV each year (CDC 2007b), representing a fraction of what must be striking mortality rates in the wild. Finding out whether these fatalities translate into population-level declines or signal parallel responses in other species (which may have been less likely to be observed by humans) has been an important focus of ecological research. Quantifying the effects of disease on host species requires careful consideration of the organism's historical population dynamics. Ideally, researchers would know background host population sizes and pathogen exposure rates, and would have validated WNV-related mortalities. These ideal data rarely exist for wildlife populations, although three studies of individually marked birds have documented WNV mortality directly in nature. A study by Caffrey and colleagues (2005) followed a group of individually marked American

crows in Oklahoma beginning in 1997. They estimated adult mortality rates between 1% and 3% annually before 2002, but then 33% of their birds died within months of WNV regional emergence in 2002, and a further 65% died in 2003 (Caffrey et al. 2005). A similar study found that 68% (19 individuals) of a group of individually marked American crows in Illinois succumbed to WNV-attributed deaths in 2003 (Yaremych et al. 2004). Finally, work by Naugle and colleagues (2005) demonstrated that WNV could have dire consequences for rare and endangered populations when they documented a 25% reduction in female survival of radio-marked greater sage-grouse (*Centrocercus urophasianus*). More than 600 bird species breed in North America during the active WNV season, and neither the detailed studies of marked birds presented above nor the laboratory challenge experiments are sufficient to predict disease impacts in this broader avian community.

The ability to estimate and interpret ecologically important impacts of WNV emergence requires preemergence population data for an unpredictable host at an unknown location. Although such information is not generally available, annual surveys can potentially be used to understand background dynamics of a wide array of potential host species over large spatial and temporal scales. During the past five decades, thousands of volunteers have contributed to the North American Breeding Bird Survey (BBS) and National Audubon Society's Christmas Bird Count (CBC) to create just such a record of avian population dynamics across the North American continent. Citizen-science projects like these generate rich data sets that have been underappreciated in quantitative research because the data present nontrivial analytical challenges. For example, population dynamics are inherently stochastic and may involve background trends and cycles that can render the isolation of signal from noise difficult. Furthermore, these surveys involve multiple sources and scales of variability, legions of observers of varied skill levels, and sporadic missing observations. Still, the emergence of WNV and its obvious impact on common bird species has led to wider recognition that these data sources are invaluable for evaluating population-level responses in a broad taxonomic array of species across large spatial scales.

Two early studies used the CBC data to evaluate WNV-related declines in wintering populations of northeastern US avifauna (Bonter and Hochachka 2003, Caffrey and Peterson 2003). Although the two analyses differed in how they defined population declines and in the spatial extent of data used, both showed declining American crow populations after WNV emergence. The study by Bonter and Hochachka (2003) also found unusual declines in black-capped and Carolina chickadee (*Poecile* spp.) and tufted titmouse (*Baeolophus bicolor*) populations, but not in blue jay, northern cardinal (*Cardinalis cardinalis*), or house sparrow populations. Although both studies (Bonter and Hochachka 2003, Caffrey and Peterson 2003) stated that some species had recovered from unexplained declines of similar magnitude in the past, Bonter and Hochachka (2003) noted that unlike the WNV-

related declines, earlier crashes were rarely synchronous across species or sites. A third study, by Hochachka and colleagues (2004), also used the CBC data to examine patterns of declines in American crow populations located specifically in and around New York City. The authors estimated that 90% of the local crow population in the Queens borough died in the first four years after WNV arrival (Hochachka et al. 2004). Similarly, breeding populations of American crow in Illinois suffered an estimated 18.3% decline between 2001 and 2005, though the population had been increasing by 1.6% annually during the preceding 25 years (Ward et al. 2006). Although they highlighted some localized declines of northern cardinal populations within Chicago, the study by Ward and colleagues (2006) generally agrees with earlier findings (Bonter and Hochachka 2003) that northern cardinal populations were not sensitive to WNV outbreaks (epizootics). Comparisons or syntheses of these studies that rely on citizen-science data sets are frustrated by inconsistencies in how analysts define and identify WNV-related declines. For example, the analysis by Caffrey and Peterson (2003) evaluated mean abundances over time across all CBC routes within the region, whereas the study by Bonter and Hochachka (2003) combined CBC and an intra-annual survey (Project FeederWatch) to identify the between-year changes in species abundance that exceeded within-year variation. The approach used by Caffrey and Peterson (2003) may be the most intuitive, but the stochasticity inherent in population data over time can easily obscure even important disturbances.

A study by LaDeau and colleagues (2007) used BBS data and Bayesian hierarchical models to draw on historical levels of site-specific stochasticity in bird abundances quantified before WNV emergence in order to identify deviations from established population trajectories. Specifically, they removed data for years after WNV emerged locally and used a hierarchical statistical model to propagate regional trends, observation error, site-specific effects, process error, and interannual stochasticity forward in time at each BBS route to quantify expected population abundances (as if WNV had never arrived). Because assessing WNV impacts was the focus of this study, the researchers chose to use BBS data instead of CBC data to reflect the importance of measuring impacts during the active viral season and because observer effort and site fidelity are more tractable in the BBS design. Like the earlier work by Caffrey and Peterson (2003), this study defined WNV impacts intuitively as declines in population abundances following WNV emergence. However, the analysis by LaDeau and colleagues (2007), which included additional years of data and comprehensive treatment of multiple types of stochasticity, revealed profound WNV-related declines across several avian species. Population abundances of American crow, American robin, eastern bluebird (*Sialia sialis*), and tufted titmouse all suffered significant declines after WNV emergence (figure 4), as did black-capped and Carolina chickadee species combined (LaDeau et al. 2007). Blue jay and house wren (*Troglodytes aedon*) populations along the East Coast remained stable until 2003, when they too declined syn-

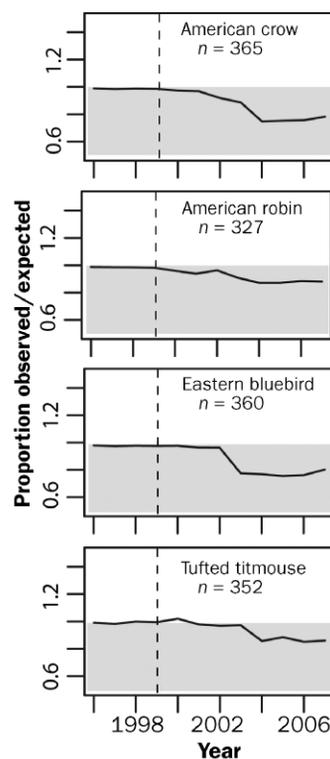


Figure 4. Deviations in observed abundances from model expectations for species with detectable West Nile virus–related declines in the eastern United States. Modeled abundances account for historical levels of stochasticity at each Breeding Bird Survey (BBS) route (n = number of routes used) before pathogen emergence and represent expected population sizes if West Nile virus exposure had not occurred. The number of BBS routes per species was determined by species range and distribution. The shaded area in the lower half of plots denotes years with lower than expected abundances.

chronously with peaks in human infections and severe declines in other impacted species. House wren and blue jay populations recovered to pre-WNV population trajectories by 2005 (LaDeau et al. 2007), although other species remained significantly reduced even through 2007 (figure 4).

We have yet to identify life history or taxon characteristics that separate the WNV-susceptible species from those species that have either survived experimental infection or have no detectable impacts in the wild. Although corvids (e.g., crows, jays) seem to be more vulnerable to WNV exposure than Passeriformes in general (Komar et al. 2003), the population consequences among corvid species are still highly variable. American crows declined dramatically after WNV emergence in each of the studies detailed above, though fish crow and blue jay populations appear more resilient (Bonter and Hochachka 2003, LaDeau et al. 2007, Wilcox et al. 2007). The majority of the birds that have declined in the wild (LaDeau et al. 2007) are species that prosper in human-

mediated landscapes. Many are also species that have been increasing during past decades, and thus changes in their growth rates may be easier to detect than in those species that were already declining (e.g., wood thrush).

It is likely that WNV emergence has already affected a much broader range of birds than those species that have been examined in laboratory studies or survey analyses. Unfortunately, general bird surveys used to evaluate many avian populations are not designed to estimate population abundances for raptors, water birds, or nocturnal species. For example, the consequences of WNV emergence for raptors are only beginning to be appreciated. Saito and colleagues (2007) reported that wildlife workers found evidence of WNV infection in 71% of the raptor carcasses collected from 12 US states since 2002. Red-tailed hawks (*Buteo jamaicensis*) and great horned owls (*Bubo virginianus*) have consistently been among the most reported birds of prey, though at least nine raptor species have been shown to harbor WNV infection, including the bald eagle (*Haliaeetus leucocephalus*) (Saito et al. 2007).

It is important to note that no studies have yet linked reduced avian host populations to dampening of WNV amplification. Changes in the avian host populations may affect local pathogen amplification in some areas, but the pathogen's diverse host pool ensures that anything less than catastrophic mortality across avian communities is unlikely to debilitate pathogen persistence. On the other hand, species that survive WNV infection are generally believed to have some acquired immunity (Fang and Reisen 2006), which could dampen the intensity of disease outbreaks over time, though the actual duration of immunity in the wild is not fully known.

Birds are not the only species that are susceptible to WNV infection. More than 20,000 cases of WNV infection in horses have been documented across North America (CDC 2008), although widespread vaccination began in 2002. More than 27,000 human WNV cases and more than 1000 human fatalities have been reported across the United States since 1999 (CDC 2008), and almost 5000 human cases were reported in Canada between 2002 and 2008 (Public Health Agency of Canada; www.phac-aspc.gc.ca/wnv-vwn/mon-hmnsurv-archive-eng.php). The CDC also reports WNV infection (though not necessarily disease) in blood samples from dogs, squirrels, bats, chipmunks, skunks, farmed alligators, and domestic rabbits.

In this area, we need to assess the role of interannual variability in WNV intensity in regulating avian populations and examine how life history characteristics (e.g., reproductive potential, juvenile development) influence host susceptibility to pathogen exposure. There is also a need to consider how interactions between WNV exposure and other stressors (e.g., storms, habitat loss) affect long-term viability of bird populations and avian communities.

Indirect consequences of WNV emergence

If there are indirect consequences of WNV emergence for North American ecosystems, they will be driven predominantly by changes in avian composition, and they are likely to vary by region and habitat type. The analyses by LaDeau

and colleagues (2007) identified dramatic declines in populations, which were on average 30% lower than expected for several common mainland species (figure 4). To date, we can only speculate as to how much these populations can decline before local or regional population recovery is unlikely, though established declines alone are likely to have important consequences for ecosystem function. Avian-mediated ecosystem services that may be affected by WNV emergence include seed dispersal, nest predation, scavenging efficiency, and regulation of insects, as well as changes in recreational birding opportunities. If WNV does reach Hawaii or other islands with endemic populations, the impacts of disease-related mortality could be devastating. The impacts over time could be severe even for mainland populations.

Pathogens that utilize multiple hosts ("generalists") can be persistent in space and time, as they are not limited by the abundance or mortality rate of any one host population (e.g., Daszak et al. 2000, Norris 2007). There are numerous examples of how changes in the abundance (or presence) of even one species can have important effects on ecosystem function. Changes in forest composition following the unexpected extinction of the passenger pigeon (*Ectopistes migratorius*) in the 19th century demonstrated how important some individual species are to ecosystem structure and function (Ellsworth and McComb 2003). Studies evaluating the impact of pathogens and insect pests on the function of North American forests demonstrate intimate connections between pathogen (or pest) effects on tree species, vertebrate food webs, and nutrient cycling (Lovett et al. 2006). Many bird species may play important roles in regulating insect pests. Finally, work in northeastern forests has consistently shown that tree seed production and trophic interactions with seed predators can influence the intensity and spread of zoonotic infections (e.g., Ostfeld et al. 2006).

Conclusions

People living in the contiguous United States have not had to face more than periodic emergences of arboviruses (e.g., SLE, EEE, WEE) and have encountered relatively few human infections in recent decades. Now, thousands of human WNV cases are reported annually, representing what is likely to be just a small fraction of the true incidence rate (Petersen and Hayes 2004). Pathogens such as WNV do not operate in a vacuum; even as WNV infection depletes avian populations, habitat loss, changing climate, and eventually new diseases also threaten population viability and challenge ecological communities. Continued globalization (e.g., intercontinental trade and movement of people and goods), human population growth, and ongoing climate change all ensure that each of these population stressors will only intensify, and we will very likely find even greater disease emergence in human and animal populations over the next century. We can learn a great deal from WNV emergence and its consequences for North American ecology that may help us to be better prepared for future threats. In this article we have reviewed a number of studies that provide valuable informa-

tion about how WNV interacts with vectors and avian hosts, but there is still much to be learned about the spatiotemporal drivers of heterogeneity in disease intensity (figures 1, 3), WNV impacts on host communities (figures 2, 4), and the longer-term indirect consequences for ecosystem structure and function. Improved understanding of the spatiotemporal dynamics of pathogen amplification or disease dampening processes will require integration across scales that are important to mosquito populations and avian communities, and those at which human observations are generally made. Such insights will be critical for managing conservation and public health risk, as well as for forecasting the ecological impacts of changing climate regimes and the next emergent zoonotic disease.

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