Surveillance for West Nile Virus Cases in Louisiana 2001-2004

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West Nile virus (WNV) was first detected in Louisiana during August of 2001. An outbreak of 204 human cases of neuro-invasive disease (NID) and 25 deaths occurred in 2002. In the 2 years following, lower numbers of human cases were identified (101 NID cases in 2003 and 84 in 2004) but intense localized foci were observed. The incidence of NID has been particularly high in the elderly (65 years and older). The distribution of West Nile cases has consisted of sporadic cases with a few very intense foci. Annually, human cases have occurred from June through December, with a peak number of new cases in August. As compared with other WNV serosurveys conducted in the United States, it appears that the WNV seroprevalence in Louisiana is not elevated.

The West Nile virus (WNV) is a single-stranded RNA virus of the family Flaviviridae, genus Flavivirus, closely related to St. Louis and Japanese encephalitis viruses. Passerine birds act as the primary amplifying host for the virus, and Culex mosquitoes are predominately responsible for maintenance of the epizootic. The virus is often responsible for an increase in avian mortality, especially among Corvidae (Blue jays, Crows), which can be used as an early warning of increased viral activity. In the Southern United States, Culex quinquefasciatus, the Southern House Mosquito, is the principal human vector. Humans develop short-lived and low grade viremias unlikely to be infectious to a mosquito.

WNV has become endemic throughout much of the United States since its introduction into the New York City area in 1999. Originally isolated from the blood of a native of Uganda in 1937, it caused widespread but infrequent outbreaks in Africa, Asia, the Middle East, and Europe. Since the 1990s the frequency and clinical severity of outbreaks has increased, coinciding with the emergence of new strains. The WNV active in the United States is the same virus that circulated in Israel from 1997 to 2000; relatively few genetic changes have occurred since its introduction in 1999.

While approximately 80% of infections are asymptomatic, clinical presentations include a spectrum of signs and symptoms from simple febrile headache to a number of severe neurologic manifestations. The risk of developing neuro-invasive disease (NID) increases with age, and those over 70 years have the greatest risk of developing fatal complications.

POPULATION AND METHODS

Cases are considered "probable" when positive by enzyme immunoassay (EIA) for WNV IgM in acute serum (< 8 days after symptom onset). Confirmed cases are positive by EIA for WNV IgM in acute-stage spinal fluid, or in paired acute-stage (< 8 days after onset) and convalescent-stage (8-14 days after onset) serum samples. Because WNV IgM antibody can persist for 6 months or longer, clinical correlation is essential.

A West Nile case was required to meet the clinical and laboratory definition and was further described as either West Nile Fever or neuro-invasive disease (WNV-NID). WN Fever cases typically presented with a mild syndrome including a febrile, influenza-like illness, headache, sore throat, myalgia, arthralgia, fatigue, and sometimes a mild and transient rash. WNV-NID cases showed signs of involvement of the nervous system, including altered mental status (altered level of consciousness, confusion, agitation, or lethargy) or other cerebral signs (cranial nerve palsies, paresis or paralysis, parkinsonian signs, tremors, ataxia or convulsions). Surveillance included passive reporting from hospital infection control and hospital laboratories, and was focused exclusively on NID cases since these are more consistently reported than WN Fever.

Reported deaths were described as deaths due to disease occurring within 6 months of diagnosis of WNV infection and having a clear clinical history indicating that the infection was one of the main contributing factors to the fatality. No additional laboratory evidence was collected to confirm this conclusion, but fatalities

J La State Med Soc. VOL 157 September/October 2005 269
were compared to death certificate data collected by the Louisiana Office of Vital Records.

**Serosurvey**

Because St. Tammany Parish was the earliest area to report an outbreak of human cases nationally in 2002, the Centers for Disease Control and Prevention (CDC) and the Louisiana Office of Public Health chose the city of Slidell (population = 45,672 in the 2000 U.S. Census) for the site of several investigations characterizing WNV occurrence in the Southeastern U.S. From October 23-28, 2002, a household-based serosurvey was conducted using a two-stage cluster method to select a representative sample of households in an attempt to establish the community-wide prevalence of recently acquired WNV infection. Consenting participants aged ≥ 5 years were interviewed with a standard questionnaire. Their sera were tested for the presence of WNV-specific IgM antibodies.

**Follow-up Interview of 2003 Cases**

In an effort to understand those risk factors that may have contributed to infection and to explain the larger number of cases later in the season, additional surveillance activities also included a follow-up interview of cases identified in 2003. Cases were interviewed by phone using a standard questionnaire.

**RESULTS**

In August of 2001 the first indication of West Nile virus in Louisiana was found in a crow from Jefferson Parish. A homeless man also from Jefferson Parish was the single human case identified in that year.

**The 2002 Outbreak**

During the epidemic year of 2002, 204 human WNV-NID cases were identified (Table). Cases ranged in age from 2 months to 94 years (Mean=50.1 years). The incidence of NID increased with age and was highest among those over 75 years (Incidence Rate=32.2 per 100,000 population) (Figure 1). The incidence among males was slightly higher than among females for all but the youngest age groups. Twenty-seven deaths (25 WNV-associated and 2 due to other causes) were reported before the end of the year, making the total case-fatality rate among NID cases 13.2%. Deaths ranged in age from 27-94 years, with the highest incidence among those over 75 years (Incidence Rate =10.7 per 100,000 population) (Figure 2).

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<th>Table: Louisiana West Nile Virus Case Summary by Year</th>
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Figure 1. Incidence of West Nile virus neuro-invasive disease, 2002-2004.

Figure 2. Mortality rate of West Nile virus cases by age, 2002-2004.

Figure 3. Epidemic curve of West Nile viral neuro-invasive disease, 2002-2004.

The first cases occurred during the second week of June in St. Tammany and Tangipahoa Parishes (Figures 3, 4). Other human foci were identified as the season continued: in late June, the Baton Rouge metropolitan area (East Baton Rouge and Ascension Parishes), in early-July, both Calcasieu and Ouachita Parishes, in mid-July, the New Orleans metropolitan area (Orleans and Jefferson Parishes) and west of Baton Rouge (Point Coupee Parish), and finally in mid-August, central Louisiana (Rapides Parish). The number of cases rapidly in-
Slidell Serosurvey Results

Among 1,226 participants in the Slidell serosurvey, 21 demonstrated serological evidence of recent WNV-infection, a 1.7% seroprevalence (95% confidence interval [CI] = 0.9%–2.7%). In a previous WNV serosurvey conducted following the 1999 New York City outbreak, the seroprevalence was estimated at 2.6% in Queens, New York (95% CI = 1.2%–4.1%). Consequently, it appears that in a warm coastal area of the Southeastern United States with very high WNV activity, the risk of WNV infection was not elevated compared to a very different setting in Queens, New York.

Nine of 20 seropositive participants reported a febrile illness (one could not recall), between June and October 2002 (48%, 95% CI = 22%–74%), compared with 212 of 1,191 (18%) seronegative participants. WNV seropositivity was thus significantly associated with a febrile illness (p = 0.01). Additional hospital-based surveillance studies identified 9 cases with severe WNV neurologic illness that resided within the surveyed area in Slidell (cumulative incidence = 19.7 per 100,000 population). On the basis of the estimated seroprevalence, 765 residents aged ≥5 years (95% CI = 367–1,164) were infected with WNV in 2002, and an estimated 1.2% (95% CI = 0.8%–2.5%) of WNV-infected Slidell residents developed severe neurologic illness.

2003-2004 – Endemic WNV in Louisiana?

In 2003, the number of human cases decreased sharply, however the duration of the arboviral season was lengthened. One-hundred and one WNV-NID human cases and 7 WNV-associated deaths were reported (Table). Incidence and mortality rates again increased with age, with the highest rate among those over 75 years (WNV-NID incidence = 10.9, mortality rate = 2.2 per 100,000 population) (Figures 1 and 2). The overall case fatality rate was 8.9% among WN NID cases (2 additional non-WNV associated deaths were reported). Fifty-one cases occurred in Caddo and Bossier Parishes, most within the Shreveport/Bossier City metropolitan area, the largest focus of human cases (41.8%). Another 47 cases occurred in 17 southeastern parishes, with only six reported cases in St. Tammany Parish, a large focus of activity in the preceding year (Figure 4). Cases again were first reported in June and continued until December (25 consecutive weeks) with a higher number of NID cases reported in October and November than in 2002 (Figure 3). Cases in Caddo Parish were reported for 14 weeks from June through mid-September. Bossier Parish cases started 6 weeks later in mid-July and continued through mid-September with two additional cases reported in November.

Follow-up Interviews of 2003 Cases

In 2003, 121 cases were identified and 9 deaths were reported. Contact with the families of deceased cases was not attempted. Among the remaining 112 cases, 67 com-
pleted the interview, 4 refused and 41 were lost to follow-up (no correct telephone number available). The cases interviewed were comparable by gender, clinical status, and date of onset to those not interviewed. Among the cases interviewed, 77% of males reported hunting during the 2003 season. None of the females reported hunting. Eighty-three percent of the hunters reported no use of insect repellents while hunting. Among the interviewed males, 40% of hunters reported an onset date during the hunting season (October 1st – January 31st), while 58% of hunters reported onset date before the start of the season (Fisher’s Exact Test p=0.036).

2004 Cases
The number of cases remained low in 2004. A total of 114 cases (84 NID, 24 Fever, and 6 asymptomatic infections) were reported (Table). Asymptomatic individuals were identified by routine screening for virus in blood donations. The incidence of WN NID (8.7 per 100,000 population) and the mortality rate (2.7 per 100,000 population) were highest among those over 75 years of age (Figures 1, 2). The case fatality rate was 8.3% among WN NID cases. The main focus of human activity was the Baton Rouge metropolitan area (East Baton Rouge and Livingston Parishes) accounting for 33.3% of cases: 28 NID and 10 Fever (Figure 4). An additional 27 cases occurred in Caddo and Bossier Parishes, 23.7% of cases: 17 NID, 6 Fever, and 4 asymptomatic blood donors. The first human case occurred 3 weeks later in previous years. Cases were reported for 16 consecutive weeks from early-July to late October with six sporadic late-season cases occurring in November and December (Figure 3). The focus of the Baton Rouge area occurred during the same 16 weeks, and there were no cases late in the season.

DISCUSSION
It is difficult to predict the future epidemiologic patterns of WNV cases in Louisiana. The history of a closely-related virus, St. Louis encephalitis (SLE), may provide clues. SLE has occurred as sporadic cases and, at times, regional outbreaks. Since 2002 WNV has caused regional outbreaks as the virus moved westward.13 The last major SLE epidemic, which occurred in 1975 and took place in states along the Mississippi River, was in many ways very similar to the 2002 WNV outbreak. Petersen et al. suggest that WNV has even greater epidemic potential than St. Louis encephalitis since human infections continue to occur in years subsequent to its initial introduction.14 Studies of the epizootic in the United States have shown that WNV causes extremely high viremias in common species of birds and many species of mosquito have been found to be infected. It is of concern that Culex mosquitoes are most often implicated in WNV transmission because vector abundance is often linked with increasing urbanization, which results in breeding sites in artificial containers and draining structures in and around homes. Surveillance for human cases is hampered by testing biases, which may include limited access to health care and misdiagnosis of older patients, missing perhaps the most severe cases. Increased screening in areas with documented activity may be useful, but testing should also include individuals whose behaviors and travel may put them at risk. Improved and timelier diagnostic testing will be essential for proper patient management.

WNV prevention should focus on possible risk groups, including those at increased risk for developing neuro-invasive disease. While it is often assumed that WNV is contracted in or around the home, our data suggest that hunting in the fall may be an important risk factor in Louisiana, and hunters here should be encouraged to use mosquito repellent. In Louisiana the arboviral season can extend into the fall when many people falsely assume that the risk has passed. Diagnosis and surveillance of West Nile virus will be a challenge to clinicians and public health officials for years to come.

REFERENCES