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THE EMERGENCE OF WEST NILE VIRUS DURING A LARGE OUTBREAK IN ILLINOIS IN 2002

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Abstract. In 2002, the world's largest outbreak of neuroinvasive West Nile virus (WNV) disease occurred. Illinois reported 21% of the total cases in the United States, the most among all states. The epidemiology of WNV in Illinois in 2002 was examined to determine factors associated with severe disease and death. A total of 884 cases were identified and there were 66 deaths. The overall attack rate of WNV infection was 7.1 per 100,000 population and this increased with age. The median ages of patients and patients who died were 56 and 78 years, respectively. Among patients who died, 91% were diagnosed with encephalitis and the case-fatality rate for patients with encephalitis was 18.6%. Patients more than 50 years old had a significantly higher risk of being reported with encephalitis (relative risk [RR] = 3.3, 95% confidence interval [CI] = 2.6–4.3%) and death (RR = 22.3, 95% CI = 5.5–90.4%). Clinicians evaluating elderly patients with WNV infection should assess patients closely for progression of disease.

INTRODUCTION

West Nile virus (WNV) is a mosquito-borne flavivirus and human neuropathogen. In Illinois, a major arboviral flavivirus epizootic occurred in 1975 during an outbreak of St. Louis encephalitis (SLE) disease. There were 578 human SLE cases reported (27% of all cases in the United States) and 47 deaths.[1] Since the SLE outbreak, Illinois has maintained a five-point arboviral surveillance program, including mosquito pool, wild bird, dead bird, equine, and human testing. In 2000, Illinois incorporated WNV testing into this surveillance system following the first recognized appearance of WNV in the Western Hemisphere in New York City in 1999.[2] In 2001, the first WNV-infected mosquitoes, birds, and horses in Illinois were identified, but no human cases were reported. On May 2, 2002, testing of a dead bird collected in Kane County, Illinois (approximately 30 miles west of Chicago), demonstrated WNV infection by immunohistochemical (IHC) staining upon necropsy. Because of this sentinel event, the Illinois Department of Public Health (IDPH) began annual seasonal arboviral testing of human specimens on May 15, 2002, one month earlier than in previous seasons. During 2002, 884 cases of WNV infection in humans were reported to the IDPH, the most cases among states in the United States during the large 2002 WNV epidemic. This report summarizes the epidemiologic investigation of the 2002 outbreak of WNV infection in Illinois and examines factors associated with severe disease and death.

METHODS

Human surveillance. In 2002, the IDPH implemented seasonal surveillance for arboviral infections in humans during from May 15 to October 31. In Illinois, aseptic meningitis and encephalitis are notifiable conditions. Hospitals and health care providers were asked to report patients with 1) aseptic meningitis (fever, meningeal signs, and abnormal findings on cerebrospinal fluid [CSF]), 2) encephalitis (fever, change in consciousness or other cortical signs, and abnormal findings on CSF) without a proven bacterial etiology, 3) CSF pleocytosis ($\geq$ 5 white blood cells/mm^3) with no other explanation, and 4) persons diagnosed with acute flaccid paralysis (or Guillain-Barré syndrome) by clinical examination. Demographic, clinical, and laboratory information for reported cases was collected by local health departments and submitted to the IDPH using a standardized non-bacterial central nervous system (CNS) infections case report form. In addition, cases of individuals with suspected WNV infection, in the absence of neurologic signs or symptoms, were also accepted by this surveillance system and designated as suspect West Nile fever cases (with or without documented fever) pending arboviral testing results. Serum and CSF specimens were requested from patients who met the above clinical criteria. A convalescent-phase serum specimen collected 2–3 weeks after onset of symptoms was requested if no CSF specimen was obtained. Clinical history of underlying medical conditions in patients was not ascertained by the IDPH report form.

Laboratory methods. Samples of serum and CSF were tested with an IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA) for antibodies to WNV, LaCrosse encephalitis virus, Eastern Equine encephalitis virus, and SLE virus at the IDPH laboratory.[3] Specimens from cases that had positive test results from reference laboratories were retested at the IDPH laboratory. All samples showing positive or equivocal antibodies for WNV through November 15, 2002, were sent to the Centers for Disease Control and Prevention (CDC) Division of Vector-Borne Infectious Diseases laboratory (Fort Collins, CO) for plaque-reduction neutralizing antibody titer (PRNT) testing. After November 15, no samples were accepted for PRNT testing at the CDC laboratory.

Definitions. A laboratory finding of at least one of the following was needed to confirm a reported case of recent infection compatible with WNV:[4] 1) isolation of WNV, or 2) identification of WNV RNA, or 3) positive IHC staining specific for WNV in any clinical specimen, or 4) demonstration of IgM antibody to WNV in CSF by MAC-ELISA per CDC protocol, or 5) a $\geq$ 4-fold increase of WNV antibodies by PRNT in paired acute- and convalescent-phase sera, or 6) demonstration of WNV IgM and IgG in a single specimen by

PRNT testing. Patients with a single serum sample that demonstrated IgM antibody only by MAC-ELISA were classified as a probable case of recent infection with WNV.

Collection and analysis of epidemiologic and clinical data. The IDPH Communicable Diseases Control Section reviewed the demographic, clinical, and laboratory data from non-bacterial CNS infections case report forms and categorized each confirmed or probable case of WNV infection into four syndromes: West Nile fever, meningitis, encephalitis, or acute flaccid paralysis (Table 1). The case report form did not solicit clinical symptoms of weakness or vomiting, but these symptoms were frequently written in as "other" symptoms and therefore included in the analysis. If there were no entries in "other" symptoms, weakness or vomiting were considered absent.

Starting on September 11, 2002, health care providers were requested to report patients with WNV infection who had received transfused blood products within four weeks before their illness, and medical records were reviewed to verify dates and unit numbers of transfused blood components. To confirm the diagnosis of WNV through receipt of a blood transfusion, available pre- and post-transfusion serum specimens were tested for WNV RNA and IgM antibody. Blood collection agencies identified donors of blood components transfused to WNV-infected recipients during the four weeks before illness onset. For those donors, blood samples available from the time of donation were retrieved and tested for WNV RNA and IgM antibody.

The attack rates of WNV disease per 100,000 population in Illinois overall and stratified by age, county, and jurisdiction were calculated using 2000 U.S. Census data.[5] Relative risks were calculated using Epi-Info version 6d (CDC, Stone Mountain, GA) and 95% confidence intervals (CIs) were adjusted by the Mantel-Haenszel method to measure the associations of age, sex, race, county or jurisdictional residence with infection. Age, rash, history of blood transfusion four weeks before infection, and travel more than 20 miles from residence within four weeks before infection were examined for associations with severity of disease and mortality.

Arbovirus environmental surveillance. For dead bird surveillance, residents were asked to report dead corvid birds (crows and blue jays) to their jurisdictional municipality for collection. Dead birds of the appropriate species and exhibiting only minor decomposition were necropsied and tissues were tested for WNV by IHC staining at the Illinois Department of Agriculture Laboratory and the University of Illinois Veterinary Diagnostic Laboratory.

Mosquito pool testing was conducted by mosquito abatement districts and public health and natural resources personnel in Illinois. Mosquito gravid traps (CDC Trap; Hausherr's Machine Works, Toms River, NJ) were stationed at designated field sites throughout the state. The mosquitoes were separated by species and then screened for WNV by the VecTest antigen capture assay (VecTest; Medical Analysis Systems, Camarillo, CA). Mosquitoes evaluated by the VecTest also underwent screening for WNV RNA by the TaqMan PCR assay (TaqMan; Applied Biosystems, Foster City, CA) at the Illinois Natural History Survey.[6] Sera from horses with neurologic symptoms were tested for WNV IgM by MAC-ELISA at the University of Illinois Veterinary Diagnostic Laboratory.[3]

TABLE 1
Diagnostic criteria

West Nile fever
1) Clinical signs and symptoms consistent with an acute viral infection in the absence of neurologic signs or symptoms
West Nile meningitis
1) Clinical signs and symptoms of an acute infection with meningeal inflammation, including fever with either headache, stiff neck, Kernig or Brudzinski sign, or photophobia and
2) Cerebrospinal fluid pleocytosis (≥ 5 white blood cells/mm^3) and
3) No proven bacterial etiology
West Nile encephalitis
1) Clinical signs and symptoms of an acute infection with encephalopathy, including fever and change in consciousness or seizures and
2) No proven bacterial etiology
West Nile acute flaccid paralysis
1) Clinical signs and symptoms of an acute neurologic process characterized by rapid onset of acute flaccid paralysis

RESULTS

Human surveillance. *Non-bacterial CNS infections surveillance.* Case reports on 6,467 persons with non-bacterial CNS infections were received by IDPH. The IDPH laboratory tested 9,497 human sera and CSF specimens; 1,516 specimens from 884 patients were positive for WNV. Among these specimens, 280 were tested for PRNT at the CDC laboratory. The 884 patients included 557 with confirmed recent WNV infection and 327 with probable recent cases of WNV infection. Among eight total cases investigated for transmission of WNV infection by blood transfusion, only one case was definitively attributed to receipt of a unit of red blood cells contaminated with WNV.

There were 66 deaths among the 884 patients. Two of the 66 deaths were reported after final case tabulations were submitted to CDC ArboNET and were not included in the data analysis. Among the 557 confirmed cases, 185 cases had positive PRNT test results for WNV, 262 cases had a positive MAC-ELISA result for WNV on both CSF and serum specimens submitted in parallel, 100 cases had a positive MAC-ELISA result for WNV by CSF only, eight cases had positive PCR results for WNV RNA, and two cases had positive IHC staining for WNV on submitted tissue specimens.

Epidemiologic characteristics. The median age of cases was 56 years (range = 3 months to 97 years). Among patients > 20 years old, the attack rate increased with age (Table 2). The median age of patients who died was 78 years (range = 49–93 years) and 77% of the deaths were in patients ≥ 70 years old. The overall case-fatality rate was 7.2%. The attack rate of WNV infection was 7.1 cases per 100,000 population. The majority of cases (635 of 884, 72%) occurred in Cook County (attack rate = 11.8 per 100,000 population; Figure 1 and Table 3). The highest attack rates within Cook County were found in the southern and northern regions of the county, particularly Evergreen Park and Oak Lawn (previously cited as areas with the highest attack rates during the 1975 SLE outbreak)[7] and Evanston and Skokie (Table 4). However, the largest number of cases was reported from the city of Chicago (225 cases) (Figure 2).

The dates of onset of illness ranged from July 10 through October 13, 2002. The peak number of cases appeared in late

TABLE 2

Demographic characteristics of 884 patients reported with confirmed or probable West Nile virus infection in Illinois in 2002 and population attack rates*

Characteristic	Number of patients (%)	Population†	Rate of infection per 100,000 population	Risk ratio (95% CI)
Age (years)				
0–19	33 (3.7)	3,605,506	0.91	Reference
20–29	38 (4.3)	1,742,602	2.2	2.4 (1.5–3.8)
30–39	107 (12.1)	1,916,801	5.6	6.1 (4.2–9.1)
40–49	169 (19.1)	1,860,796	9.1	10.0 (6.9–14.5)
50–59	148 (16.7)	1,330,677	11.1	12.2 (8.4–17.8)
60–69	141 (16.0)	860,229	16.4	18.0 (12.3–26.3)
70–79	144 (16.3)	691,752	20.8	22.9 (15.7–33.4)
≥ 80	103 (11.7)	410,830	25.1	27.5 (18.6–40.8)
Sex				
Male	448 (49.3)	6,080,336	7.4	1.07 (0.94–1.22)
Female	436 (50.7)	6,338,957	6.9	Reference
Race				
White	717 (89.2)	9,125,471	7.9	1.9 (1.5–2.4)
Black	79 (9.8)	1,876,875	4.2	Reference
Asian/Pacific Islander	6 (0.7)	428,213	1.4	0.3 (0.2–0.8)
Native American	1 (0.1)	31,006	3.2	0.8 (0.1–5.5)
Other	1 (0.1)	722,712	0.13	0.03 (0.0–0.2)

* Percentages do not add up to 100% because of rounding. CI = confidence interval.
† Population figures are from the 2000 U.S. Census.

August (Figure 3). Of the eight cases that were investigated for transmission of WNV infection by blood transfusions, one case that had a positive IgM antibody result and a positive PCR result for WNV tested on a serum specimen collected on October 15 was definitively linked to a PCR-positive, IgM antibody-negative unit of red blood cells, from which a segment was tested for WNV retrospectively, that was transfused to the patient on October 4.[8] Serum from the patient obtained 11 days before the blood transfusion was IgM antibody negative and PCR negative for WNV. Travel history was completed on 518 case report forms. Only 94 (18%) patients reported having traveled more than 20 miles from their primary residence within 4 weeks before onset of their symptoms.

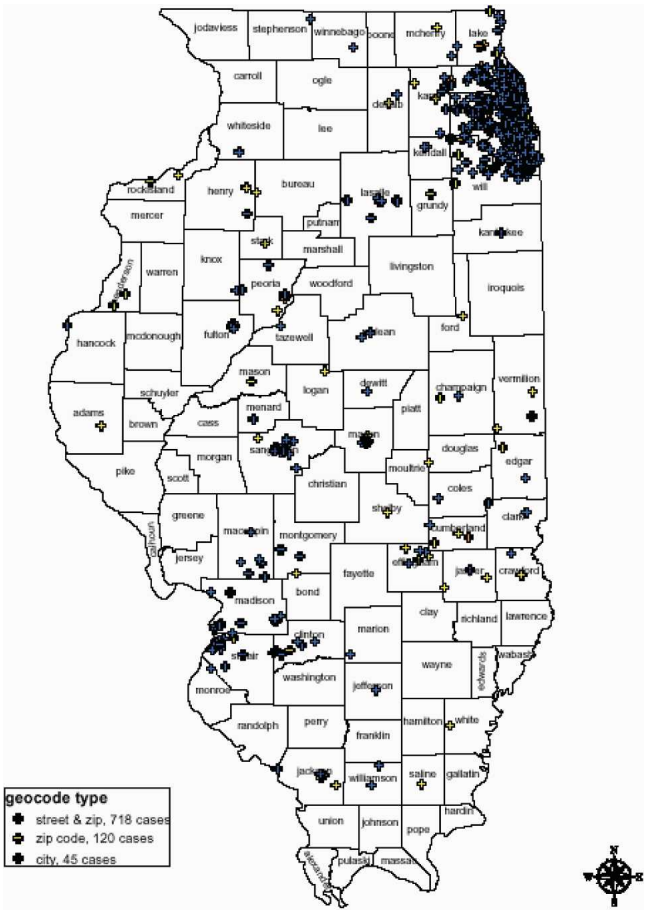

FIGURE 1. Geographic location of residence of West Nile virus cases in Illinois in 2002. This figure appears in color at www.ajtmh.org.

Clinical characteristics. Of the 884 patients with confirmed or probable WNV infection, 331 (37.4%) had West Nile fever, 311 (35.2%) had encephalitis, 232 (26.2%) had aseptic meningitis, and 10 (1.1%) had illness classified as acute flaccid paralysis. The majority (61%) of patients with aseptic meningitis were less than 50 years of age. In contrast, 54% of the patients with West Nile fever and 84% of patients with encephalitis were ≥ 50 years old (Figure 4 and Table 5). Among patients who died, 58 of (91%) 64 were diagnosed with encephalitis and the case-fatality rate for patients with encephalitis was 18.6%. There were four deaths among patients with West Nile fever. The median age of patients who died with West Nile fever was 78 years (range = 59–83 years) and

TABLE 3

Counties in Illinois with the highest number of West Nile virus human cases in 2002 and population attack rates*

County	Number of cases	Rate of infection per 100,000 population	Risk ratio (95% CI)
Cook	635	11.8	Reference
Dupage	51	5.6	0.47 (0.36–0.63)
Will	18	3.6	0.31 (0.19–0.49)
St. Clair	15	5.9	0.50 (0.30–0.83)
Madison	14	5.4	0.46 (0.27–0.78)
Sangamon	13	6.9	0.58 (0.34–1.01)
LaSalle	11	9.9	0.84 (0.46–1.52)
Macon	9	7.9	0.67 (0.35–1.29)
Kane	9	2.2	0.19 (0.10–0.36)
Fulton	8	20.9	1.77 (0.88–3.56)
Lake	8	1.2	0.10 (0.05–0.21)

* CI = confidence interval.

TABLE 4
Cities in Cook County with the highest number of West Nile virus cases in 2002 and population attack rates

City	Number of cases	Rate of infection per 100,000 population
Skokie	48	75.8
Evanston	45	60.6
Chicago	225	7.8
Oak Lawn	35	63.4
Evergreen Park	18	86.5

comorbid conditions among these patients included acute myelocytic leukemia in a 59-year-old patient and Crohn's disease with bowel resection and restrictive lung disease in a 78-year-old patient. Two other patients 78 and 83 years old were otherwise healthy prior to onset of illness.

Hospitalization was reported for 649 (73%) cases. Hospital length of stay was available for 328 patients (Table 6). The 10 cases of acute flaccid paralysis were excluded from analysis. The mean length of stay was 6.1 days (range = 1–37 days). Nearly all (98%) patients with encephalitis were hospitalized and among the 139 encephalitis cases for which length of stay information was available, the mean length of stay was 8.1 days (range = 1–37 days). This was longest mean length of stay of all the clinical categories. Ninety percent of patients with aseptic meningitis were hospitalized, but this group had the shortest mean length of stay (4.0 days, range = 0–13 days) among 105 cases for whom data were available. Only 38% of patients with West Nile fever were hospitalized, with

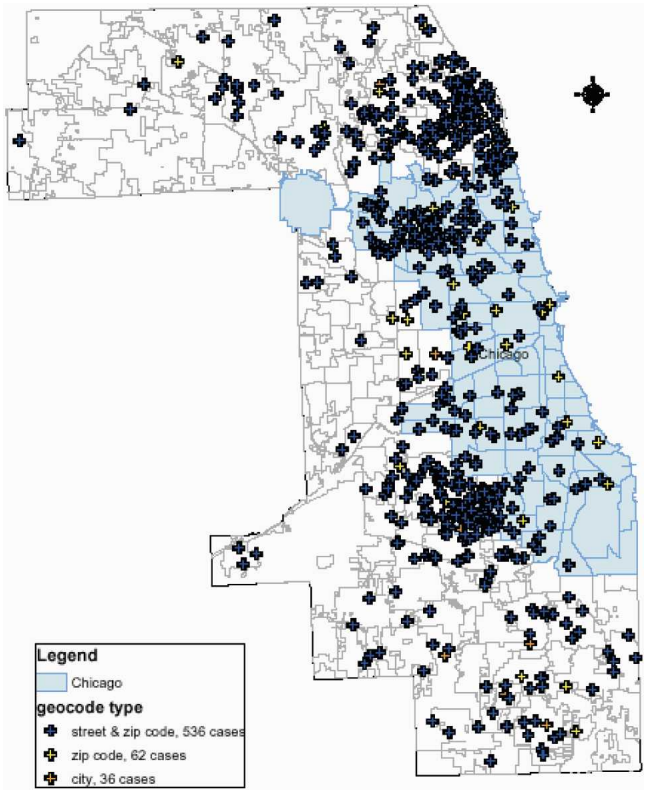

FIGURE 2. Geographic location of residence of human West Nile virus cases in Cook County, Illinois in 2002. This figure appears in color at www.ajtmh.org.

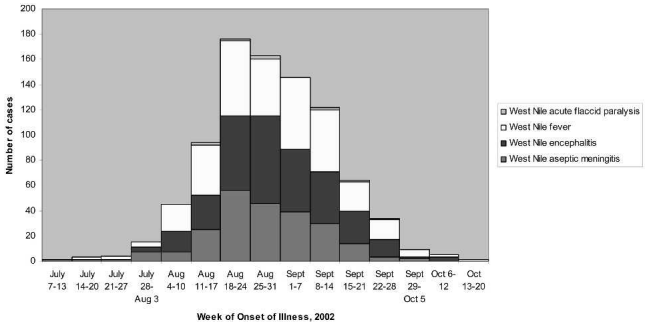

FIGURE 3. Number of reported cases of West Nile virus infection in Illinois in 2002. This figure appears in color at www.ajtmh.org.

a mean length of stay of 5.4 days (range = 1–20 days) among 84 cases for whom data were available.

In patients with neurologic manifestations of aseptic meningitis and encephalitis, fever (95%) and headache (83%) were the most commonly reported symptoms (Table 7). Change in consciousness was documented in 59% of the cases, all in patients with encephalitis. Other symptoms included stiff neck (49%), rash (39%), vomiting (23%), and weakness (22%).

A lymphocytic-predominant pleocytosis in CSF, consistent with viral infection, was seen in 424 (95%) of 446 patients with aseptic meningitis or encephalitis (median CSF white blood cell count = 63/mm^3, range = 0–1,753). Protein levels in CSF were also elevated (> 40 mg/dL) in 398 (94%) of 425 patients with aseptic meningitis or encephalitis (median = 75 mg/dL, range = 6–18,329) (Table 8).

Factors associated with disease severity and death. Patients > 50 years old had a significantly higher risk of being reported with encephalitis (relative risk [RR] = 3.3; 95% CI = 2.6–4.3) and death (RR = 22.3, 95% CI = 5.5–90.4) compared with patients ≤ 50 years of age. Patients with rash had a lower likelihood of having encephalitis (RR = 0.54, 95% CI = 0.42–0.69) or dying (RR = 0.26, 95% CI = 0.12–0.55). When stratified by an age > 50 years, patients with rash maintained a lower likelihood of having encephalitis (RR = 0.67, 95% CI = 0.53–0.84) or dying (RR = 0.39, 95% CI = 0.19–0.81). A white blood cell count in CSF > 168 cells/mm^3 (75th percentile of cases with CSF data reported) was not significantly associated with encephalitis or death (Table 9).

Arbovirus environmental surveillance. From March 31 to September 22, 793 dead birds were tested for WNV; 517

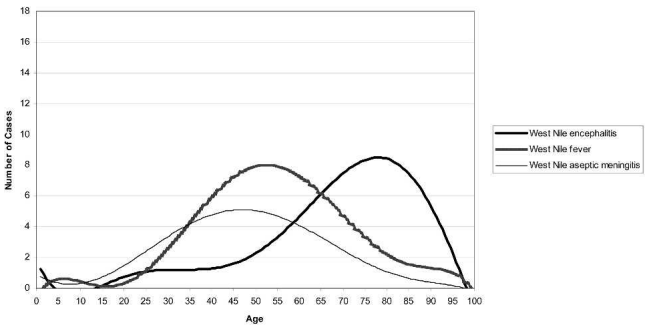

FIGURE 4. Age (years) distribution of human West Nile virus cases in Illinois in 2002. This figure appears in color at www.ajtmh.org.

TABLE 5
Disease syndromes by age groups in patients reported with confirmed or probable West Nile virus infection in Illinois in 2002*

Characteristic	WNV fever (n = 331)	Aseptic meningitis (n = 232)	Encephalitis (n = 311)	Deaths
Median age in years (range)	51 (3–97)	44 (0–86)	71 (2–93)	78 (49–93)
Number (%) of cases, age group (years)				
0–19	10 (3%)	18 (8%)	5 (2%)	0 (0%)
20–49	141 (43%)	123 (53%)	45 (14%)	1 (1%)
50–69	123 (37%)	67 (29%)	94 (30%)	14 (22%)
≥ 70	56 (17%)	24 (10%)	167 (54%)	49 (77%)
Number of deaths (%)	4 (1.2%)	1 (0.4%)	58 (18.6%)	64 (7.2%)

* There were 10 cases of acute flaccid paralysis, including 1 death.

(65%) birds were positive for WNV, mostly from the northeast Illinois area. Sixty-three percent of WNV-positive birds were crows and 36% were blue jays. The first WNV-positive dead crow was identified on May 2.

From February 3 to October 27, 624 (28%) of 2,268 mosquito pools from traps were positive for WNV; the first WNV-positive mosquito pool was identified June 16. West Nile virus was found in 12 mosquito species. The mosquito species most frequently positive for WNV were *Culex pipiens*, *Cx. restuans*, and mixtures of the two species, designated as *Culex (Culex)* species. From January 6 to November 17, 1,721 horses were tested for IgM antibody to WNV; 1,268 (74%) were positive for WNV.

DISCUSSION

The world's largest outbreak of West Nile neuroinvasive disease ever recorded occurred in the United States in 2002. West Nile virus was detected in 44 states and the District of Columbia. From June to December, 4,156 cases of human WNV infection (including 284 deaths) were reported to CDC.[9] During this outbreak, Illinois was among 30 states to report human WNV cases for the first time. Illinois reported 21% of the total cases in the United States, the most among all states.

In areas with endemic activity, WNV usually causes a mild illness categorized in our surveillance system as West Nile fever.[10,11] Serosurveys have shown that approximately 20% of all WNV infections manifest West Nile fever symptoms, while fewer than 1% of infections result in neurologic illness.[12,13] In the United States, surveillance efforts since 1999 had emphasized neuroinvasive disease, especially encephalitis.[14] In Illinois, although West Nile fever is not a notifiable disease, reported cases of West Nile fever and West Nile encephalitis, comprising 37% and 35% of total cases, were approximately equal in number. The reporting of West Nile fever cases is likely due to several factors, including frequent communications with the media to heighten awareness among clinicians and the public of the spectrum of WNV infection signs and symptoms, arboviral testing of all serum and CSF specimens submitted to IPDH laboratory regardless of disease status (some state health department laboratories tested only cases of meningoencephalitis), as well as intense enzootic transmission in heavily affected areas, particularly Cook County.

The median age and average hospital length of stay for West Nile fever cases were higher and longer than for aseptic meningitis cases. This may explain why the case-fatality rate for West Nile fever cases (1.2%) was higher than cases of aseptic meningitis (0.4%). Two of the four patients with West Nile fever who died also had serious underlying medical conditions that may have compounded the severity of disease. Slight genetic variations in the virus itself during recent outbreaks might have conferred virulence factors contributing to higher morbidity and mortality than observed during earlier outbreaks.[15–17] There may have been a bias towards diagnosing and reporting West Nile fever in persons with more fulminant illness that may also account for this finding. A prospective study in Louisiana of long-term outcome for patients with neurologic manifestations during the 2002 outbreak found that all patients with West Nile meningitis had normal or near-normal function at the eight-month follow-up.[18] Similar assessment for patients with West Nile fever requires further investigation.

In our study, an age > 50 years old was associated with an approximately 20-fold higher risk of severe disease and death. This marked risk of neuroinvasive disease and death in the elderly has been described in recent WNV outbreaks.[2,15,19] Rash was identified in close to 50% of all cases and patients with rash were less likely to be reported with severe disease or death, even when stratified for age. In earlier epidemics, almost half of the patients displayed a generalized roseolar or

TABLE 6
Hospitalization rates and average hospital length of stay for patients reported with confirmed or probable West Nile fever, meningitis, and encephalitis in Illinois in 2002

Characteristic	Total	WNV fever	Aseptic meningitis	Encephalitis
Patients hospitalized number/total number (%)	649/884 (73)	125/331 (38)	208/232 (90)	306/311 (98)
Mean length of stay in days	6.1 (1–37)	5.4 (1–20)	4.0 (1–13)	8.1 (1–37)
(range)	n = 328	n = 84	n = 105	n = 139
± SD	5.2	4.2	2.5	6.4
Median length of stay (days)	5	4	4	6
Interquartile range 25/75	3/7	3/7	2/6	4/10

TABLE 7
Clinical characteristics in patients reported with confirmed or probable West Nile virus meningitis and encephalitis and overall cases in Illinois in 2002

Characteristic	Total cases (n = 884) number/total number (%)	Total neurologic (aseptic meningitis and encephalitis) cases (n = 543) number/total number (%)	Aseptic meningitis (n = 232) number/total number (%)	Encephalitis (n = 311) number/total number (%)
Fever	764/816 (94)	495/521 (95)	212/220 (96)	283/301 (94)
Headache	636/764 (83)	390/473 (83)	205/217 (95)	185/256 (72)
Rash	301/654 (46)	151/390 (39)	83/174 (48)	68/216 (32)
Stiff neck	291/632 (49)	198/402 (49)	105/176 (60)	93/226 (41)
Altered mental status/change in consciousness	264/627 (42)	249/424 (59)	0/142 (0)	249/282 (88)
Photophobia	155/583 (27)	101/369 (19)	57/165 (35)	44/204 (22)
Weakness*	201/884 (23)	120/543 (22)	30/232 (13)	90/311 (29)
Tremor	103/543 (19)	76/339 (22)	6/142 (4)	70/197 (36)
Vomiting*	154/884 (17)	124/543 (23)	65/232 (28)	59/311 (19)
Coma/stupor	78/550 (14)	74/356 (21)	0/141 (0)	74/215 (34)
Paresis/paralysis	56/572 (10)	46/361 (9)	3/144 (2)	43/217 (20)
Kernig/Brudzinski sign	31/496 (6)	25/302 (8)	12/130 (9)	13/172 (8)
Seizures	28/557 (5)	26/355 (7)	2/144 (1)	24/211 (11)
Cranial nerve palsies	18/519 (4)	14/327 (3)	2/139 (1)	12/188 (6)

* Written in as "other" symptom on case report form.

maculopapular rash. The predominant syndrome in these outbreaks was West Nile fever.[20–23] In more contemporary outbreaks, characterized by West Nile meningitis and encephalitis cases, skin rashes have not been as evident.[2,15,24–26] The reason behind this discrepancy and the pathophysiologic relationship between rash and severity of disease remains unknown and requires further study.

Because data were derived from a passive surveillance system, our study had at least two major limitations. Passive surveillance data can have an inherent reporting bias towards cases with more severe illness. Therefore, these data may not have reflected the age distribution, symptoms, and severity of disease found in all possibly infected persons in Illinois. Second, we did not ascertain the presence or absence of symptoms and hospitalization dates for cases with incomplete case report forms. This may have affected our results, particularly with regard to frequency of symptoms and risk factors associated with severity of disease in WNV infection.

The magnitude of this WNV epizootic in Illinois shares parallels with the largest human arboviral encephalitis outbreak ever reported in the United States before 2002, the St. Louis Encephalitis outbreak of 1975. Similar to the 2002 WNV outbreak, 27% of all SLE cases in the United States were from Illinois, more than any other state. Cook County was the most highly affected area during both outbreaks, with 72% (attack rate = 11.8 per 100,000 population) of WNV cases in 2002 and 50% (attack rate = 5.3 per 100,000 population) of SLE cases in 1975.[7]

Because WNV and SLE virus amplify in similar avian hosts and mosquito vectors,[14,27] the regional and local epidemiologic patterns of transmission traced in Illinois during these major outbreaks appear to reflect a temporal and spatial in-

TABLE 8
Cerebrospinal fluid (CSF) white blood cell (WBC) count and chemistry results for patients reported with confirmed or probable West Nile virus meningitis and encephalitis in Illinois in 2002

Characteristic	Total cases with CSF data	Aseptic meningitis	Encephalitis
CSF WBC (per mm^3) mean (range) ± SD	144.1 (0–1,753) ± 231.9	144.3 (5–1,540) ± 198.9	160.0 (0–1,753) ± 265.5
CSF WBC median (interquartile range 25/75)	n = 473 63 (23/168)	n = 211 75 (32/175)	n = 235 61 (28/175)
Neutrophils (%) mean (range) ± SD	42.0 (0–99) ± 27.8	42.0 (0–99) ± 25.8	43.8 (0–99) ± 29.8
Median (interquartile range 25/75)	n = 383 42 (18/65)	n = 187 42 (20/62)	n = 184 45 (18/69)
Lymphocytes (%) mean (range) ± SD	47.2 (0–99) ± 28.1	49.0 (0–99) ± 26.1	44.6 (0–99) ± 29.2
Median (interquartile range 25/75)	n = 424 46 (22/71)	n = 196 47.5 (29.5/71)	n = 212 42.5 (18.5/66)
Monocytes (%) mean (range) ± SD	13.4 (0–98) ± 14.1	13.7 (0–98) ± 15.1	12.6 (0–80) ± 11.8
Median (interquartile range 25/75)	n = 357 9 (5/17)	n = 170 9 (5/17)	n = 175 9 (5/16)
Eosinophils (%) mean (range) ± SD	2.7 (0–82) ± 12.3	0.5 (0–90) ± 1.9	2.0 (0–56) ± 9.1
Median (interquartile range 25/75)	n = 64 0 (0/0)	n = 23 0 (0/0)	n = 38 0 (0/0)
Glucose (mg/dL) mean (range) ± SD	71.3 (15–223) ± 24.7	66.7 (33–146) ± 18.9	76.4 (15–223) ± 28.3
Median (interquartile range 25/75)	n = 457 64 (57/77)	n = 205 62 (56/71)	n = 224 67.5 (59/86)
Protein (mg/dL) mean (range) ± SD	122.8 (6–18,329) ± 859.2	73.2 (7–197) ± 29.8	177.6 (6–18,329) ± 1,223.1
Median (interquartile range 25/75)	n = 453 75 (54/101)	n = 202 69 (52/87)	n = 223 84 (64/112)

TABLE 9

Relative risks of encephalitis and death associated with various potential prognostic factors in patients reported with confirmed or probable West Nile virus infection in Illinois in 2002*

Characteristic	Relative risk (95% confidence interval)		
	Encephalitis	Encephalitis plus death	Death
Age > 50 years (n = 520/884)	3.32 (2.56–4.31)	20.24 (4.98–82.36)	22.26 (5.48–90.40)
Rash (n = 301/654)	0.54 (0.42–0.69)	0.30 (0.14–0.65)	0.26 (0.12–0.55)
Rash, stratified by age > 50 years old (n = 130/362)	0.67 (0.53–0.84)	0.44 (0.21–0.92)	0.39 (0.19–0.81)
CSF WBC count > 168 cells per mm^3 (75^{th} percentile) (n = 120/473)	1.05 (0.86–1.29)	0.82 (0.40–1.66)	0.82 (0.42–1.60)
Receipt of blood transfusion 4 weeks before symptom onset (n = 8/260)	1.20 (0.38–3.79)	3.50 (0.54–22.77)	2.94 (0.46–18.89)
Travel 20 miles from primary residence 4 weeks before symptom onset (n = 94/518)	1.02 (0.76–1.38)	0.78 (0.31–1.96)	0.86 (0.37–1.99)

* CSF = cerebrospinal fluid; WBC = white blood cell.

teraction of vectors, hosts, and pathogen populations modulated by meteorologic and ecologic factors.[28] Vector competency, vector abundance, vector infection rate, and rate of vector-host contact are primary determinants of arboviral transmission.[28–32] Illinois has more than 60 native species of mosquitoes,[33] including most of those species listed by CDC as competent vectors for WNV and SLE.[32,34] *Culex restuans* and *Cx. pipiens*, the common WNV-positive species, are abundant in urban areas throughout the state, frequently found in human-made containers and catchbasins with organic rich water.[35] In 2002, early season moderate temperatures and plentiful rainfall followed by above average temperatures and a period of low rainfall in the late summer were optimal conditions for increases in *Culex*.[28,36] In August 2002, the percentage of positive *Culex* (*Culex*) mosquito pools in Chicago ranged from about 60% to almost 95%, which coincided with the peak transmission period to humans in Cook County. Estimates of the mosquito infection rate were as high as 70 per 1,000 female *Culex*, based on collections in gravid traps in Chicago (Novak RJ, Lampman RL, unpublished data). These rates of infection exceeded those recorded from many outbreaks in the eastern United States.[37]

The large number of crows in transmission areas was also crucial for the enzootic amplification of WNV in 2002. Illinois has three of the largest crow wintering sites in the Midwest, with major roosting sites in central, northeastern, and southeastern areas of the state. Estimates of wintering crows approach 4.8 million in Illinois.[38]

More than 80% of the 12.4 million residents in Illinois live in nine metropolitan areas. More than 5.3 million people reside in Chicago and surrounding suburbs in Cook County, making this the most densely populated region in the state. Since epidemic WNV transmission appears to involve urban mosquito and bird species, it would be reasonable to assume that metropolitan areas would be susceptible to periodic outbreaks.

Although many areas in the United States experienced extensive WNV activity in 2002, because Illinois reported the greatest proportion of cases of human WNV infection, opportunities to better understand the interaction between ecologic conditions and risk factors for human transmission might be found by examining the outbreak in this region. Large urban and suburban populations in Illinois live in close proximity to mosquito vector breeding sites. The abundant mosquito species harboring WNV, many of which are indigenous to Illinois, might partially explain the greater magnitude of the WNV outbreak than previously seen during SLE outbreaks.[39] Enhanced surveillance during 2002 may have also contributed to this difference. Geographic information system (GIS) technology was used to record human cases of WNV infection in Illinois and should be expanded in the future to map mosquito breeding sites. In Cook County, there are an estimated 625,000 catchbasins. Efforts to quantitatively link human disease with indices of mosquito exposure may need to incorporate catchbasins into these models.

Early detection of WNV human cases is important to guide preventive arboviral strategies, such as mosquito larvicide and adulticide programs, educational campaigns for personal protection against mosquito exposure, and financial resource allocation. In Illinois, the first 12 cases of WNV had an onset of illness in July 2002; 10 were from Cook County. Half of these cases in Cook County were West Nile fever cases, sentinel events that triggered awareness of escalating local WNV activity and influenced arboviral containment measures. In addition to tracking incidence of neurologic disease as WNV migrates westward and becomes endemic across the United States, surveillance for West Nile fever should be continued regionally to promote aggressive arboviral control policy.

In 2002, arboviral surveillance detected a broad spectrum of human WNV disease that challenged health care providers, public health officials, and community leaders in Illinois. Because the largest burden of severe disease and death occurred in older age groups, prevention programs should target elderly persons living in areas with WNV transmission and should emphasize restricting outdoor activity during dusk to dawn, wearing long-sleeved shirts and pants while outdoors during the early evening and night hours, and the use of mosquito repellent containing DEET (N,N-diethyl-*m*-toluamide) to clothing and exposed skin.[40] Clinicians evaluating patients with WNV encephalitis and elderly patients with West Nile fever should assess patients closely for progression of disease.

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