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Commentary

Resurgence of West Nile neurologic disease in the United States in 2012: What happened? What needs to be done?

David W.C. Beasley *, Alan D.T. Barrett, Robert B. Tesh

Departments of Microbiology and Immunology, and Pathology, Sealy Center for Vaccine Development, Institute for Human Infections and Immunity, The University of Texas Medical Branch, 301 University Blvd., Galveston, TX 77555-0609, USA

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ABSTRACT

The resurgence in cases of neurologic disease caused by West Nile virus (WNV) in the United States in 2012 came as a surprise to the general public and to many non-arbovirus researchers. Following the introduction of WNV into the US in 1999, the number of human infections rose dramatically, peaking in 2002–03. However, cases declined from 2008–11, and it was unclear if the virus would continue to have a low-level endemic transmission pattern with occasional outbreaks, like the related flavivirus, Saint Louis encephalitis virus, or a more active pattern with annual outbreaks, including occasional years with large epidemics, like Japanese encephalitis virus. The large epidemic in 2012 suggests that the United States can expect periodic outbreaks of West Nile fever and neurologic disease in the coming years. In this paper, we consider the causes of the upsurge in WNV infections during the past year and their implications for future research and disease control measures.

Following the introduction of West Nile virus (WNV) into the United States in 1999, the number of human cases of WN fever and neurologic disease rose dramatically, peaking in 2002–3. However, cases declined from 2008–11, and it was unclear if the virus would continue to have a low-level endemic transmission pattern with occasional outbreaks, like the related flavivirus, Saint Louis encephalitis virus (SLEV), or a more active pattern with annual outbreaks, including occasional years with large epidemics, like Japanese encephalitis virus (JEV). The resurgence in cases of WNV neurologic disease in 2012 therefore came as a surprise to the American public and to many non-arbovirus researchers. The size of the 2012 outbreak suggests that the US can expect periodic epidemics of WN fever and neurologic disease in the coming years. In this paper, we consider the causes of the upsurge in WNV infections during the past year and their implications for future research and disease control measures.

1. Background: West Nile virus

WNV is a mosquito-borne RNA virus in the genus *Flavivirus*, family *Flaviviridae*, that is maintained in nature in a basic transmission cycle involving wild birds and *Culex spp.* mosquitoes. For many years following its first isolation in Uganda in 1937, WNV was considered a relatively unimportant member of the flavivirus family. It was known to exist in Africa, southern Europe, the Middle East and Central Asia, where it caused sporadic cases of febrile disease and occasional outbreaks of encephalitis in elderly people and in equines. In 1999, WNV was detected in New York City and surrounding areas, where it caused a large die-off in crows, exotic zoo birds and other bird populations and an outbreak of encephalitis in elderly humans. During the next few years, the virus spread rapidly north, west and south across North America, with the largest epidemics occurring in 2002 and 2003 (Figs. 1 and 2).

WNV has a wide global distribution, and molecular phylogenetic studies have identified multiple lineages or genotypes (Fig. 3). Strains associated with outbreaks of neurological disease in the US clustered together as a subgroup of genotype/lineage 1, suggesting that this subgroup had evolved a more virulent phenotype (Lanciotti et al., 1999). However, later studies in mice demonstrated that strains from lineage 2, the other major genotype, were also capable of causing neuroinvasive disease (Beasley et al., 2002). In the past few years, epidemics in Europe and individual cases of disease in humans and horses in South Africa have been associated with strains from both lineages (Papa et al., 2010; Venter and Swanepoel, 2010), verifying the earlier experimental observations in mice.

WNV is found in all regions of the continental US as well as in southern Canada, Mexico, the Caribbean, and parts of Central and South America. Molecular phylogenetic studies suggest that all isolates are derived from the virus originally introduced into New York City (e.g. May et al., 2011; Osorio et al., 2012; Pesko and Ebel, 2012). The exact manner in which WNV was first introduced is

* Corresponding author.
E-mail addresses: dwbeasle@utmb.edu (D.W.C. Beasley), abarrett@utmb.edu (A.D.T. Barrett), rtesh@utmb.edu (R.B. Tesh).

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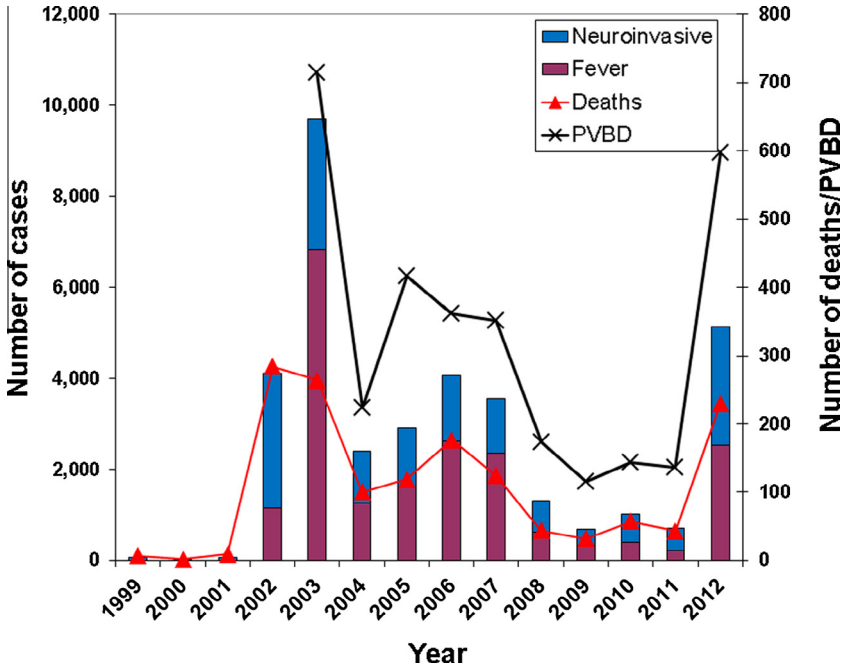

Fig. 1. Numbers of West Nile fever and neuroinvasive disease cases, deaths and presumptive viremic blood donors (PVBD) reported to the US. Centers for Disease Control and Prevention during each year since the introduction of WNV into the US in 1999. (Data from <http://www.cdc.gov/westnile>.)

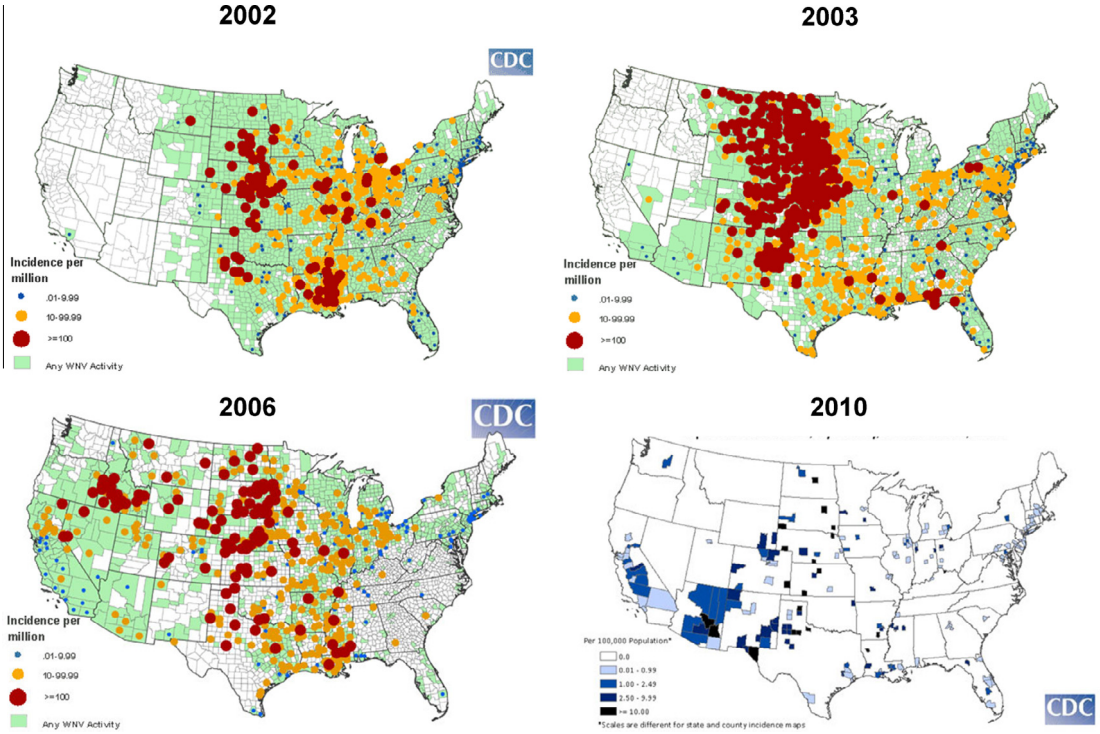

Fig. 2. The varying incidence of West Nile neuroinvasive disease cases by county reported to CDC in selected years, since the peak outbreak years of 2002–03. Note the emergence of individual foci of intense transmission in individual years, such as in Louisiana in 2002, Idaho in 2006 and Arizona in 2010.

unknown, but the most likely scenarios are through the migration or smuggling of an infected bird, or by an infected mosquito "hitching a ride" in an airplane or container cargo coming from the Mediterranean region or North Africa. Regardless, WNV is now firmly established (endemic) in the US. Virus activity is seen mainly during summer, but it may vary, depending on latitude and seasonal temperatures. The largest annual numbers of human neuroinvasive disease cases and deaths were reported in 2002, with 2946 neuroinvasive cases and 284 deaths, with similar numbers in 2003 (Fig. 1). From 2004–7, cases of neuroinvasive disease and deaths declined to about half of the 2002–3 peak years, then declined further during 2008–11, reaching a nadir of 373 neuroinvasive cases