A decade of West Nile virus in South Dakota: 
human epidemiology 2002 – 2011

(Lon Kightlinger)

West Nile virus (WNV), a mosquito-borne flavivirus, was first detected in North America during the summer of 1999 in New York City. Over the next several years WNV swarmed across North America, reaching South Dakota in 2002 and all contiguous 48 United States by 2006. During the 10 years since WNV was first detected in South Dakota 1,759 people have been reported and confirmed ill and 26 individuals have died. Although we are unable to predict WNV’s activity during the next decade, it is prudent to expect it to persist as a public health threat to South Dakota into the foreseeable future.

*Culex tarsalis* mosquitoes are the insect vector of WNV in South Dakota and birds are the primary reservoir of the virus. Humans are among the accidental mammalian hosts. Human infection is generally asymptomatic, but approximately 20% of human infections cause acute febrile illness (West Nile fever) and about 1% develops more severe neuroinvasive syndromes including meningitis, encephalitis and acute flaccid paralysis or poliomyelitis. Approximately 10% of WNV neuroinvasive cases are fatal. Since WNV disease is a relatively recent occurrence in the United States the long-term health problems of those infected are not yet well understood.

**West Nile cases and deaths in South Dakota and the United States, 1999-2011**

<table>
<thead>
<tr>
<th>Year</th>
<th>Neuro-invasive</th>
<th>Fever</th>
<th>Total cases</th>
<th>Deaths</th>
<th>Neuro-invasive</th>
<th>Fever</th>
<th>Total cases</th>
<th>Deaths</th>
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<td>0</td>
<td>474</td>
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<td>17,393</td>
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*2011 United States data is provisional, South Dakota is complete

Since 1999 there have been 31,392 reported cases of human WNV disease and 1,263 WNV-associated deaths in the United States. In South Dakota 1,759 human WNV disease cases, including 332 cases of WNV neuroinvasive cases and 26 WNV-associated deaths, have been reported since 2002. The peak outbreak year in South Dakota was 2003 when 1,039 human WNV cases and 14 deaths were reported, while 2011 had the fewest with only 2 confirmed cases. During the 2003 WNV outbreak South Dakota had 10.5% of reported WNV cases in the
nation and 5.3% of deaths. During the past 10 years there have also been 119 viremic blood donors, 2 cases of WNV transmission through blood transfusion, and 16 cases of pregnancy-associated WNV illness reported in South Dakota.

Human WNV cases have been reported in residents of all 66 South Dakota counties over the past decade. The annual average rate of disease in South Dakota has been 21.6 cases per 100,000 population over the past 10 years. Brown County reported the most cumulative WNV cases, 203, and Deuel and Jerauld counties have had the fewest case, 4. Sanborn County had the highest average annual incidence of WNV disease was (84.9 cases per year per 100,000 population), whereas Minnehaha County had the lowest incidence (5.8 cases per year per 100,000 population). Nearly every city, town and village in the state had human WNV cases reported over the past decade. Ten communities reported 20 or more cases during the 10-year period: Rapid City 160, Aberdeen 154, Sioux Falls 81, Mitchell 62, Pierre 62, Belle Fourche 37, Spearfish 27, Huron 22, Sturgis 20 and Vermillion 20.

**West Nile cases reported 2002-2011 (upper number) and average annual disease rate per 100,000 population (lower number in parenthesis), South Dakota.** State rate 21.6.

- White counties: low incidence <20 cases per 100,000 population per year.
- Yellow (light gray) counties: medium incidence 20-39 cases per 100,000 population per year.
- Blue counties (dark gray): high incidence ≥40 cases per 100,000 population per year.

People in all age groups have been infected, sickened and killed by WNV in South Dakota. The youngest death was a baby less than 6 months of age, while the oldest case was 96 and the oldest death was 92 years of age. People in their 70’s had the highest risk of developing neuroinvasive disease, while middle-age people in their 40’s had the highest rate of WNV fever diagnosis. The elderly had the highest death rate with 77% of all WNV-associated deaths being among people 70 years and older. The WNV disease rates appeared to be normally distributed among the race groups in South Dakota with White people accounting for 91% of reported cases and 81% of
deaths, while American Indians accounted for 9% of cases and 15% of deaths. Other race groups comprised <1% of cases. People who are immunocompromised, pregnant or have had organ transplants are at higher risk of severe WNV disease.

West Nile disease is a seasonal illness in South Dakota associated with the ecology, distribution and infectiousness of the *Culex tarsalis* mosquito vector and the bird reservoirs. Following the bite of a WNV infectious mosquito there is a 2 to 15 day incubation period before a person becomes ill. Although cases have occurred from May to October in South Dakota, 98% of cases became ill during July, August and September, with 64% of cases occurring during August. The earliest case onset was 8 May 2004 and the latest case in the season was 17 October 2005.
As we enter the eleventh season of WNV transmission in South Dakota, and the fourteenth year in the United States, a human vaccine is still not licensed, and specific treatment regimens are still experimental. The lack of vaccine prevention and solid medical treatment leaves mosquito avoidance and mosquito control as the primary means of WNV prevention. The screening of donated blood has made blood transfusions safer.

The most important WNV prevention measures are mosquito avoidance and mosquito control. Mosquito avoidance includes limiting time outdoors, wearing protective clothing, screening windows and doors, sleeping under bed nets, avoiding infested areas and discouraging mosquito bites by using repellents containing DEET, Picaridin, Oil of Lemon Eucalyptus or IR3535. Mosquito control measures include elimination of standing water on personal and public property, and community-wide mosquito larval control and adulticide spraying. South Dakota communities have made considerable progress fighting the mosquitoes. In 2001, prior to the emergence of WNV, 8 South Dakota communities claimed to have mosquito control programs. Six years later, of the 233 South Dakota municipalities and tribes surveyed, 65% said they were using larvicidal control, 84% were doing adulticide spraying mosquito control, and 63% of communities were doing both.

Over the past 10 years human WNV infection has caused extensive disease and death in South Dakota. Although the infection rate has decreased since 2003 this mosquito-borne disease is unpredictable and may persist as a public health threat into the foreseeable future.

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**Public health surveillance case definition for West Nile disease and other arboviral diseases**

[California Serogroup Viruses, i.e., California encephalitis, Jamestown Canyon, Keystone, La Crosse, Snowshoe hare, and Trivittatus viruses], Eastern Equine Encephalitis Virus, Powassan Virus, St. Louis Encephalitis Virus, West Nile Virus, Western Equine Encephalitis Virus]


**Background:** Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies, or midges. Other modes of transmission for some arboviruses include blood transfusion, organ transplantation, perinatal transmission, consumption of unpasteurized dairy products, breast feeding, and laboratory exposures.

**Clinical description:** Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purposes of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: neuroinvasive disease and non-neuroinvasive disease.

**Neuroinvasive disease:** Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with stiff neck, altered mental status, seizures, limb weakness, cerebrospinal fluid (CSF) pleocytosis, or abnormal neuroimaging. AFP may result from anterior ("polio") myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barré syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

Non-neuroinvasive disease: Most arboviruses are capable of causing an acute systemic febrile illness (e.g., West Nile fever) that may include headache, myalgias, arthralgias, rash, or gastrointestinal symptoms. Rarely, myocarditis, pancreatitis, hepatitis, or ocular manifestations such as chorioretinitis and iridocyclitis can occur.

**Clinical criteria for diagnosis:** A clinically compatible case of arboviral disease is defined as follows:

**Neuroinvasive disease**
- Fever (\(\geq 38.3^\circ C\)) as reported by the patient or a health-care provider, **AND**
- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurologic dysfunction, as documented by a physician, **AND**
- Absence of a more likely clinical explanation.

**Non-neuroinvasive disease**
- Fever (\(\geq 38.3^\circ C\)) as reported by the patient or a health-care provider, **AND**
- Absence of neuroinvasive disease, **AND**
- Absence of a more likely clinical explanation.
Laboratory criteria for diagnosis
- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- 4-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred, OR
- Virus-specific IgM antibodies in CSF or serum.

Case classification
**Confirmed cases:**
*Neuroinvasive disease:* A case that meets the above clinical criteria for neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:
- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- 4-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

*Non-neuroinvasive disease:* A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:
- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- 4-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

**Probable cases:**
*Neuroinvasive disease:* A case that meets the above clinical criteria for neuroinvasive disease and the laboratory criteria for a probable case:
- Virus-specific IgM antibodies in CSF or serum but with no other testing.

**Virus-specific IgM antibodies in CSF or serum but with no other testing.**

Comments on Interpreting arboviral laboratory results
- **Serologic cross-reactivity.** In some instances, arboviruses from the same genus produce cross-reactive antibodies. In geographic areas where two or more closely-related arboviruses occur, serologic testing for more than one virus may be needed and results compared to determine the specific causative virus. For example, such testing might be needed to distinguish antibodies resulting from infections within genera, e.g., flaviviruses such as West Nile, St. Louis encephalitis, Powassan, Dengue, or Japanese encephalitis viruses.

- **Rise and fall of IgM antibodies.** For most arboviral infections, IgM antibodies are generally first detectable at 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented (e.g., up to 500 days for West Nile virus). Serum collected within 8 days of illness onset may not have detectable IgM and testing should be repeated on a convalescent-phase sample to rule out arboviral infection in those with a compatible clinical syndrome.

- **Persistence of IgM antibodies.** Arboviral IgM antibodies may be detected in some patients months or years after their acute infection. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a 4-fold or greater change in virus-specific antibody titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient’s recent illness. Clinical and epidemiologic history also should be carefully considered.

- **Persistence of IgG and neutralizing antibodies.** Arboviral IgG and neutralizing antibodies can persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of these antibodies alone is only evidence of previous infection and clinically compatible cases with the presence of IgG, but not IgM, should be evaluated for other etiologic agents.

- **Arboviral serologic assays.** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed. Confirmatory testing involves the detection of arbovirus-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test (PRNT).

- **Other information to consider.** Vaccination history, detailed travel history, date of onset of symptoms, and knowledge of potentially cross-reactive arboviruses known to circulate in the geographic area should be considered when interpreting results.