

# Endemic Human Mosquito-borne Disease in Wisconsin Residents, 2002-2006

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## ABSTRACT

*Introduction:* West Nile virus (WNV) and La Crosse virus (LAC) are the primary mosquito-borne arboviruses associated with human disease in Wisconsin. We examined WNV and LAC human illness surveillance data collected during 2002 through 2006.

*Methods:* ELISA-based tests developed by the Centers for Disease Control and Prevention (CDC) were used to detect acute WNV and LAC infection in patient sera or cerebral spinal fluid. Public health personnel conducted patient follow-up using standard arbovirus reporting forms. CDC/Council of State and Territorial Epidemiologists definitions were used to determine cases.

*Results:* From 2002 through 2006, 114 confirmed human cases of WNV illness were reported in Wisconsin residents; 82% of illness onsets occurred during August or September. Median age of WNV case patients was 51 years, 49% reported neuroinvasive disease, 56% were hospitalized, and 7 cases were fatal. Confirmed LAC illnesses declined from a high of 27 cases during 2003 to a low of 3 cases during 2005 and 2006. Most LAC illnesses occurred in residents of Western Wisconsin; median age of LAC cases was 9 years. Mean annual incidences of reported confirmed WNV illnesses calculated for high, medium, and low population density groupings were very similar (range: 0.40-0.46 cases/100,000 population).

*Conclusions:* Humans are at risk for mosquito-borne diseases in Wisconsin. Protection and prevention mea-

asures are important statewide, especially during July through September when the risk is greatest.

## INTRODUCTION

Since the initial detection of West Nile virus (WNV) infections among Wisconsin birds in 2001, followed by the initial reports of WNV human illnesses among Wisconsin residents in 2002,<sup>1</sup> WNV has joined La Crosse virus (LAC) as the primary mosquito-borne arboviruses associated with human disease in Wisconsin. Because both viruses remain endemic in wildlife and mosquito populations within the state, humans are at risk of infections during mosquito seasons. A comprehensive well-established statewide arbovirus surveillance program exists in Wisconsin to facilitate understanding of trends of illness and virus transmission among humans, domestic animals, wildlife, and mosquitoes. This report provides a summary of human case data collected during routine surveillance follow-up of reported WNV and LAC illnesses during 2002 through 2006.

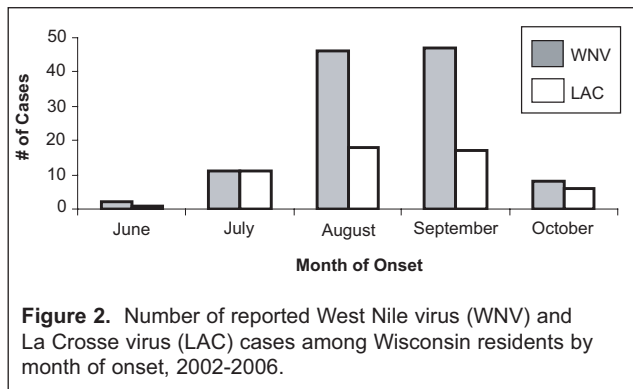
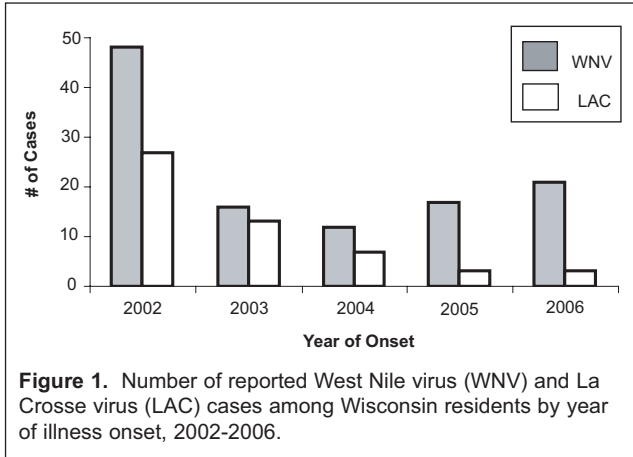
## METHODS

### Laboratory Testing

Human arboviral illnesses in Wisconsin residents are primarily diagnosed by laboratory testing of serum or cerebral spinal fluid (CSF) specimens using the Centers for Disease Control and Prevention (CDC) testing protocols that were used for this investigation. For WNV, commercial laboratories and the Wisconsin State Laboratory of Hygiene (WSLH) conducted ELISA-based screening tests of serum and CSF specimens to detect the presence of WNV IgM antibody, an indicator of acute WNV infection. WSLH or CDC performed fee-exempt confirmatory testing using a CDC WNV IgM antibody-capturing assay (MAC-ELISA)<sup>2</sup> on all specimens that were WNV-IgM-positive with ELISA-based screening. In addition, beginning in 2003, the American Red Cross and other blood banks nationwide screened donated blood units for the presence of WNV markers.<sup>3</sup> Testing for LAC

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was conducted at the WSLH using a CDC MAC-ELISA assay; positive specimens were sent to the CDC arbovirus laboratory for confirmation. Samples with equivocal or uninterpretable IgM results by MAC-ELISA testing were further analyzed by plaque reduction neutralization testing at the WSLH or CDC.

#### *Case Follow-up Activities and Case Classification*

Our routine surveillance protocols were followed for this investigation. Patient follow-up upon laboratory confirmation of WNV or LAC infection was conducted by local health department personnel using a standard report form that included demographic, clinical, recent travel, mosquito exposure, and repellent use data. As a component of the statewide arboviral-related passive surveillance activities coordinated by the Wisconsin Division of Public Health (WDPH), completed report forms were submitted to the Bureau of Communicable Diseases and Preparedness, WDPH. CDC/CSTE (Council of State and Territorial Epidemiologists) case definitions<sup>4</sup> were used to determine cases and classify them as neuroinvasive disease (meningitis or encephalitis) and non-neuroinvasive illness (such as WNV fever). According to the CDC/CSTE case definition,

arboviral meningitis is characterized by fever, headache, stiff neck, and pleocytosis; arboviral encephalitis is characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction (e.g., paresis or paralysis, cranial nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, and abnormal movements.) The WDPH reported confirmed cases with clinical correlation to the CDC. At this time, long-term follow-up of WNV and LAC case patients is not routinely conducted by public health agencies in Wisconsin.

For this report, clinical and diagnostic data were reviewed for all WNV and LAC illnesses reported with onsets during 2002-2006. During this review,<sup>4</sup> patients previously reported with WNV did not have illnesses meeting the CDC/CSTE WNV case definition criteria and their cases were excluded; 3 of the 4 had onset during 2002, the first year with reported human cases in Wisconsin. Another patient originally reported as having a WNV case was determined to be LAC positive and WNV negative by diagnostic IgM antibody testing; the case patient was reclassified from WNV to LAC.

#### *Data Analyses*

Variable frequencies were determined using Epi Info software, version 3.3.2 (Centers for Disease Control and Prevention, Atlanta, Ga). To examine WNV incidence by population density as a measure of urbanicity, counties were placed into 1 of 3 groups using 2000 US Census population density data: high (>100 persons per square mile), medium (40-99 persons per square mile), and low (<40 persons per square mile). Annual incidence rates per 100,000 persons by population density grouping were obtained using case data and total population obtained from 2005 population estimates (Wisconsin Department of Administration).

## RESULTS

### *West Nile Virus Cases*

During the 2002 through 2006 study interval, 114 human cases of West Nile virus (WNV) illness were reported in Wisconsin residents, an average of 23 cases per year. WNV case totals were highest during 2002 (48 cases), the first year human cases were reported in Wisconsin, and ranged between 12 and 21 cases annually during the subsequent 4 years (Figure 1). Since screening of donated blood units was initiated,<sup>6</sup> WNV fever cases (non-neuroinvasive illness) were detected as a result of this screening, representing 9% of the WNV cases reported in Wisconsin residents during 2003-2006. In addition, 10 WNV-positive asymptomatic blood do-

nors were identified by donor blood unit screening; 8 of these were detected during 2006.

Most of the 114 WNV case illness onsets (82%) occurred during August or September (Figure 2), with the earliest onset occurring on June 14 and the latest on October 14. WNV cases occurred in residents of 42 (58%) of 72 Wisconsin counties, with 61 (54%) cases occurring in the 10 most populous counties (Figure 3). However, when WNV incidence was examined using county-level population density data, similar annual incidence was observed for counties with high, medium, and low population densities, ranging from 0.40 cases per 100,000 persons for counties with high population densities to 0.46 cases per 100,000 persons for counties with low population densities (Table 1).

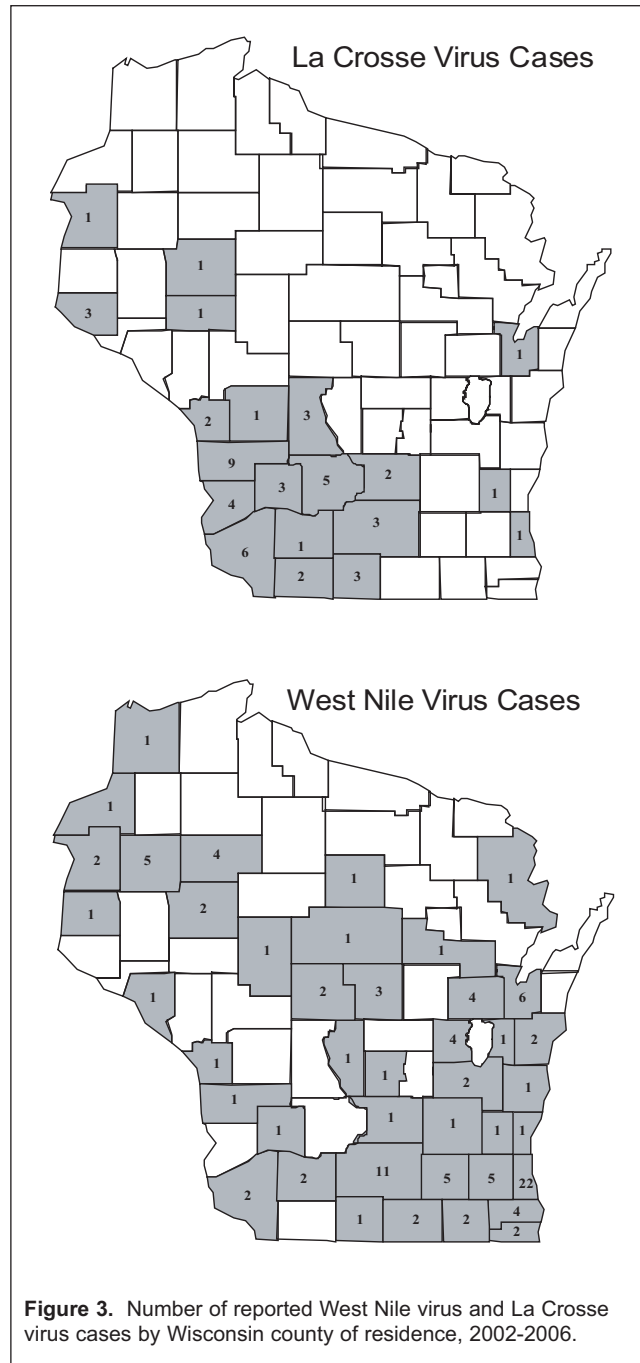
Among the 114 reported WNV cases, 69 (61%) occurred in males, and the median WNV case patient age was 51 years (range: 6-93 years). Among 93 patients for whom race was reported, 90 were white and 3 were nonwhite. Only 1 WNV case patient was ill while pregnant.

Among the 114 WNV case patients, 56 (49%) had reported WNV neuroinvasive disease (WNND) and of these 56, the median age was 56 years (range 6-93) and the greatest number of cases occurred among 40-49 year olds (Table 2). The proportion of WNV case patients with WNND illness increased with increasing age.

Among the 114 WNV case patients, 64 (56%) were hospitalized for their illnesses, 7 cases were fatal (case fatality rate of 6%), and the median age of case patients who died was 80 years (range: 55-93 years). The case fatality rate among case patients aged >80 years was 44%. The 55-year-old case patient who died was an organ transplant recipient on immunosuppressive medications when infected with WNV.

When comparing case patients with WNV fever to those with WNND, fever, headache, and fatigue were the most prominent symptoms in both, myalgias and rash were noted less frequently in WNND, and neck stiffness was observed equally frequently in WNV fever and WNND (Table 3). In addition to confusion, impaired memory, and slurred speech, substantial proportions of case patients with WNND had disorientation (64%), difficulty with balance or gait (40%), and coma (23%).

During the 2 weeks prior to their illness onsets, 13 (11%) WNV case patients reported travel to other states with areas reporting substantial WNV human caseloads during the related mosquito season. Destinations included Illinois (2 cases) during 2002; South Dakota (3 cases), Colorado (2 cases), North Dakota (2 cases) and



**Figure 3.** Number of reported West Nile virus and La Crosse virus cases by Wisconsin county of residence, 2002-2006.

Nebraska (1 case) during 2003; California (2 cases) during 2005 and Nebraska (1 case) during 2006.

Data regarding mosquito exposure within 2 weeks prior to illness onset were provided for 83 (73%) WNV case patients among whom 42 (51%) reported receiving mosquito bites, 20 (24%) reported mosquito exposure but did not recall bites, and 21 (25%) reported neither exposure nor bites. Reported mosquito repellent use among 37 case patients with data provided included 1 (3%) always using repellent, 6 (16%) using repellent

**Table 1.** Mean Annual Laboratory Confirmed West Nile Virus Illness Incidence by Population Density Grouping, 2002-2006, Wisconsin

Population Density*	No. of Counties	No. of Cases	Total Population†	Annual Incidence‡
High§	19	76	3,800,004	0.40
Medium¶	20	22	1,083,795	0.41
Low**	33	16	696,958	0.46

\* County-level population density data from the 2000 US Census used (US Census Bureau)

† County-level population data used from year 2005 (Wisconsin Department of Administration)

‡ Per 100,000 persons

§ (>100 persons/square mile)

¶ (40-99 persons/square mile)

\*\* (<40 persons/square mile)

**Table 2.** Reported West Nile Virus (WNV) Cases in Wisconsin Residents by Age Group and Presence or Absence of WNV Neuroinvasive Disease (WNND), 2002-2006

Age Group (years)	All Cases No. (%)	WNND No. (% cases, age group)	% of All WNND Cases
0-10	1 (1)	1 (100)	2
10-19	2 (2)	0 (0)	0
20-29	13 (11)	3 (23)	5
30-39	15 (13)	5 (33)	9
40-49	25 (22)	13 (52)	23
50-59	20 (18)	9 (45)	16
60-69	18 (16)	9 (50)	16
70-79	11 (10)	8 (73)	14
>80	9 (8)	8 (89)	14
Total	114 (100)	56 (49)	100

most of the time, 12 (32%) using repellent sometimes and 18 (49%) never using repellent.

### *La Crosse Virus Cases*

Reported LAC illnesses declined from a high of 27 cases during 2003 to a low of 3 cases during 2005 and 2006 (Figure 1). Illness onsets occurred in June through October; two-thirds occurred during August or September (Figure 2). LAC case illnesses occurred in residents of 20 Wisconsin counties, mostly in Western Wisconsin and in counties bordering either the Mississippi or Wisconsin rivers (Figure 3), which reflects the focal regional distribution of the LAC vector mosquitoes.

Of the 53 reported LAC cases, 31 (58%) occurred in males, 40 (75%) occurred in persons aged <19 years, the median case patient age was 9 years (range: 1-83 years), 36 (69%) occurred in patients hospitalized for their illnesses, and 1 death occurred in a 12 year-old patient.

Among 36 patients with race data provided, 35 were white and 1 was nonwhite. No female case patients indicated illness while pregnant.

Associated neuroinvasive illness (NI) was reported in 33 (62%) of 53 LAC case patients. In contrast with WNND disease in which all but 1 case occurred among adults aged >20 years, 24 (73%) of the 33 LAC NI illnesses occurred in persons <19 years, with 16 (48%) occurring in children aged <9 years. Fever (92%), headache (92%), fatigue (76%), and vomiting (73%) were common among all patients with LAC case illnesses. Nausea, neck stiffness, confusion, slurred speech, and convulsions were reported in sizeable proportions of LAC NI case patients (Table 3).

Only 1 LAC case patient reported travel to another state (Michigan) during the 2 weeks prior to illness onset. Information regarding mosquito exposure during the 14 days prior to illness onset was reported for 44 (83%) case patients among whom 36 (82%) reported receiving mosquito bites, 3 (7%) reported mosquito exposure but did not recall bites and 5 (11%) reported neither exposure nor bites. No mosquito repellent use data were available for LAC case patients.

## DISCUSSION

During 2002 through 2006, WNV illness became the most important endemic arboviral human illness in Wisconsin and 114 total cases were reported among Wisconsin residents. Approximately half of the reported cases involved WNV neuroinvasive disease (WNND), the more serious illness associated with WNV infection. WNND may result in severe debilitation and death<sup>5-8</sup> and 7 reported deaths in Wisconsin have been attributed to WNV illness since 2002; the mortality (44%) among case patients >80 years of age was particularly striking.

The Wisconsin case data were consistent with other reports indicating older persons are at greater risk for WNND.<sup>6,8</sup> Currently, the CDC WNV Web site information indicates persons >50 years of age are at greatest risk of WNND;<sup>9</sup> however, about 25% of all cases in this report were in the 40-49 year old age group, of whom >50% developed WNND. In fact, the 40-49 year olds accounted for the greatest number of WNND cases compared with other age groups; nearly a quarter of all the WNND cases occurred in 40-49 year-olds. These data indicate that persons <50 years old may also be at greater risk than previously thought, and that persons in this age group should also be targeted to take extra precautions when *Culex* mosquitoes are active throughout Wisconsin.

Risk for WNV infection in Wisconsin is assumed to exist statewide due to the presence of the *Culex sp.* mos-

quito vector throughout the state. During the 5-year period from 2002 to 2006, at least 1 reported human WNV case occurred in 58% of Wisconsin's 72 counties, and the 10 most populous Wisconsin counties reported more than half of the total WNV cases. However, examination of incidence data by population density category indicated that a similar risk exists for residents living in both urban and rural areas of Wisconsin. These data suggest that conditions such as significant active circulation of WNV among avian hosts, sufficient *Culex* mosquito numbers to facilitate virus transmission to humans, and a sizable population of humans at risk for mosquito interaction and subsequent infection are present in areas of the state with high, medium, and low population densities and are not primarily confined to Wisconsin population centers. In contrast, human LAC cases exhibit a geographic pattern of clustering with greatest risk in Western Wisconsin, particularly the southwestern corner of the state, which is an area traditionally rich in hardwood forests.

Recent federal funding has helped enhance an existing active program in LAC-endemic counties in Western Wisconsin to reduce exposure to *Ochlerotatus triseriatus* (the Eastern treehole mosquito, formerly named *Aedes triseriatus*), a mosquito confined to specific ecological environments and the vector for LAC virus.<sup>10</sup> Efforts of this program include aggressive prevention education initiatives and active elimination of known mosquito breeding sites, such as the collection and shredding of discarded tires. Site visits to case patient residences are conducted to eliminate mosquito breeding sites and to reduce the potential for multiple human cases in the same geographic location. Mosquito trapping data is used for *Oc. triseriatus* population and viral surveillance, facilitating *Oc. triseriatus* population reduction. This work is ongoing. With only 3 confirmed cases of LAC illness reported in Wisconsin during both 2005 and 2006, it appears that this enhanced program may be having a positive impact on human health, although 2 years is not sufficiently long to determine the impact. These enhanced activities should be sustained and human surveillance continued to reduce human risk and determine whether these low human case totals continue over time.

Our data indicate August and September are peak months of onset of both human WNV and LAC illnesses; >80% of WNV and >65% of LAC case onsets occurred during these 2 months. Protection and prevention efforts in Wisconsin should be enhanced from July through September when human risk is greatest. Approximately half of WNV case patients with avail-

**Table 3.** Signs and Symptoms of Illness for 58 Case Patients with West Nile Virus (WNV) Fever, 56 Case Patients with WNV Neuroinvasive Disease (WNNND), and 33 Patients with La Crosse Virus Neuroinvasive Illness (LAC NI), 2002-2006, Wisconsin

Sign/ Symptom	WNV Fever		WNNND		LAC NI	
	n*	Yes	n*	Yes	n*	Yes
Fever	57	86%	56	98%	33	91%
Headache	58	88%	56	73%	32	91%
Myalgias	58	79%	54	59%	33	42%
Fatigue	57	77%	55	89%	33	85%
Rash	58	59%	53	17%	33	3%
Arthralgias	57	54%	53	57%	32	34%
Nausea	57	58%	55	58%	33	70%
Vomiting	57	42%	56	45%	33	70%
Diarrhea	57	21%	52	31%	33	6%
Photophobia	57	44%	52	33%	33	30%
Neck Stiffness	58	47%	55	47%	32	53%
Confusion	57	12%	54	80%	33	50%
Impaired Memory	57	0%	53	57%	33	9%
Slurred Speech	57	4%	52	33%	31	24%
Convulsions	57	0%	52	6%	31	29%

\*Number of patients with reported data for specific sign or symptom.

able mosquito exposure information indicated they had received mosquito bites during the 2 weeks prior to the onset of their illness; >80% of LAC case patients reported mosquito bites. This difference may reflect more aggressive behavior by the eastern treehole mosquito compared with *Culex* species, the main vector for WNV transmission to humans. Alarming, reported mosquito repellent use by WNV case patients during that same time period was low; 49% of case patients reported never using repellants. Efforts should continue to advise Wisconsin residents on the use of mosquito repellants with active ingredients approved by the US Environmental Protection Agency to protect themselves from WNV and LAC infections.

Surveillance for human arboviral illnesses remains an important component of public health activities in Wisconsin. Mosquito-borne arboviral diseases are complex by nature and dependent on a large array of factors including weather conditions, host-vector interaction, human exposure, local ecology, and other variables, some of which remain unknown.<sup>1</sup> Currently, there is limited ability to predict the number of human cases of arboviral illnesses that will occur in any given year. Because of the morbidity and risk of mortality from acute illness, and the long-term disability and other lasting sequelae that may occur in surviving case patients,<sup>7,8,11,12</sup> reporting and prevention of cases of arboviral illness is essential. Furthermore, there is recent evidence that long-term se-

quellae associated with WNV illness, such as multiple somatic complaints, tremor, and abnormalities in motor skills and executive functioning are not confined to patients who develop neuroinvasive illness but also occur more frequently in patients with the more mild WNV fever illness than previously indicated.<sup>7,12</sup>

## CONCLUSION

Based on data presented in this report and previous surveillance data, it is likely that WNV and LAC will remain endemic in Wisconsin, with human cases occurring annually during mosquito seasons. Outbreaks of human disease, like the outbreak of 6 WNV-IgM-confirmed illnesses that occurred among turkey breeder farm workers in northeastern Wisconsin during 2002, may also occur.<sup>13</sup> Also, although no recent human cases have been reported in Wisconsin residents, the potential exists for other mosquito-borne viruses that cause human illnesses, such as eastern equine encephalitis (EEE) virus and St. Louis encephalitis (SLE), to re-emerge. Human cases of EEE and SLE have been previously reported in Wisconsin<sup>14-15</sup> and a recent human outbreak of EEE occurred in other states.<sup>16</sup> In addition, a large equine outbreak of EEE occurred in northwestern Wisconsin during 2001, although fortunately no human cases associated with the outbreak were reported (Unpublished data – Wisconsin Division of Public Health). There is also the potential for mosquito-borne arboviruses not traditionally seen in Wisconsin to emerge in the state, as WNV did in 2001. A case of Cache Valley fever found to be indigenously acquired in Wisconsin was reported in a Wisconsin resident during 2003, the second case ever reported in the United States.<sup>17</sup>

Because mosquito vectors for this wide variety of arthropod-borne viruses remain active throughout Wisconsin, humans will remain at risk from them and the need for public education and intervention to control them will continue statewide. In addition, the current practice of annual seasonal statewide wild dead bird surveillance as a surveillance mechanism for early warning of WNV presence continues to be justified.

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# Wisconsin Medical Journal

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