
Eastern Equine Encephalitis Virus — Old Enemy, New Threat

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Last summer, Vermont documented its first human cases of eastern equine encephalitis (EEE), a mosquito-borne disease that is endemic in the eastern United States. Since the discovery of the EEE virus in the 1930s, cases in humans had been sporadic and restricted to areas south of northern New England until a disease outbreak struck New Hampshire in 2005.¹ Over the past decade, we have witnessed a sustained resurgence of EEE virus activity within long-standing foci in the northeastern United States and northward expansion into regions where the virus was historically rare or previously unknown, including northern New England and eastern Canada.

Although the specific factors responsible for the reemergence of EEE virus are unknown, vector-borne diseases are ecologi-

cally complex and exquisitely sensitive to environmental changes. For example, Lyme disease arose, in part, because of landscape changes that increased the habitat and wild-animal hosts of vector ticks. West Nile virus is highly sensitive to heat waves and drought that promote the breeding of mosquitoes in standing water in urban storm drains and accelerate virus amplification. Similarly, EEE virus transmission is highly seasonal and dependent on weather conditions, occurring within specific forested swamp habitats where the main mosquito vector (*Culiseta melanura*) resides.

The EEE virus causes severe disease in horses and humans, resulting in high mortality as well as neurologic impairment in survivors. Although cases in humans are relatively rare, as compared with those of other vector-borne diseases, an estimated

case-fatality rate of 35 to 75% makes the EEE virus the most deadly mosquito-borne pathogen in North America.^{2,3} Half of survivors suffer permanent neurologic sequelae and require long-term care, which is estimated to cost as much as \$3 million per patient over the rest of their lifetime.⁴ Currently, there is no vaccine or effective treatment available for infection in humans, although veterinary vaccines exist for horses. To curtail infections in humans in affected states, public health authorities routinely implement prevention and control measures that include enhanced mosquito surveillance, public education and outreach that emphasize personal protection measures, and insecticide spraying designed to limit rates of infection when epidemic conditions arise. The costs for implementing aerial applica-

tion of chemical insecticides in affected regions impose a considerable financial burden on already-stretched public health budgets. Moreover, these measures are often met with resistance and controversy by a public that is increasingly apprehensive, justifiably or not, about the possible effects of insecticides on human health and the environment.

The EEE virus was first discovered in 1933 during a large-scale equine epizootic in the mid-Atlantic region of the United States. Fatal encephalitis in humans soon followed during a 1938 outbreak of EEE in southeastern Massachusetts involving 34 cases in humans and 25 deaths. More than 20 years later, another epidemic struck in New Jersey in 1959, resulting in 32 cases in humans, with a similar fatality rate. Since then, a series of more limited outbreaks have recurred in southern New Jersey and Massachusetts, with additional cases in humans in central New York and Rhode Island and, more recently, in New Hampshire and Vermont. In addition, cases have occurred in horses in these and other northeastern states, including Connecticut and more recently Maine, and in southeastern Canada. The figure shows that EEE infections in humans have become more frequent and have extended northward in New England over the past 10 years.

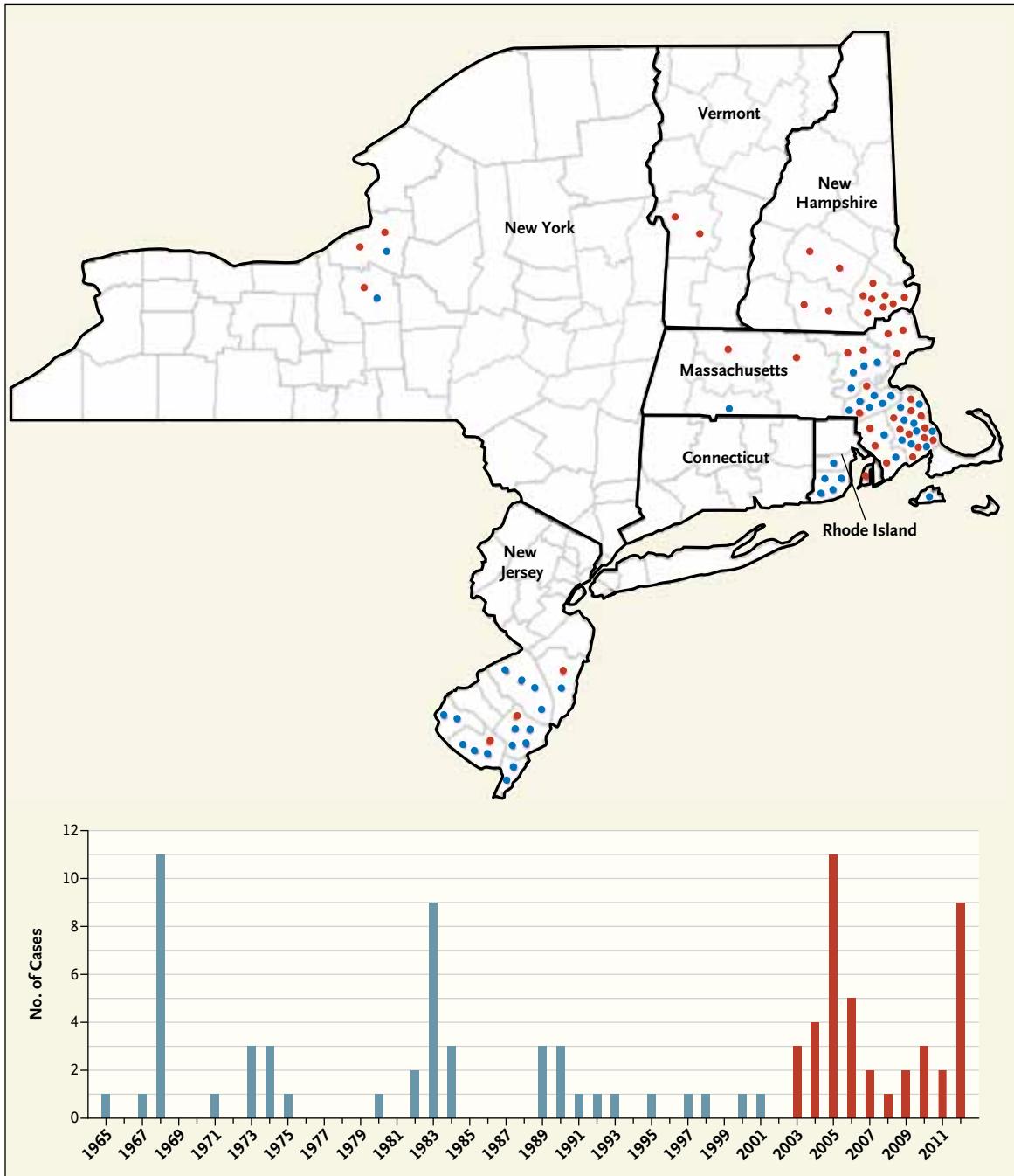
EEE outbreaks occur intermittently when environmental conditions favor virus amplification followed by virus overflow into human and horse populations. The EEE virus is amplified in a bird-mosquito transmission cycle involving primarily *C. melanura*

mosquitoes and song birds inhabiting freshwater swamp foci.³ *C. melanura* is a particularly efficient enzootic vector because it feeds mainly on avian hosts. This mosquito also occasionally feeds on mammals; however, other mosquito species, such as *Coquillettidia perturbans*, that feed more opportunistically on both avian and mammalian hosts have been implicated as bridge vectors from viremic birds to humans.

Active transmission of the EEE virus is highly seasonal in temperate regions, occurring from summer to early fall and then terminating each winter when mosquito feeding ceases. The mechanisms responsible for the seasonal reemergence of the EEE virus in sites where it is endemic are not well understood. Virus transmission may be reinitiated each season by locally overwintering virus through an unknown mechanism (perhaps persistence in resident hosts or mosquito vectors). New strains of the EEE virus may also be reintroduced annually by migrating birds into northeastern United States from more southerly regions, such as Florida, where transmission is continuous throughout the year. Phylogenetic analyses indicate that genetically identical virus strains may persist in the northeastern United States but disappear after 1 to 5 years.⁵ Northeastern populations of the EEE virus also share recent common ancestry with strains circulating in the southeastern United States, which suggests that long-range viral dispersal occasionally occurs among these locations. These findings may help explain the periodicity of EEE virus epidemics in northern regions that tend to cluster

over 2 or more consecutive years, separated by periods of dormancy.

The factors responsible for re-emergence of EEE are certainly complex and probably reflect ongoing changes in the ecology and epidemiology of this virus. Long-term changes in land use, including wetlands restoration and suburban development, and increases in human population density near critical habitats may be important components. However, weather conditions, in particular, are known to have more immediate effects on mosquito abundance and levels of virus activity. Historical risk factors have included above-average rainfall, mild winters, and greater amount of EEE virus activity during the previous year. In the context of climate change, records show a trend toward milder winters and hotter summers, marked by extremes in both precipitation and drought in the northeastern United States. Rainfall and accumulated ground water increase the abundance of *C. melanura* mosquitoes by creating aquatic habitats in freshwater swamps that are favorable for larval development. Milder winters, in turn, may enhance the overwintering survival of mosquito vectors and allow mosquitoes to extend their range northward. Warmer summer conditions accelerate the generation time of mosquitoes, their frequency of blood feeding, and the rate of virus replication within mosquitoes. These environmental changes have the potential to alter disease risk by increasing the abundance and distribution of the vector, lengthening the virus-transmission season, and increasing the intensity of virus transmission.



Eastern Equine Encephalitis Cases in Humans in Part of the Northeastern United States, 1965–2012.

The map shows the annual distribution of cases of eastern equine encephalitis in humans according to county. The histogram indicates the annual number of cases in humans. Red represents cases in humans occurring during the previous 10 years.

Climate change has been predicted to have a number of effects on vector-borne diseases, including the northward expansion

of mosquito vectors and their pathogens as temperatures become warmer. This prediction has raised concerns about the

possible expansion of tropical diseases such as dengue and malaria into the United States; however, we should not lose sight of

already-established vector-borne diseases that occur in temperate zones and may more readily exploit regional climate changes. We are now seeing recurrent EEE cases each year and their expansion into northern New England for the first time, a phenomenon that requires further scrutiny. In the meantime, comprehensive surveillance programs complemented by science-based mosquito control and timely public outreach provide the best hedge against

this and other vector-borne disease threats.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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