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Unprecedented Outbreak of West Nile Virus — Maricopa County, Arizona, 2021

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West Nile virus (WNV) is a mosquitoborne disease primarily transmitted through bites of infected *Culex* species mosquitos (*1*). In the United States, WNV is the leading domestically acquired arboviral disease; it can cause severe illness affecting the brain and spinal cord with an associated case fatality rate of 10% (*2*,*3*). On September 2, 2021, Maricopa County Environmental Services Department, Vector Control Division (MCESD-VCD) notified the Maricopa County Department of Public Health (MCDPH) and the Arizona Department of Health Services (ADHS) that the WNV vector index (VI), a measure of infected Culex mosquitoes, was substantially elevated. By that date, at least 100 WNV cases had already been reported among Maricopa County residents to MCDPH by health care providers and laboratories. Within 2 weeks, the VI reached its highest ever recorded level (53.61), with an associated tenfold increase in the number of human disease cases. During 2021, a total of 1,487 human WNV cases were identified; 956 (64.3%) patients had neuroinvasive disease, and 101 (6.8%) died. MCESD-VCD conducted daily remediation efforts to mitigate elevated VI and address mosquito-related complaints from residents (i.e., large numbers of outdoor mosquitoes from an unknown source and unmaintained swimming pools potentially breeding mosquitoes). MCDPH increased outreach to the community and providers through messaging, education events, and media. This was the largest documented focal WNV outbreak in a single county in the United States (*4*). Despite outreach efforts to communities and health care partners, clinicians and patients reported a lack of awareness of the WNV outbreak, highlighting the need for public health agencies to increase prevention messaging to broaden public awareness and to ensure that health care providers are aware of recommended testing methods for clinically compatible illnesses.

Investigation and Results

WNV, an arthropod-borne arbovirus, is primarily transmitted through bites of infected Culex mosquitoes and is the leading cause of domestically acquired arbovirus infections in the United States (*1*). Transmission is also possible through blood transfusions; since 2005, the Food and Drug Administration has recommended WNV nucleic acid testing of minipools consisting of combined individual blood donation samples, with an automatic switch to individual donation testing upon detection of a positive result (*5*). Persons with a WNV-positive

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reverse transcription–polymerase chain reaction (RT-PCR) or immunoglobulin M (IgM) blood or cerebrospinal fluid (CSF) test result are reported to public health. Health care providers are required to report patients within 5 working days of detection, diagnosis, or treatment of a suspected or confirmed WNV infection; laboratories are required to report positive WNV test results within the same period. WNV case reports are stored within the Arizona Medical Electronic Disease Surveillance Intelligence System.*,† MCDPH investigates reports of positive WNV laboratory test results, classifies them according to national case definitions (*6*), and regularly communicates with health care providers via a mass notification system (SurvAlert) regarding community health threats. MCDPH responds to WNV outbreaks in partnership with MCESD-VCD, with support from ADHS.

No vaccine or specific therapy exists for WNV; thus, treatment is supportive. The case fatality rate in persons with neuroinvasive disease is 10% (*2*,*3*). The frequency and location of outbreaks vary annually and are challenging to predict (*1*). In Arizona, WNV was first detected in 2003 (12 cases); the majority of cases occurred among Maricopa County residents (*2*). The largest outbreak previously recorded in Maricopa County occurred in 2004 (355 cases).

MCESD-VCD conducts vector surveillance and abatement§ based on resident complaints of mosquito abundance and routine mosquito trap deployments in specific locations throughout the county.¶ When mosquitoes are found in traps, MCESD-VCD organizes them into groups (pools) of up to 50 female *Culex* spp. mosquitoes to be tested as one sample. Each pool is then tested for WNV using RT-PCR; a positive mosquito pool is one in which the sample is WNV-positive. From this testing, MCESD-VCD calculates a VI (the estimated proportion of infected mosquitoes of a particular species in a specific area collected during weekly mosquito surveillance). The highest VI previously recorded in Maricopa County was 19.4 in 2019 (*7*). When the VI exceeds 3.0 (based on analysis of data from previous seasons), MCESD-VCD notifies MCDPH that an increase in human WNV cases is anticipated within 2–3 weeks. Laboratory processing and notification of VI to MCDPH lags throughout the season (approximately 1–2 weeks). ADHS coordinates confirmatory human WNV testing with the Arizona State Public Health Laboratory and CDC, monitors WNV surveillance data statewide, provides resources, and issues health alert notifications (HANs).

On May 4, 2021, MCESD-VCD notified MCDPH of the first 2021 WNV-positive mosquito pool. MCESD-VCD

* https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/communicable-disease-reporting/reportable-diseases-list.pdf
† https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/communicable-disease-reporting/lab-reporting-requirements.pdf

§ https://codes.findlaw.com/az/title-36-public-health-and-safety/az-rev-st-sect-36-601.html.
¶ https://www.maricopa.gov/632/Vector-Control

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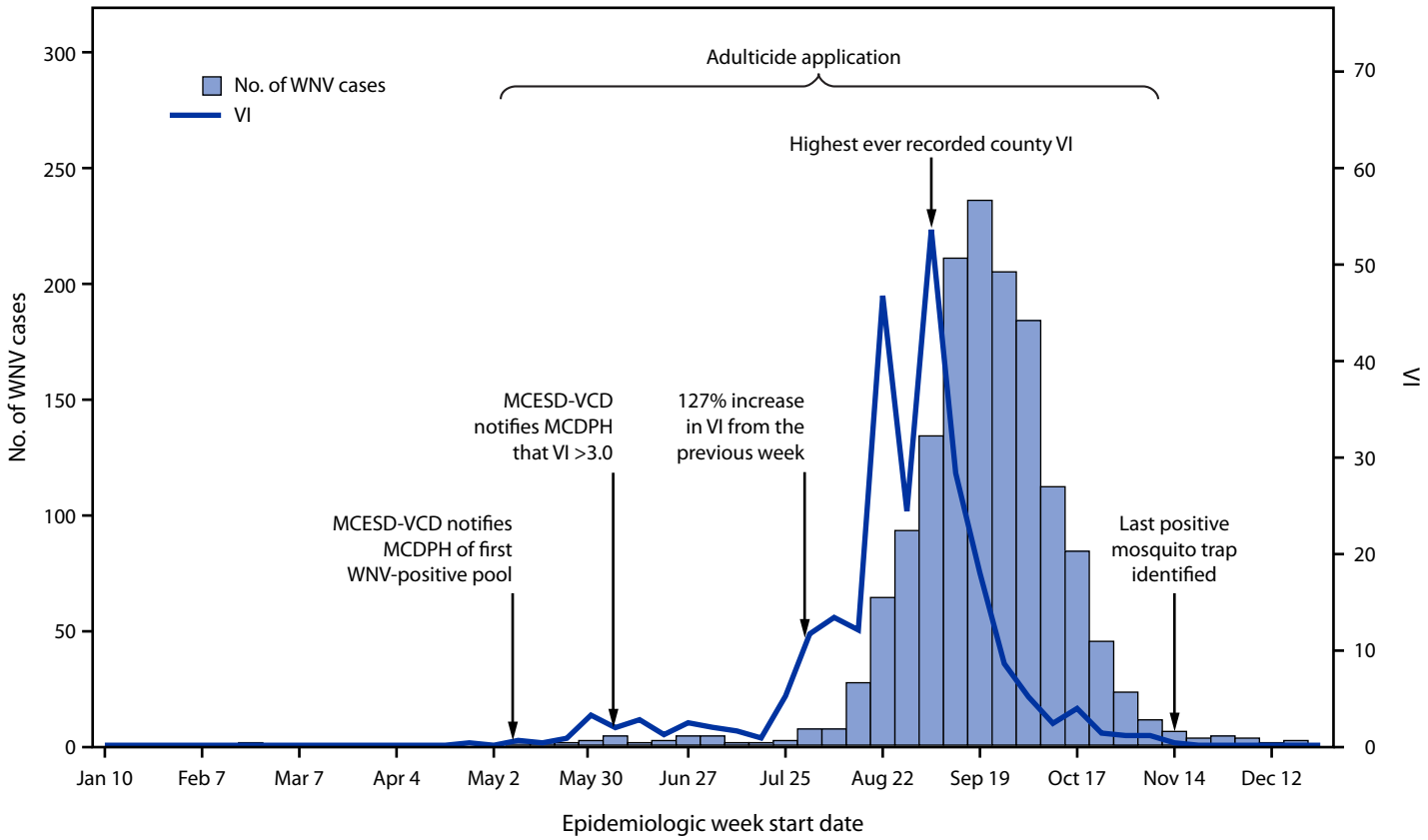
continued mosquito surveillance and commenced application of adulticides based on WNV-positive pools. On June 11, MCESD-VCD notified MCDPH that the VI had exceeded 3.0 (Figure). MCDPH enhanced routine surveillance by forwarding WNV IgM-positive serum and CSF specimens collected from persons with suspected WNV cases to the Arizona State Public Health Laboratory (ASPHL) for confirmatory testing. WNV-positive RT-PCR samples are considered confirmatory tests and were not forwarded to ASPHL. On August 12, the VI had increased by approximately 127% from the previous week (from 5.11 to 11.57). By September 2, the WNV VI was 46.72, peaking the week of September 11 at 53.61; the highest level ever recorded in the county. A VI peak this late in the season (i.e., in September) has occurred twice before in Maricopa County, in 2014 (VI = 9.6) and 2018 (VI = 7.9).

During 2021, MCDPH identified 1,487 confirmed or probable human WNV cases and an additional 78 asymptomatic viremic blood donors. The majority (95%) of persons with WNV had illness onset during a 12-week period during August 15–November 6, 2021. On September 25, the outbreak peaked at 236 cases reported in a single week. The last adulticide application occurred November 9. The last positive mosquito trap was identified the week of November 14; adulticide was not applied because the temperatures had decreased to <50°F (<10°C); according to manufacturer instructions, the material cannot be applied at these temperatures.**,††

Among the 1,487 WNV cases, 956 (64.3%) were classified as neuroinvasive disease, and 101 (6.8%) patients died; all deaths occurred among patients with neuroinvasive disease (Table). In addition to the 78 asymptomatic WNV reports identified through routine blood donation screening, 25 of the 1,487 WNV cases were identified as blood donors with symptomatic WNV; one of these symptomatic patients was

** https://www3.epa.gov/pesticides/chem_search/ppls/008329-00109-20180110.pdf
†† https://www3.epa.gov/pesticides/chem_search/ppls/002724-00791-20131118.pdf

FIGURE. Number of West Nile virus cases (N = 1,487),§ vector indices,* and public health responses, by epidemiologic week start date† — Maricopa County, Arizona, 2021



Abbreviations: MCDPH = Maricopa County Department of Public Health; MCESD-VCD = Maricopa County Environmental Services Department, Vector Control Division; VI = vector index; WNV = West Nile virus.
* The VI is the estimated proportion of infected mosquitoes of a particular species in a specific area collected during weekly mosquito surveillance.
† The number of persons with WNV each week is based on date of symptom onset; VI data are based on date of mosquito collection, which lags from MCDPH notification date by approximately 1-2 weeks.
§ Neuroinvasive and nonneuroinvasive cases are shown.

TABLE. Characteristics of residents with West Nile virus (N = 1,487), by clinical syndrome* — Maricopa County, Arizona, 2021

Characteristic	No. (%)							
	Neuroinvasive disease, clinical syndrome*						Nonneuroinvasive disease¶	Total cases
	All	Encephalitis†	Meningitis†	GBS	AFP†	Not specified†,§		
Total (%)	**956 (64.3)**	618 (64.6)	319 (33.4)	1 (<1.0)	1 (<1.0)	17 (1.8)	531 (35.7)	**1,487**
Age, yrs, median (IQR)	70 (58–78)	73 (63–80)	61 (48–71)	79 (NA)	59 (NA)	67 (57–72)	59 (48–69)	**66 (53–75)**
Sex								
Female	393 (41.0)	250 (40.5)	139 (43.6)	1 (100)	0 (—)	3 (17.6)	247 (46.5)	**640 (43.0)**
Male	563 (58.9)	368 (59.5)	180 (56.4)	0 (—)	1 (100)	14 (82.4)	284 (53.5)	**847 (57.0)**
Race**								
AI/AN	2 (<1.0)	2 (<1.0)	0 (—)	0 (—)	0 (—)	0 (—)	1 (<1.0)	**3 (<1.0)**
Asian	6 (<1.0)	1 (<1.0)	5 (1.6)	0 (—)	0 (—)	0 (—)	6 (1.1)	**12 (<1.0)**
Black or African American	16 (1.7)	10 (1.6)	6 (1.9)	0 (—)	0 (—)	0 (—)	1 (<1.0)	**17 (1.1)**
NH/OPI	1 (<1.0)	1 (<1.0)	0 (—)	0 (—)	0 (—)	0 (—)	0 (—)	**1 (<1.0)**
White	814 (85.1)	518 (83.8)	282 (88.4)	0 (—)	1 (100)	13 (76.5)	345 (65.0)	**1,159 (77.9)**
Other	18 (1.9)	12 (1.9)	6 (1.9)	0 (—)	0 (—)	0 (—)	13 (2.4)	**31 (2.1)**
Unknown	99 (10.4)	74 (12.0)	20 (6.3)	1 (100)	0 (—)	4 (23.5)	165 (31.1)	**264 (17.8)**
Ethnicity††								
Hispanic or Latino	58 (6.1)	33 (5.3)	24 (7.5)	0 (—)	0 (—)	1 (5.9)	19 (3.6)	**77 (5.2)**
Not Hispanic or Latino	787 (82.3)	501 (81.1)	272 (85.3)	0 (—)	1 (100)	13 (76.5)	346 (65.2)	**1,133 (76.2)**
Unknown	111 (11.6)	84 (13.6)	23 (7.2)	1 (100)	0 (100)	3 (17.6)	166 (31.3)	**277 (18.6)**
Hospitalized	923 (96.5)	600 (97.1)	309 (96.9)	1 (100)	1 (100)	12 (70.6)	91 (17.1)	**1,014 (68.2)**
Length of stay, days, median (IQR)	7 (4–11)	9 (6–13)	5 (3–7)	9 (NA)	16 (NA)	4 (2–7)	4 (2–6)	**6 (4–10)**
Deaths§§	101 (10.6)	99 (16.0)	2 (0.6)	0 (—)	0 (—)	0 (—)	0 (—)	**101 (6.8)**
Decedent age, yrs, median (IQR)	79 (71–83)	79 (71–83)	76 (65–86)	NA	NA	NA	NA	**79 (71–83)**

Abbreviations: AFP = acute flaccid paralysis; AI/AN = American Indian or Alaska Native; GBS = Guillain-Barré syndrome; NA = not applicable; NH/OPI= Native Hawaiian or other Pacific Islander.

* The constellation of physical symptoms associated with a person's illness. https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/mosquito-borne/wnv-sle-case-classification-algorithm.pdf

† Percentages of cases of encephalitis, meningitis, GBS, AFP, and unspecified neurologic signs or symptoms are percentages of neuroinvasive cases.

§ Not specified encompasses other neurologic or neuroinvasive clinical syndromes not covered under the categories of encephalitis, meningitis, GBS, or AFP.

¶ Nonneuroinvasive case classification indicates an acute systemic febrile illness with absence of neuroinvasive disease.

** Race is a mutually exclusive category self-reported by the patient. The Other category includes those who did not identify with the provided options.

†† Ethnicity is a mutually exclusive category self-reported by the patient.

§§ Deaths from West Nile virus are deaths for which West Nile virus was listed as a contributing or underlying cause of death on the death certificate.

diagnosed with neuroinvasive disease. The median age among all patients was 66 years (IQR = 53–75 years), and among those who died, the median age was 79 years (IQR = 71–83 years). Most cases occurred in persons who were White (78%), non-Hispanic or Latino (76%), and male (57%). In total, 1,014 (68.2%) patients were hospitalized, with 91% of hospitalizations occurring among persons with neuroinvasive disease. The median length of hospitalization for persons with neuroinvasive disease was 7 days (IQR = 4–11 days), compared with 4 days (IQR = 2–6 days) for those with nonneuroinvasive disease. During the investigation, cross-reactivity with mumps IgM testing was reported for 11 cases. MCDPH clinical staff members reviewed patient clinical courses, including symptoms, comorbidities, and potential exposures to determine compatibility with WNV and mumps; all patients' clinical illnesses were considered to be more consistent with WNV than with mumps.

Public Health Response

After identification of the first confirmed human case during the 2021 WNV transmission season, MCDPH issued a SurvAlert on June 25, advising health care providers to consider WNV and other arboviruses in patients with clinical signs or symptoms compatible with WNV neuroinvasive disease.[§§] MCDPH also alerted local blood banks to trigger individual donor screening rather than pooled screening. MCESD-VCD continued applying pesticide and larvicides, conducting mosquito surveillance, and responding to resident complaints of large quantities of mosquitoes or unmaintained swimming pools. In August, in anticipation of an increase in mosquitos during the Arizona monsoon

§§ Provider messaging advised that clinicians consider testing in the following scenarios: all cases of viral encephalitis; all cases of acute flaccid paralysis or Guillain-Barré syndrome of unknown etiology, with or without presence of viral meningitis or viral encephalitis; and cases of aseptic meningitis, especially those with at least one of the following: altered mentation, profound muscle weakness, flaccid paralysis, spastic paralysis, Guillain-Barré syndrome, or seizure.

season (June 15–September 30),[¶] MCDPH increased social media messaging regarding mosquito breeding and WNV prevention strategies after each rain. In September, MCDPH added the local social networking service for neighborhoods, Nextdoor.com, to their social media outreach targeting populations at higher risk. ADHS worked with community partners, including the Arizona office of AARP and the Arizona Geriatric Society, to prioritize outreach to persons aged ≥60 years, who are at increased risk for WNV-associated morbidity and mortality (*3*).

On September 1, MCDPH issued a press release regarding the first death in a patient with confirmed WNV. Based on the substantially elevated VI, MCESD-VCD, MCDPH, and ADHS coordinated an enhanced response including distribution of insect repellent and information packets and participated in interviews across multiple media platforms to increase public awareness. ADHS also issued a HAN notifying providers of the record-breaking season. On October 13, MCDPH, MCESD-VCD, ADHS, and CDC met to discuss outbreak response strategies, including issuing a SurvAlert reiterating the unprecedented number of WNV cases and recommending that providers test the serum and CSF of patients being evaluated for suspected WNV. Throughout the 2021 season, MCESD-VC fogged >400,000 acres with adulticide (twice the 10-year per-acre average), applied larvicide to approximately 25,000 sites, and received approximately 9,500 mosquito abundance or green pool complaints (40% more than average).

Discussion

The largest recorded WNV outbreak in a U.S. county occurred during May–December 2021 in Maricopa County, Arizona, and included more than four times the number of cases reported (355) in the previous largest outbreak in the county during 2004 (*8*). The reason for the unprecedented 2021 WNV outbreak is unknown, but is likely multifactorial, potentially related to increased rain (*9*), recent population growth and housing development, and changes in health care-seeking behavior during the COVID-19 pandemic. In response to this large number of human cases, local and state public health and vector agencies worked together to increase public and health care provider awareness, reinforce prevention messaging, and expand vector control activities.

The majority of identified cases resulted in neuroinvasive disease and occurred among older adults (aged ≥60 years). More than 1,000 patients required hospitalization, taxing a health care system that was already stressed as a result of the COVID-19 pandemic. Although COVID-19 cases exceeded WNV cases in Maricopa County (19,656 COVID-19 patients were hospitalized during May–December 2021) (*8*), health care facilities anecdotally reported intensive care units at full capacity with approximately one half of patients infected with SARS-CoV-2 and one half with WNV.

Summary

What is already known about this topic?

West Nile virus (WNV) is endemic in Maricopa County, Arizona. Since WNV was first detected in 2003, four outbreaks have occurred.

What is added by this report?

In 2021, Maricopa County experienced its fifth, and largest, WNV outbreak reported in the county: 1,487 cases, 1,014 (68%) hospitalizations, and 101 (7%) deaths, taxing a stressed health care system during the COVID-19 pandemic.

What are the implications for public health practice?

Clinicians should consider WNV testing in serum and cerebrospinal fluid in patients with a clinically compatible illness. Public health agencies should continually review messaging to improve awareness. Human and mosquito surveillance is essential to mounting a rapid, coordinated response and limiting further spread.

In spite of increased community and health care partner outreach through social and other media and health care provider messaging, anecdotally, clinicians and patients reported a lack of awareness of the WNV outbreak, highlighting the need for a more effective messaging strategy to increase public and provider awareness, case diagnosis, and WNV prevention. Based on provider reports, public health reminders to clinicians to consider WNV testing of both serum and CSF for ill patients are needed, especially among those patients with possible neuroinvasive disease. In addition, providers should be aware of potential cross-reactivity with other flaviviruses (e.g., St. Louis encephalitis and dengue) and potential false-positive results of the mumps IgM test; this has not been described previously and requires further evaluation.

The findings in this report are subject to at least three limitations. First, most cases identified were neuroinvasive disease, suggesting underrecognition of nonneuroinvasive disease, either because of mild illness, consideration of alternative etiologies (e.g., COVID-19), or low provider awareness about WNV. Previous estimates indicate that approximately 30–70 nonneuroinvasive cases occur for every neuroinvasive case identified (*10*); thus, surveillance data likely underestimate the true magnitude of this outbreak. Second, it was not possible to determine receipt of public messaging to ensure outreach to all areas of the county. Health education messaging materials developed for previous WNV outbreaks might be outdated; local, state, and federal agencies are currently partnering to update media campaigns. Finally, delays in laboratory testing affected timeliness of case investigation and implementation

[¶] https://www.weather.gov/fgz/Monsoon

of prevention measures, slowed identification of response thresholds, and delayed the public health response.

WNV continues to cause serious illness and affects health care capacity, especially when outbreaks co-occur with other diseases, such as COVID-19. Increasing temperatures might extend the period during which mosquitos can multiply, potentially prolonging the WNV season in relation to the local environmental conditions (*9*). Analyses are underway to identify data thresholds for increased public and provider messaging on prevention, diagnosis, and testing. Timely and coordinated mosquito and human case surveillance are critical to identifying outbreaks and guiding prevention efforts.

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