



Published in final edited form as:

Pediatrics. 2014 September ; 134(3): e642–e650. doi:10.1542/peds.2014-0498.

Neuroinvasive Arboviral Disease in the United States: 2003 to 2012

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Abstract

OBJECTIVE—To describe the epidemiologic and clinical syndromes associated with pediatric neuroinvasive arboviral infections among children in the United States from 2003 through 2012.

METHODS—We reviewed data reported by state health departments to ArboNET, the national arboviral surveillance system, for 2003 through 2012. Children (<18 years) with neuroinvasive arboviral infections (eg, meningitis, encephalitis, or acute flaccid paralysis) were included. Demographic, clinical syndrome, outcome, geographic, and temporal data were analyzed for all cases.

RESULTS—During the study period, 1217 cases and 22 deaths due to pediatric neuroinvasive arboviral infection were reported from the 48 contiguous states. La Crosse virus (665 cases; 55%) and West Nile virus (505 cases; 41%) were the most common etiologies identified. Although less common, Eastern equine encephalitis virus (30 cases; 2%) resulted in 10 pediatric deaths. La Crosse virus primarily affected younger children, whereas West Nile virus was more common in older children and adolescents. West Nile virus disease cases occurred throughout the country, whereas La Crosse and the other arboviruses were more focally distributed.

CONCLUSIONS—Neuroinvasive arboviral infections were an important cause of pediatric disease from 2003 through 2012. Differences in the epidemiology and clinical disease result from complex interactions among virus, vector, host, and the environment. Decreasing the morbidity and mortality from these agents depends on vector control, personal protection to reduce mosquito and tick bites, and blood donor screening. Effective surveillance is critical to inform clinicians and

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Dr Gaensbauer participated in conceptualization of the study, data analysis, and drafted the initial manuscript; Ms Lindsey and Drs Messacar and Staples contributed to conceptualization of the study, data analysis, and reviewed and revised the manuscript; Dr Fischer conceptualized and designed the study and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

public health officials about the epidemiologic features of these diseases and to direct prevention efforts.

Keywords

arboviruses; epidemiology; child; United States

Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes or ticks. Most human arboviral infections are asymptomatic. Symptomatic infections most often manifest as a systemic febrile illness and, less commonly, as neuroinvasive disease (meningitis, encephalitis, or acute flaccid paralysis). Because of the considerable morbidity associated with neuroinvasive disease, case detection and reporting is assumed to be more consistent and complete than for nonneuroinvasive disease.¹

West Nile virus is the leading cause of arboviral disease in the United States.² However, La Crosse virus infections occur primarily among children and several other arboviruses (eg, Eastern equine encephalitis, St Louis encephalitis, and Powassan viruses) cause sporadic cases and seasonal outbreaks.^{2,3} Domestic neurotropic arboviruses belong to 3 virus families (ie, Bunyaviridae, Flaviviridae, and Togaviridae). Different vectors, animal hosts, and tissue tropisms contribute to variations in geographic distribution, disease incidence, clinical manifestations, and outcomes. Understanding the epidemiology and burden of arboviral disease is essential to directing diagnostic testing and improving public health control efforts. We describe the epidemiology of neuroinvasive arboviral infections among children in the United States from 2003 through 2012.

METHODS

Case Definitions and Reporting

We defined a case as a child (<18 years of age) with domestically acquired neuroinvasive arboviral disease in the United States from 2003 through 2012. Cases were identified from reports to ArboNET, the national arboviral surveillance system. Human disease due to Eastern equine encephalitis virus, La Crosse and other California serogroup viruses, Powassan virus, St Louis encephalitis virus, Western equine encephalitis virus, and West Nile virus are nationally notifiable conditions.⁴ State health departments report arboviral disease cases to US Centers for Disease Control and Prevention (CDC) through ArboNET by using standard surveillance case definitions that include clinical and laboratory criteria.⁴ Laboratory confirmation may be performed by viral culture, nucleic acid amplification, immunohistochemical staining, or serology, but the specific tests used to confirm each case are not reported to ArboNET. All confirmed and probable cases were included.

Data routinely collected in ArboNET include patient age, gender, county and state of residence, date of illness onset, case status (ie, confirmed, probable, suspect, or not a case), clinical syndrome (eg, meningitis, encephalitis, acute flaccid paralysis, uncomplicated fever), and outcome (hospitalization or fatality). Cases reported as meningitis, encephalitis, or acute flaccid paralysis were classified as neuroinvasive disease; others were considered

nonneuroinvasive disease. Cases reported as meningoencephalitis were classified as encephalitis; cases reported as acute flaccid paralysis (with or without another clinical syndrome) were classified as acute flaccid paralysis only and not included in the other clinical syndrome categories. Information regarding hospitalization and acute flaccid paralysis was collected starting in 2004. A previous publication describing the epidemiology of neuroinvasive arboviral disease in the United States from 1999 to 2007 included 4 years of data presented here but did not focus on pediatric disease.³

Data Analysis

We described the number of reported cases and calculated national incidence per 1 000 000 children by using US Census Bureau annual population estimates.^{5–7} County-level incidences were calculated by using 2010 census data.⁸ Categorical variables were summarized using counts and proportions; continuous variables were summarized by using median and range. Statistical analyses were performed using Stata version 11.2 (Stata Corp, College Station, TX). Maps were generated by using ArcGIS version 10.1 (ESRI, Redlands, CA).

RESULTS

From 2003 through 2012, a total of 14 163 cases of domestically acquired neuroinvasive arboviral disease were reported to ArboNET, including 12 897 (91%) in adults, 1217 (9%) in children, and 49 (<1%) with unknown age (Table 1). Among adults, 12 554 (97%) of the cases were caused by West Nile virus. In contrast, only 505 (41%) of the pediatric cases were caused by West Nile virus and 665 (55%) were caused by La Crosse virus. The remaining pediatric neuroinvasive disease cases were caused by Eastern equine encephalitis virus (30 cases; 2%), Powassan virus (8; 1%), St Louis encephalitis virus (4; <1%), and unspecified California serogroup viruses (5; <1%). There were no reported cases of pediatric neuroinvasive disease caused by Jamestown Canyon or Western equine encephalitis viruses.

West Nile Virus

From 2003 through 2012, a total of 13 108 West Nile virus neuroinvasive disease cases were reported to ArboNET (Table 1). Of these, 505 (4%) occurred in children with a median of 49 cases per year (range 7–137). The average annual incidence was 0.68 cases per million children (range 0.09–1.85); almost eightfold lower than the rate in adults. Incidence was highest in 2003 and 2012 and lowest from 2008 through 2011 (Fig 1).

Pediatric West Nile virus neuroinvasive disease cases were reported from 299 counties in 41 states (Fig 2A). States with the highest annual incidence were in the North Central and Mountain regions, including South Dakota (10.36 per million children), Wyoming (5.91), North Dakota (5.34), and Nebraska (5.23). Seven states reported more than half of all cases: Texas (77 cases), California (49), Louisiana (34), Colorado (32), Arizona (29), Nebraska (24), and South Dakota (21). In the 2012 resurgence of West Nile virus, most cases occurred in the south, with 27 (33%) of the 83 reported cases of pediatric neuroinvasive disease occurring in Texas.

Of the 505 pediatric West Nile virus disease cases reported from 2003 through 2012, 306 (61%) were boys (Table 2). The median age of patients was 12 years (range: 1 month–17 years) and 173 (34%) were 15 to 17 years of age (Fig 3). Cases peaked in August, with 444 (88%) having illness onset during July through September (Fig 4). Half of the cases ($n = 295$) were classified as meningitis, 236 (47%) as encephalitis, and 14 (3%) as acute flaccid paralysis; 7 (50%) of the patients with acute flaccid paralysis also had meningitis or encephalitis (Table 2). Three patients (1%) died. Of the 356 cases with available data, 312 (88%) were hospitalized.

La Crosse Virus

Over the 10-year period, 754 La Crosse virus neuroinvasive disease cases were reported to the CDC (Table 1). Most (665 cases, 88%) occurred in children <18 years of age with a median of 59 pediatric cases per year (range 39–102). The average annual incidence was 22 times higher in children than adults, with a rate of 0.90 cases per million children per year (range 0.53–1.51). The incidence was highest in 2003, 2004, and 2011, and lowest from 2007 through 2009 (Fig 1).

La Crosse virus neuroinvasive disease cases were reported from 204 counties in 21 states (Fig 2B). States with the highest average annual incidence rates were in the Appalachian and Midwestern regions, including West Virginia (37.69 per million children), Tennessee (6.28), North Carolina (6.22), and Ohio (5.86). Those 4 states reported 81% of all cases: Ohio (160 cases), West Virginia (146), North Carolina (142), and Tennessee (94). Furthermore, 372 (56%) of the 665 cases reported nationally occurred in residents of just 29 (9%) of the 336 counties in these 4 states (10 counties in central Ohio, 8 in southern West Virginia, 7 in western North Carolina, and 4 in eastern Tennessee); the median average annual incidence in these 28 counties was 91.65 cases per million children (range 2.16–309.07).

Of the 665 pediatric La Crosse virus disease cases, 412 (62%) were boys (Table 2). The median age of patients was 7 years (range 1 month–17 years) and 309 (46%) were 5 to 9 years of age (Fig 3). Although most cases (544; 82%) had illness onset during July through September, 56 (8%) occurred in June and 54 (8%) had onset in October (Fig 4). Most cases (521; 78%) were classified as encephalitis; 134 (20%) were classified as meningitis and 10 (2%) as acute flaccid paralysis (Table 2). All of the patients with reported acute flaccid paralysis also had meningitis or encephalitis. Nine patients (1%) died. Of the 562 cases with available data, 543 (97%) were hospitalized.

Eastern Equine Encephalitis Virus

Of 89 cases of neuroinvasive disease caused by Eastern equine encephalitis virus from 2003 through 2012, 30 (34%) occurred in children, with a median of 2 cases per year (range 1–7) (Table 1). The average annual incidence of 0.04 cases per million children (range 0.01–0.09) was similar to that in adults (0.03). The number of cases reported was highest in 2003 and 2005 and lowest from 2006 through 2011 (Fig 1).

Cases were reported from 25 counties in 11 states along the Atlantic and Gulf Coasts (Fig 2C). States with the highest average annual incidence rates were New Hampshire (0.70 per million children), Massachusetts (0.49), Alabama (0.26), Louisiana (0.18), and Florida

(0.18). Seven states accounted for 87% of the reported cases: Florida (7 cases), Massachusetts (7), Alabama (3), North Carolina (3), New Hampshire (2), Louisiana (2), and Georgia (2).

Of the 30 pediatric cases, half were boys (Table 2). The median age of patients was 5 years (range 3 months–16 years); 15 (50%) were <4 years of age and 6 (20%) were infants <1 year of age. Most of the cases (27; 90%) occurred from July through September and were classified as encephalitis. The case-fatality was 33% (10 deaths). Of the 22 patients with available data, 21 (95%) were admitted to the hospital.

Powassan Virus

During the 10 years from 2003 through 2012, 45 cases of Powassan virus neuroinvasive disease were reported to ArboNET; of these, 8 (17%) cases were in children <18 years of age (Table 1). A median of 1 pediatric case was reported per year from 2003 through 2012 (range 0–2). The annual incidence of 0.01 cases per million children (range 0.00–0.03) compared with 0.02 per million adults. All of the cases were reported between 2007 and 2011.

Cases were reported from 8 counties in 3 states: Minnesota (3 cases; 0.23 per million children), New York (3 cases; 0.07 per million children), and Wisconsin (2 cases; 0.15 per million children) (Fig 2D). Six (75%) of the pediatric case-patients were boys and their median age was 6 years (range 3 months–14 years) (Table 2). Five (63%) cases had onset during the spring, whereas 2 (38%) occurred during summer. Six (75%) were classified as encephalitis; 7 (88%) were hospitalized and there were no deaths.

St Louis Encephalitis Virus

Although 109 cases of neuroinvasive disease caused by St Louis encephalitis virus were reported from 2003 through 2012, only 4 (4%) cases occurred in children, with 2 cases in 2007 and 2 cases in 2009 (Table 1). Cases were reported from 4 counties in 3 states (Arkansas, Louisiana, and Texas). All 4 cases were classified as encephalitis; all were hospitalized but there were no deaths.

DISCUSSION

Neurotropic arboviruses have been a significant cause of pediatric disease over the past 10 years in the United States, with more than 1200 cases of central nervous system infection and 22 resulting deaths reported. La Crosse and West Nile viruses were the most important etiologies of pediatric neuroinvasive arboviral disease during this period, with incidence rates of 0.90 and 0.68 cases per million, respectively. Although the number of cases was low, Eastern equine encephalitis virus had the highest case-fatality rate, consistent with previous reports.^{3,9,10} These differences in epidemiology and clinical disease result from complex interactions among virus, vector, host, and the environment.^{3,11,12}

It is difficult to compare the incidence rates for neuroinvasive arboviral disease with that of herpes simplex virus or enterovirus, as the latter are not nationally notifiable conditions. For herpes simplex virus, researchers estimate there are 750 encephalitis cases among neonates

and another 400 cases in older children each year in the United States.^{13–15} Other researchers have speculated there are at least 75 000 cases of enteroviral meningitis annually in the United States among all age groups but there are limited empirical data and the incidence in children is not known.^{16,17}

Our results confirm that La Crosse virus neuroinvasive infection is predominantly a pediatric disease. Almost 90% of reported cases occur in children, particularly those younger than 10 years of age.³ In contrast, <4% of reported West Nile virus neuroinvasive disease cases occurred in children, and we observed a higher rate in adolescents than in younger children. Previous reports also have shown that West Nile virus disease incidence and severity were highest among older adults.^{1,3,18–21}

The predilection of La Crosse virus to affect younger children is incompletely understood. Mouse models of La Crosse virus infection have correlated young age with a higher initial viremia, which is thought to be a critical factor for neuroinvasion, and age appears to be a critical factor for control of viral dissemination after direct central nervous system inoculation.²² Although the reasons for higher incidence and severity of West Nile virus neuroinvasive disease in older age groups are not fully understood, possible explanations include changes in innate and adaptive immune function resulting in increased duration and magnitude of viremia or enhanced viral entry into the central nervous system due to disruption of the cerebral endothelium from conditions such as hypertension and cerebrovascular disease.^{23,24}

La Crosse virus, an orthobunyavirus, is transmitted by *Aedes triseriatus*, a mosquito that lives and breeds in the water holes of trees and other vessels, with gray squirrels and chipmunks serving as primary amplifying hosts.¹² Accordingly, La Crosse virus has been reported in distinct geographic regions with wooded areas that support its transmission cycle. From 1963 to 1981, the vast majority of cases reported were from the upper Midwest.²⁵ Our data confirm more recent observations that the highest burden of La Crosse virus disease has now shifted to the Appalachian region of West Virginia, Tennessee, North Carolina, and Ohio.^{26–28}

West Nile virus, a flavivirus, is transmitted primarily by *Culex* mosquitoes, with birds as its natural reservoir.^{23,29} This virus now affects children from all regions of the contiguous United States, demonstrating less specificity for particular ecologic and geographic regions than other arboviral etiologies. Nevertheless, the higher incidence of disease in the northern plains and mountain regions is likely in part because of the predominance of *Culex tarsalis* as the primary vector in the region, and the convergence of zoonotic hosts and ecologic conditions that promote efficient amplification and transmission.^{30,31} Similarly, large outbreaks in Arizona in 2010 and north Texas in 2012 were likely due to a confluence of favorable weather and environmental conditions resulting in an abundance of susceptible vertebrate hosts and vector mosquitoes.^{32–37}

Eastern equine encephalitis virus is an alphavirus. It is maintained in enzootic cycle between birds and mosquitoes by *Culiseta melanura*, which breeds in a specific hardwood swamp environment.¹² Several mosquito species function as bridge vectors, transmitting the virus

from birds to humans and other mammals. Accordingly, human disease cases occur in limited geographic areas, mostly along the Atlantic and Gulf Coasts.

Powassan virus is unique among the reportable viruses in that it is transmitted by *Ixodes* ticks, rather than mosquitoes, and small woodland mammals as serve as the major environmental reservoir.¹² From 2001 to 2012, a total of 47 cases of neuroinvasive Powassan virus disease were reported in the United States. Most were classified as encephalitis and ~10% of cases were fatal.^{38–40} Pediatric Powassan virus neuroinvasive disease cases were limited to Minnesota, New York, and Wisconsin. Historically, the virus was known to occur in the northeastern United States and Canada and parts of Russia, but is increasingly being identified in the upper Midwest.^{39,40}

Few St Louis encephalitis virus disease cases were reported during the surveillance period. Historically, St Louis encephalitis virus disease occurred in intermittent epidemics every 10 to 20 years and recent patterns also may reflect normal fluctuations.³ However, there is some evidence that birds infected with West Nile virus develop cross-reactive immunity, leading to speculation that West Nile virus may competitively displace St Louis encephalitis virus by reducing the numbers of susceptible zoonotic hosts.^{41,42}

Seasonal and geographic patterns of arboviral diseases are largely driven by their ecology. The vast majority of mosquito-borne disease cases were reported during the summer months corresponding to the peaks in the vector populations, viral amplification in zoonotic hosts, and human activity outdoors.⁴³ In contrast, most Powassan virus disease cases were reported during the spring, corresponding to the period of highest nymphal tick activity. Temporal trends in La Crosse and West Nile virus disease showed notable fluctuations, with peaks in disease incidence occurring ~7 to 10 years apart for each virus. Reasons for these patterns are unknown but likely depend on viral pathogenesis, human behavior, weather, and variations in the abundance and distribution of vectors and zoonotic hosts.^{44–49}

There are no specific treatments for arboviral infections; clinical management is supportive. Diagnosis is usually confirmed by measuring virus-specific immunoglobulin M antibody in serum or cerebrospinal fluid.⁵⁰ This is in contrast to molecular testing used for other common neurologic viral infections, such as enterovirus and herpes simplex virus. Commercial laboratories perform immunoglobulin M antibody testing for many domestic arboviral infections, but West Nile virus testing may need to be ordered separate from an “arboviral panel.” Powassan virus testing is available only at the CDC and several state health departments. Health care providers can contact their state or local health department to facilitate arboviral diagnostic testing.

This report has some important limitations. ArboNET is a passive surveillance system that depends on clinicians to consider the diagnosis of a possible arboviral infection and order appropriate diagnostic tests, and on health care providers and laboratories to report laboratory-confirmed cases to public health departments. Reported cases of neuroinvasive disease are considered the most accurate and consistent measure of arboviral disease in humans because the severity of disease increases the likelihood that a patient will seek medical care and have appropriate diagnostic testing performed. Nonetheless, ArboNET

reports likely underestimate the burden of domestic neuroinvasive arboviral diseases and may vary by jurisdiction or over time. By not including nonneuroinvasive disease cases in this report, the true burden of domestic arboviral diseases among children is further underestimated. Data from previous studies suggest there are an estimated 30 to 70 non-neuroinvasive disease cases for every reported case of West Nile virus.^{51–53} However, most of these data were derived from adult blood donors and there are not similar estimates for non-neuroinvasive West Nile virus disease in children or for non-neuroinvasive disease caused by other arboviruses. In addition, preconceptions about arboviral disease epidemiology may impact diagnostic practices, with La Crosse virus testing more likely to be performed on children in selected states and West Nile virus testing considered more in older adults.⁵⁴ Additionally, because ArboNET does not routinely collect information regarding clinical signs and symptoms or specific laboratory findings (eg, cerebrospinal fluid findings), misclassification as neuroinvasive disease or a specific clinical syndrome (ie, meningitis, encephalitis, or acute flaccid paralysis) cannot be detected. For example, spinal cord involvement resulting in acute flaccid paralysis has only rarely been described with La Crosse virus or other orthobunyaviruses but 10 cases of acute flaccid paralysis were reported after La Crosse virus infections in our series.^{25–28,55–60} This finding should prompt further investigation to determine if these cases were classified as acute flaccid paralysis due to generalized weakness or true spinal cord infection.

CONCLUSIONS

This report confirms that La Crosse virus, West Nile virus, and other arboviruses are important causes of central nervous system infections among children in the United States. Outbreaks are unpredictable and result from a complex interaction among virus, vector, host, and environmental factors. These variables are dynamic because of changes in weather and ecology, demographic shifts in human populations, and the introduction and evolution of new viruses. There are no specific vaccines or therapeutics for domestic arboviral diseases. Decreasing the morbidity and mortality from these agents depends on vector control, personal protection to reduce mosquito and tick bites, and blood donor screening. Effective surveillance is critical to direct these prevention efforts. Understanding the epidemiology, seasonality, and geographic distribution of these viruses will assist with clinical recognition, development of vaccines and therapeutics, and implementation of public health preventive measures.

Acknowledgments

We thank Jennifer Lehman and the state and local health department personnel who collected and reported the data used in this analysis.

FUNDING: Drs Gaensbauer and Messacar received funding from the Centers for Disease Control and Prevention for this study.

ABBREVIATION

CDC Centers for Disease Control and Prevention

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WHAT'S KNOWN ON THIS SUBJECT

Arthropod-borne viruses are important causes of neurologic infections among children in the United States. The epidemiology of these diseases is complex and relates to multiple factors, including vector biology, animal reservoirs, weather, and human behavior.

WHAT THIS STUDY ADDS

National surveillance data from 2003 to 2012 will improve understanding of the geographic, temporal, and clinical trends in pediatric neuroinvasive arboviral disease, and will inform decision-making for clinicians, public health authorities, and the general public.

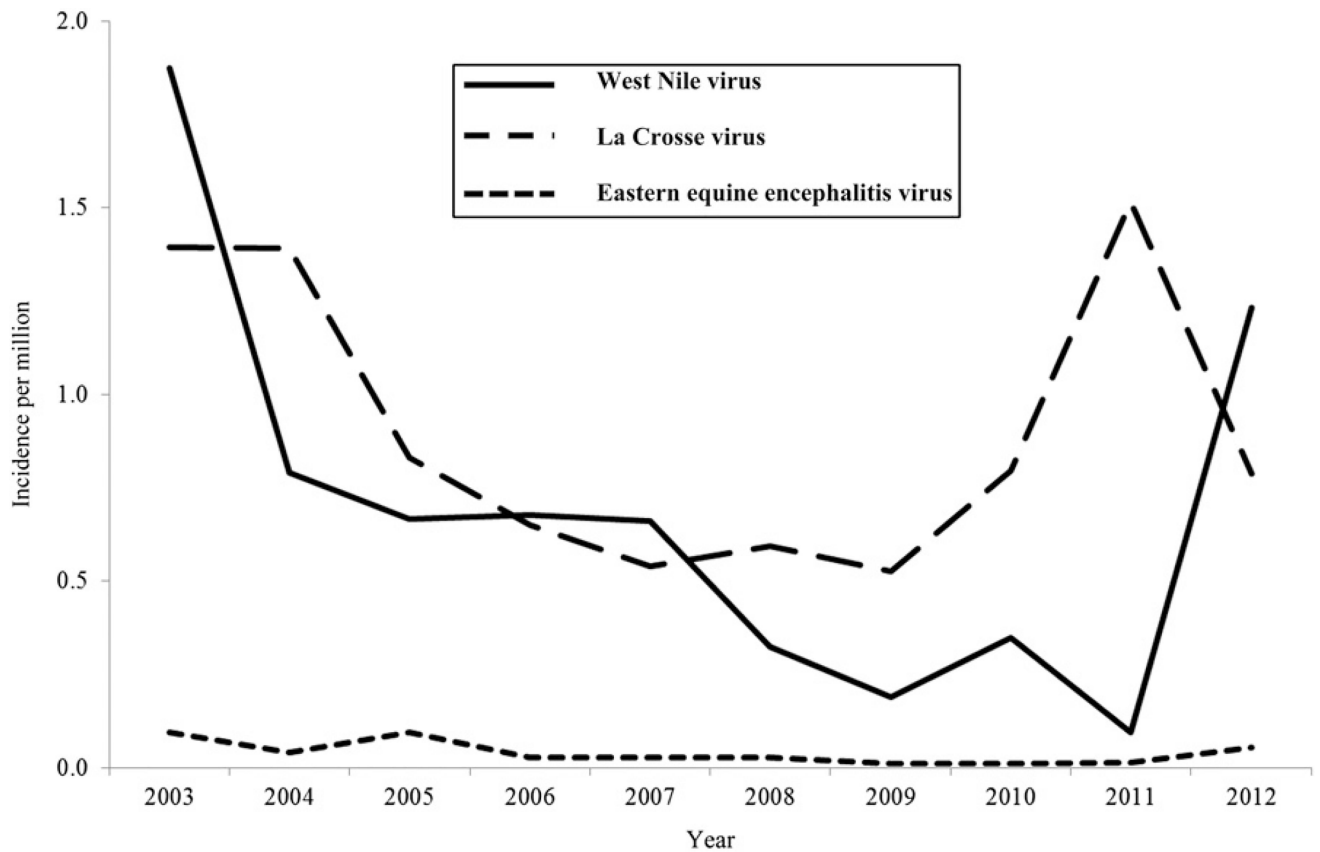
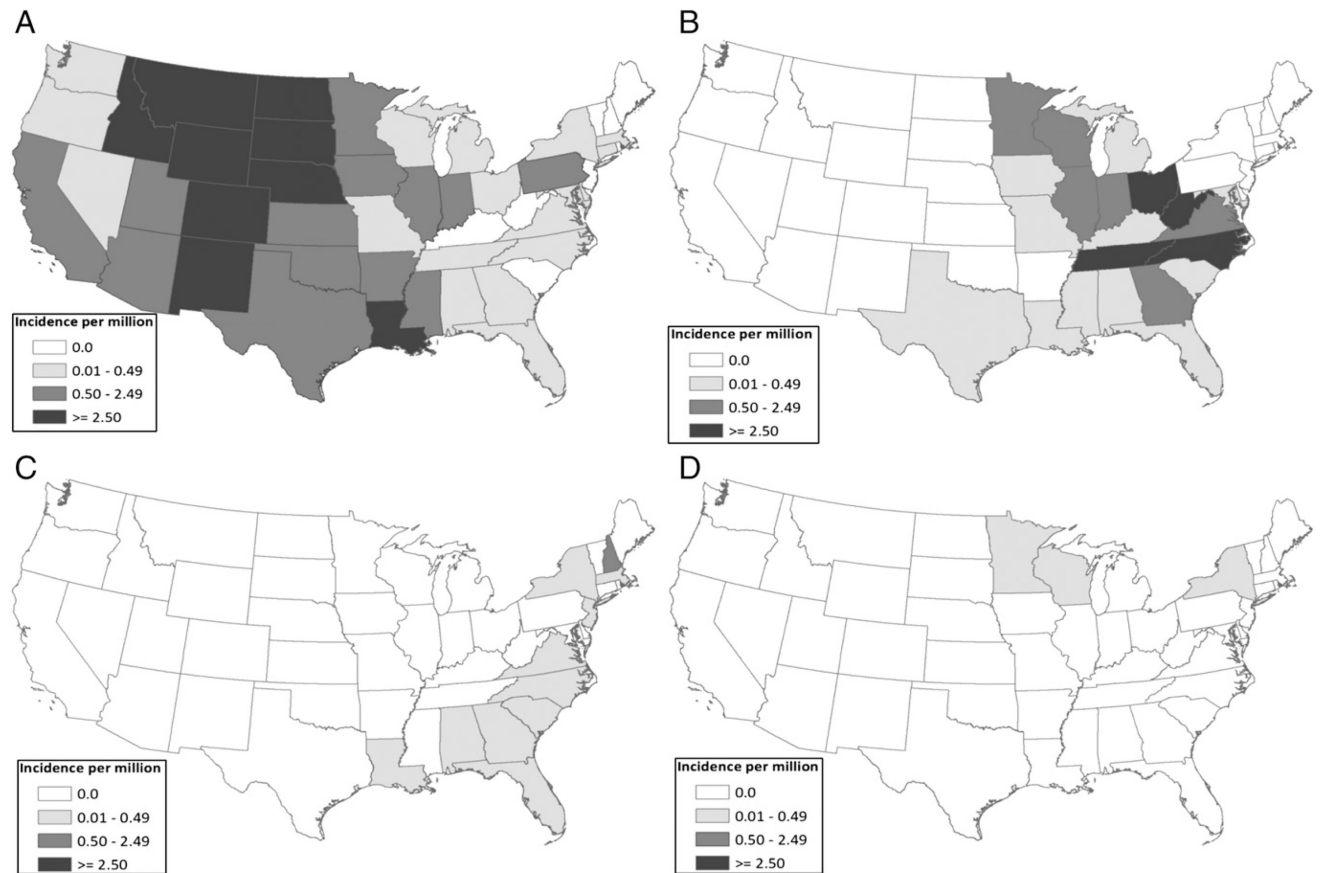


FIGURE 1. Incidence per million children (<18 years) of reported neuroinvasive arboviral disease due to West Nile, La Crosse, and Eastern equine encephalitis viruses, by year: United States, 2003 through 2012.

**FIGURE 2.**

Average annual incidence per million children (<18 years) of neuroinvasive arboviral disease reported in the United States from 2003 through 2012, by state. A, West Nile virus; B, La Crosse virus; C, eastern equine encephalitis virus; and D, Powassan virus.

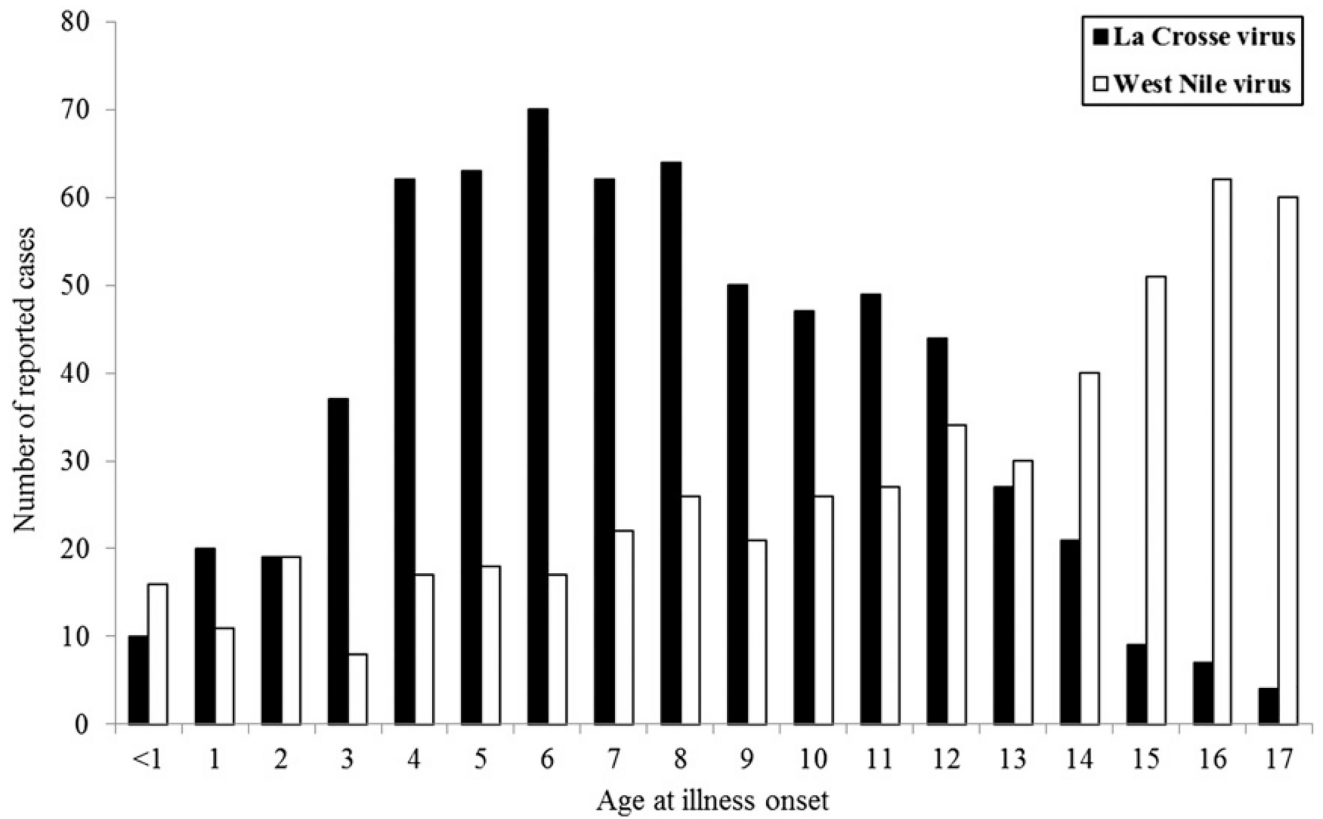


FIGURE 3.

Number of reported pediatric neuroinvasive arboviral disease cases due to La Crosse and West Nile viruses, by age at illness onset: United States, 2003–2012.

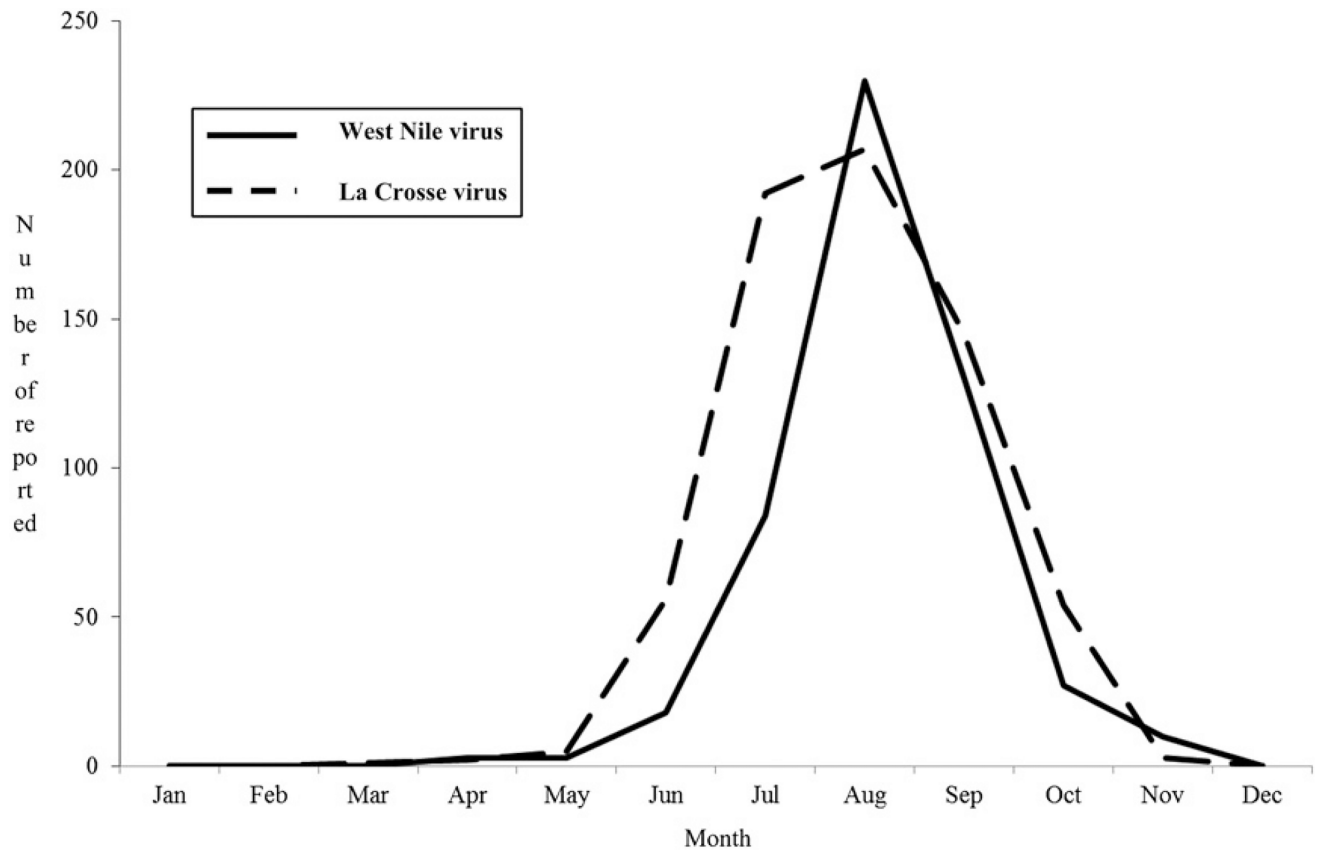


FIGURE 4. Number of reported pediatric neuroinvasive arboviral disease cases due to La Crosse and West Nile viruses, by month of illness onset: United States, 2003–2012.

TABLE 1

Reported Neuroinvasive Arboviral Disease Cases and Average Annual Incidence Rate per Million, by Virus and Age Group: United States, 2003–2012

Virus	Adults, 18 y		Children, <18 y		Incidence Rate Ratio
	No.	(Rate)	No.	(Rate)	
West Nile ^a	12 554	(5.35)	505	(0.68)	7.87
La Crosse	89	(0.04)	665	(0.90)	0.04
Eastern equine encephalitis	59	(0.03)	30	(0.04)	0.75
Powassan	37	(0.02)	8	(0.01)	2.00
St Louis encephalitis	105	(0.04)	4	(0.01)	4.00
Other ^b	53	(0.02)	5	(0.01)	2.00
Total	12 897	(5.50)	1217	(1.63)	3.37

^a An additional 49 cases of West Nile virus neuroinvasive disease had unknown age.

^b For adults, includes cases reported as unspecified flavivirus ($n = 36$), unspecified California serogroup virus ($n = 11$), Jamestown Canyon virus ($n = 3$), Cache Valley virus ($n = 2$), and Colorado tick fever virus ($n = 1$). For children, includes cases reported as an unspecified California serogroup virus ($n = 5$).

Demographics and Clinical Characteristics of Reported Pediatric Neuroinvasive Arboviral Disease Cases: United States, 2003–2012

TABLE 2

Characteristic	Virus									
	West Nile, <i>n</i> = 505		La Crosse, <i>n</i> = 665		Eastern Equine Encephalitis, <i>n</i> = 30		Powassan, <i>n</i> = 8		St Louis Encephalitis, <i>n</i> = 4	
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
Gender										
Girls	198	(39)	252	(38)	15	(50)	2	(25)	3	(75)
Boys	306	(61)	412	(62)	15	(50)	6	(75)	1	(25)
Unknown	1	(<1)	1	(<1)	0	(0)	0	(0)	0	(0)
Age group, y										
0–4	71	(14)	148	(22)	15	(50)	2	(25)	2	(50)
5–9	104	(21)	309	(46)	7	(15)	4	(50)	0	(0)
10–14	157	(31)	188	(28)	7	(23)	2	(25)	2	(50)
15–17	173	(34)	20	(3)	1	(3)	0	(0)	0	(0)
Period of onset										
January–March	0	(0)	1	(<1)	0	(0)	0	(0)	0	(0)
April–June	24	(5)	63	(9)	1	(3)	5	(63)	2	(50)
July–September	444	(88)	544	(82)	27	(90)	3	(38)	2	(50)
October–December	37	(7)	57	(9)	2	(7)	0	(0)	0	(0)
Clinical syndrome										
Meningitis	255	(50)	134	(20)	3	(10)	2	(25)	0	(0)
Encephalitis ^a	236	(47)	521	(78)	27	(90)	6	(75)	4	(100)
Acute flaccid paralysis ^b	14	(3)	10	(2)	0	(0)	0	(0)	0	(0)
Died										
Yes	3	(1)	9	(1)	10	(33)	0	(0)	0	(0)
No	493	(98)	643	(97)	20	(67)	8	(100)	4	(100)
Unknown	9	(2)	13	(2)	0	(0)	0	(0)	0	(0)

^aIncludes meningoencephalitis.

Acute flaccid paralysis status was not collected until 2004. Of the 14 patients with acute flaccid paralysis due to West Nile virus infection, 7 (50%) also had meningitis or encephalitis. All of the 10 patients with acute flaccid paralysis due to La Crosse virus infection also had meningitis or encephalitis.

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