SPREAD OF EQUINE WEST NILE VIRUS ENCEPHALOMYELITIS DURING THE 2002 TEXAS EPIDEMIC

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Abstract. Using reports of clinical West Nile virus (WNV) encephalomyelitis in Texas equids during 2002, the distribution of disease was analyzed using cluster statistics and spatial modeling to develop hypotheses of disease spread during the first year of its detection. Significant (P < 0.05) clusters of cases reported early during the outbreak were identified in east, northcentral, and north Texas, and significant (P < 0.05) clusters late during the outbreak were detected in central, south, and west Texas. Two counties on the south Texas coast first reported disease significantly (P < 0.05) earlier than their 10 nearest neighboring counties. The estimated incidence of disease was greatest in the high plains of north Texas and in northcentral Texas. Higher rates were also estimated in eastern and southern areas of the Gulf Coast. The spatial and temporal distribution observed indicates that the equine WNV epidemic began in two parts of Texas and spread elsewhere throughout the state. The mechanism of introduction and spread remains speculative.

INTRODUCTION

The geographic distribution of West Nile virus (WNV) infection is still evolving in North America and factors that promote epidemics are not well understood.1 Disease outbreaks may occur if a habitat suitable for a mosquito-to-avian transmission cycle is established near susceptible populations.2 The environmental conditions that promote outbreaks of WNV disease are presently unknown; however, extrapolation of results from ecological studies of St. Louis encephalitis (SLE) virus may prove useful. WN and SLE viruses are antigenically related, and their natural histories and epidemiology in North America seem to be quite similar. SLE virus is endemic in many regions because of the presence of competent mosquito vectors and amplification hosts, and these regions will likely be predisposed to WNV epidemics in the future.3 Since first being identified as a cause of human disease after a large urban epidemic in St. Louis in 1933, numerous outbreaks of SLE have occurred, but epidemics do not occur annually.3 Epidemic transmission of SLE virus requires synchronization of mosquito and amplification host population dynamics, and a pre-existing high level of SLE virus infection. Once biotic primers (conditions that predispose geographical regions to epidemics; for example, a susceptible host population) are in place, triggers are required to set an epidemic in motion.3 Triggers including meteorological events—for example, mild, wet spring conditions—may favor both insect reproduction and avian breeding.3

Since the mid-1990s, the number of severe WNV disease outbreaks in equine populations has increased. Recent outbreaks include Morocco (1996, 2003), Israel (1998–2000), Italy (1998), and France (2000).4 The North American outbreak of equine WNV encephalomyelitis exploded during 2002, with nearly 15,000 laboratory confirmed cases in 41 American states,5 as well as in Canada and in Mexico.5–8 Susceptible mammals are typically infected by ornithophilic mosquito vectors. Mosquito species that feed on both birds and mammals may act as bridge vectors, spreading infection from birds to horses and humans. The bridge vectors that are responsible for equine WNV infections in most of North America are unknown.

WNV was first detected in the state of Texas in 2002. During 2001, no human or equine cases were reported (United States Geologic Survey; http://cindi.usgs.gov/hazard/event/west_nile/west_nile_2001.html). WNV infection was not detected in sentinel flocks maintained during 2001 nor from mosquito collections. A total of 1,698 laboratory-confirmed (IgM-ELISA) equine cases were reported during 2002 from 204 of 254 Texas counties. The first cases were reported on June 27 from eastern coastal Texas. The epidemic peak occurred on October 5, and 50% of cases were reported during a 6-week period, September 3 to October 17. The epidemic lasted 25 weeks. The objective of this study was to describe the spread of WNV encephalomyelitis cases in the Texas equine population during 2002 and thereby generate hypotheses regarding how infection might have been introduced and spread throughout the state during the first year that WNV was detected.

MATERIALS AND METHODS

Data source. Clinical cases of WNV encephalomyelitis occurring in the Texas equine population during 2002 and reported to the Texas Department of State Health Services’ (TDSHS) Zoonoses Control Branch were used as the data source. All cases were confirmed by IgM enzyme-linked immunosorbent assay (MAC-ELISA). Clinical signs and a positive MAC-ELISA are sufficient criteria for a probable case,9 the MAC-ELISA being a highly sensitive assay. WNV IgM antibodies are detectable 6–10 days after infection, and persist for < 2–3 months.4,9 Vaccination against WNV infection is unlikely to produce false-positive IgM ELISA results.10

Data available for cases included date of onset, street address, latitude and longitude coordinates of the location where equine cases were stabled or pastured at the time of disease onset, and county. In addition, most cases were investigated by Zoonoses Control Branch staff and a standard equine neurologic disease report was completed. Ancillary data available from these reports included vaccination status and date, and history of travel outside county of residence in the preceding 60 days. In this report, only results of analyses of data describing the locations and dates of occurrence of confirmed cases in Texas are presented.

Descriptive analysis. Based on visual inspection of an epidemic curve of reported cases, the 2002 epidemic seemed to consist of three phases: 27 June to July 25, July 26 to Sep-
sember 27, and September 28 to December 17), and 44 (2.6%), 637 (37.5%), and 1,018 (59.9%) cases, respectively. For analysis, only cases that had no history of vaccination during the 12 months preceding the date of disease onset \( (N = 1,268) \), and which had no reported travel history during the 60 days preceding date of disease onset \( (N = 1,035) \), were included. Thus, the data set consisted of 979 cases of disease. Cases were described by date-of-onset and longitude (\(^{\circ}\)W) and latitude (\(^{\circ}\)N) coordinates.

The mean center of cases occurring during each week of the epidemic in which at least five cases were reported (weeks 1–20; 27 June–13 November) was estimated, as previously described, and plotted. The correlation between date of onset of cases and latitude and longitude was estimated using Spearman’s rank correlation statistics. The spatial distribution of cases during the course of the epidemic was investigated for clustering and outliers using a local indicator of spatial association (LISA) Moran’s test. This test detects local spatial autocorrelation (regions where adjacent areas have similar values) and can also be used as a diagnostic test for outliers in global spatial patterns. The variable of interest in this analysis was the date-of-onset (the date that the first clinical signs were noted by the owner) of the first case reported from each county. County date-of-onset was coded as serial date using the 1900 date system. LISA analyses were performed based on the 10 nearest county neighbors in the neighborhood of each case county. Cases were weighted using both a standardized by count (weights for each case normalized by its neighbor count, so that the sum of the weights for each case was 1) and indirect distance (so that the farther apart a case was located from its neighbor, the less influence it had; an inverse distance to the power of 2 was used) neighbor weighting methods. \( P \) values were calculated by Monte Carlo conditional randomization procedures: after calculation of the statistic using the observed data, observations were randomized and the statistic was recalculated for the randomized data a total of 999 times; \( P \) values were calculated by comparing (ranking) the observed statistic to the reference distribution. In each randomization, the proportion of index case counties was held fixed for the nearest 10 neighboring counties within the neighborhood of each index case county of interest, and the remaining values were randomly assigned new locations, so that randomization was conditional, sequentially, on each index county case in the data set. \( P \) values were corrected for multiple testing using Simes adjustment, because LISA statistics calculated were likely not independent of one another. To detect outliers, scatterplots of LISA neighbor values for each county and standardized (z-distribution) serial county dates-of-onset were created. The four quadrants of such a scatterplot provide a classification of four types—clusters and outliers—of spatial autocorrelation. These groups are areas (clusters) in which the first reported county cases occurred early (low-low) or late (high-high) in the epidemic and areas (outliers) where the first reported county cases occurred late (high-low) in the outbreak but neighboring county cases occurred early. To interpret LISA analysis results, these groups of counties were mapped.

Spatial modeling. The spatial distribution of date-of-onset of individually reported equine cases, and of county incidence risk of disease, was modeled using kriging techniques. Model parameters were derived by fitting directional semivariograms to serial dates of disease onset or estimated county risk of disease. The latter was calculated as the proportion of the estimated county equine population during 2002 (http://www.nass.usda.gov/census/census02/profiles/tx/index.htm) reported to have been affected by WNV. County centroids were identified and were used to spatially locate each of the 254 estimated county disease risks. Distances between all possible cases or county risk pairs were estimated. Directional variograms were created by selecting lag parameters (number of lags and lag spacing). Scatterplots of the semivariance of date-of-onset by the lag in date-of-onset were visually inspected and the semivariograms that included the greatest amount of detail with a smoothed appearance were selected. The semivariograms were characterized by iteratively manipulating nugget, range, and sill parameters, and by fitting spherical, exponential, or Gaussian models and minimizing a goodness-of-fit statistic. These parameters were used to define the kriging models of date of disease onset and estimated disease risk. For mapping purposes, estimated date of disease onset of individual cases and of the first case reported from each county was categorized by the month in which the case was reported to have occurred.

RESULTS

Two foci of cases reported in July were detected in east Texas. Within a broader area of east Texas, cases were reported during August and September. During August, cases were also reported from several areas of north and northcentral Texas. Most areas of Texas reported equine cases during October. Cases were reported from 204 counties. Those 50 Texas counties not reporting cases were mostly located in southern and western Texas.

The mean center of cases occurring during each week of the epidemic in which at least five cases were reported moved northwest during weeks 1–10 and moved southeast during weeks 11–20. The onset date of cases was significantly \( (P < 0.001) \) correlated with latitude (0.32) and longitude (−0.29). For cases occurring during weeks 1–10 and weeks 11–20, estimated correlations were 0.45 and −0.50 and 0.30 and −0.26, respectively.

Significant \( (P < 0.05) \) clusters of counties reporting cases early during the outbreak were identified in east and northwest Texas (Figure 1), and counties reporting cases significantly \( (P < 0.05) \) late during the outbreak were observed in central, south, and west Texas. Two counties on the south Texas coast reporting cases significantly \( (P < 0.05) \) earlier than their nearest neighbors were identified. Semivariograms were identified using a lag spacing of 1° and number of lags of 20 days, and a direction of 0° and angular tolerance of 90°. The best-fitting model of disease onset case pairs was a Gaussian model with nugget, range, and sill of 160, 3.3, and 800, respectively. Using these model parameters, a map of estimated onset date of cases in Texas during 2002 was produced (Figure 2). The best-fitting model of county disease rates was a Gaussian model with nugget, range, and sill of 45, 8.0, and 63, respectively. Estimated incidences of disease are displayed in Figure 3A. For comparison, the estimated distribution of horses in Texas is shown in Figure 3B. The inci-
Equine WNV disease in 2002, the first year that disease was reported in Texas, initially occurred at two foci. At the beginning of the outbreak, cases were progressively reported from coastal regions of east Texas. Within a month, substantial numbers of cases were also reported from the high plains region of northwest Texas. There are several reasons that could explain the observed spatial and temporal spread of disease, including differential environmental conditions and different vector species populations in parts of the state, separate sites of WNV introduction and intersite spread, and study biases.

A plausible explanation of the observed pattern of WNV disease reported in Texas equids during 2002 is differential environmental conditions and different vector species populations in parts of the state. In Texas, WNV has reportedly (http://www.tdh.state.tx.us/zoonzoonis/diseases/Arboviral/westNile/) been isolated from a range of mosquito species (including Aedes aegypti, Ae. albopictus, Culex [Melanocol- nion] spp., Cx. restuans, Cx. salinarius, and Cx. tarsalis), but mostly (> 85%) from Cx. pipiens quinquefasciatus. WNV-infected Cx. quinquefasciatus have been collected from throughout the state. Infected Aedes spp., Culex (melanococ nion) spp., and Cx. salinarius have only been collected from eastern coastal Texas, and WNV-infected Cx. tarsalis have only been collected from far western Texas (El Paso county) and the high plains of northwest Texas (Lubbock and Randall counties). Although the vector species responsible for WNV transmission within the Texas equine population are unknown, it has been suggested that Aedes and Ochlero- tatus species, and possibly Cx. pipiens and Cx. restuans, may act as bridge vectors for equine infections in the northeast region of the United States. In a study conducted in coastal east Texas (bayou floodplain), > 25% of Ae. taenio rhynchus, Anopheles crucians-bradleyi, and Psorophora cili ata caught had fed on equine. Cx. tarsalis is a potential vector of WNV in the western United States. In Lubbock county (northwest Texas), adult mosquitoes collected (using New Jersey light traps and CO2-baited encephalitis vector survey light traps) during 2002 and 2003 represented seven genera, with Cx. tarsalis and Oc. sollicitans being the predominant species collected. WNV-positive pools of mosquitoes were detected in 2002 and 2003, with the majority of the positive pools consisting of Cx. tarsalis. Cx tarsalis as a vector of WNV in equine populations may explain the unusual cluster of cases in northwest Texas. Mosquito species responsible for transmission in east and central Texas are unknown, although Ochlerotatus species likely play a role. Environmental conditions in east and northwest Texas in early- to mid-2002 may have favored expansion of these vector popula tions—to a greater extent than in other areas of the state— leading to the early outbreaks of disease observed. Such triggering events that favor breeding and rapid maturation of mosquito populations, as well as breeding in resident avian species, are known to be important precursors to SLE epi demics.

The two WNV disease foci observed are separated by a distance of nearly 1,000 km. Whether these foci of cases were epidemiologically linked is unknown. Although migratory birds have been suggested as critical long distance transport agents of WNV in North America, it is unlikely that migra-
tory birds transported WNV from east Texas to the high plains of north Texas during August 2002 through the known existing flyways (http://www.birdnature.com/allflyways.html). However, WNV could have entered east Texas along either the Mississippi or central flyways, and the source of WNV would have been migratory birds infected with WNV in states such as Louisiana, Arkansas, and Missouri. During 2001, WNV was detected within the dead bird surveillance program in all of these states, as well as in Illinois, Iowa, and Wisconsin (http://westnilemaps.usgs.gov/2002/usa_avian_mar_04.html). The source of introduction in northwest Texas is less clear. If WNV was introduced through the central flyway, it would have originated in states such as Colorado, Wyoming, and Montana. A large outbreak of WNV encephalomyelitis occurred in Colorado during 2002, but the first detection of WNV in wildbirds and horses was made on August 15 (http://www.cdphe.state.co.us/dc/zoonosis/wnv/WNVUpdateFinal02.pdf), about the same time the disease was first reported in northwest Texas. Lack of a clear spatiotemporal pattern suggests that other factors may have been responsible for WNV introduction and the subsequent large outbreak in the equine population of this region of Texas. Wild birds as a vehicle for WNV spread is speculative. If movement of birds is important, short-distance travel of resident, nonmigratory birds, and long-range travel of migratory birds may both be contributing factors. Although one modeling study has suggested that the observed patterns of long distance spread can adequately be explained by migratory birds as transport agents, this theory has also been discounted for several reasons: the potential rates of movement calculated for migratory birds greatly exceed the rate of WNV spread observed in North America; inconsistencies in direction of movement; consistent patterns of recurrence of WNV disease in subsequent years, whereas migratory stopover sites tend to be variable; host competence, precluding migratory birds that suffer high case fatality rates from acting as dispersal agent; and insufficient duration of viremia.

Spread of WNV from east Texas to northwest Texas during the spring or summer of 2002 through migratory birds is speculative.

The same spatial and temporal patterns of WNV occurrence in Texas equids in 2002 were not apparent in data generated by mosquito monitoring and wild bird mortality and human disease surveillance (http://westnilemaps.usgs.gov/2002/). These inconsistencies could be caused by study biases and reporting issues: passive surveillance systems are known to produce biased results in terms of the spatial distribution of disease, because they are often based on clinical disease reports. Reporting of equine cases in Texas during 2002 relied on owners observing signs of disease, contacting their veterinarian or TDSHS personnel, who investigated each case, and completed and submitted an investigation form. It is probable that mild cases of disease were not reported. Vector monitoring may be biased by the disease risk perceived by local communities and public health authorities. Mosquito surveillance data reported from Texas in 2002 reflects high intensity monitoring in some counties, for example, Harris County and the Houston metropolitan area, and missing data in other counties. Wild bird mortality surveillance depends on public awareness, which can be geographically inconsistent within a large state such as Texas. In addition, variation in the population distributions of various bird species, humans and equines may influence disease reporting. Although there are inconsistencies between data sources and systems that were operational during 2002 in Texas—and attempts to integrate data and draw overall conclusions may not be useful—the lack of consistency in WNV patterns observed suggests that the outbreaks in the equine and human populations was substantially different. Ecological factors operating at a local or district geographical level could be responsible for these differences.

Recent advances in geographical information systems (GISs) and spatial techniques have allowed epidemiologists and public health specialists to systematically produce disease risk maps as part of surveillance programs. Data smoothing and analysis techniques can be used to produce risk maps, in
which the risk of disease occurrence, generally relative to some baseline and avoiding artificial administrative boundaries, can be estimated. These types of maps have a direct use in public health campaigns and for targeted control programs. Monthly risk maps showing the relative danger of regional arbovirus transmission can be constructed. At the beginning of the mosquito season—March in the subtropics of North America—risk maps can be updated weekly as epidemic triggers are identified and quantified. The maps of monthly risk developed in the present study serve as a guide to potential seasonal risk of WNV disease within the equine population of Texas. However, the data on which this study was based are unique because the population was highly susceptible to infection, and the infection of wildbird populations as reservoir hosts and horses and humans as accidental hosts was an evolving system. In subsequent years, the epidemiology of WNV infection is likely to evolve, perhaps following the model of SLE in human populations or eastern equine encephalitis in horse populations, where outbreaks of disease occur every 5–10 years in some areas. Forecasting systems need to be developed to capture the dynamic behavior of this system. It may be possible to identify WNV foci based on specific habitat components, such as vegetation and standing water; control strategies can be implemented or enhanced. Remote sensing using proxy variables is an attractive approach, because it overcomes issues associated with ground observations, including sample size, lack of adequate spatial data coverage, and cost. More recently, the use of hydrology models has been proposed for forecasting WNV and SLE virus in southern Florida. Advantages include measurement of a variable directly related to mosquito abundance, real-time prediction, fine-scale, and the ability to make medium- to long-range forecasts.

Reporting of cases of equine WNV encephalomyelitis was used in this study to characterize the spread of the WNV in Texas during 2002. In another study based on Texas data from 2002, the median date of occurrence of human cases of WNV disease occurred on average 14 days after that of the nearest (within 5 km) equine disease case. Using time series analysis, human cases were best described by the number of equine cases occurring and reported 30 days previously. Although dead bird surveillance is known to be a sensitive indicator of the presence of WNV in a district, reporting of equine disease cases in Texas during 2002 also seems to be a sensitive indicator of the spread of WNV throughout the state. Knowing when and where the risk of WNV disease is elevated is important, so that prevention strategies—including vaccination, mosquito population suppression, and reduction in the exposure of equines to mosquitoes—can be implemented in a timely manner. As the ecology of this disease evolves, accumulation of data and knowledge will allow a more accurate identification of locations and time periods during which disease risk in both equine and human populations is elevated, thus enhancing disease control efforts.

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