

WEST NILE VIRUS DISEASE

(West Nile Virus Encephalitis, WNV)

REPORTING INFORMATION

- **Class B1:** Report by the end of the next business day in which the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
 - [Ohio Confidential Reportable Disease form](#) (HEA 3334, rev. 1/09), [Positive Laboratory Findings for Reportable Disease form](#) (HEA 3333, rev. 8/05), the local public health department via the Ohio Disease Reporting System (ODRS) or telephone.
- The Centers for Disease Control and Prevention (CDC) [Mosquito borne Illness Case Investigation worksheet](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS not send to ODH, unless otherwise requested. If requested, the mailing address for this form is: Ohio Department of Health, Outbreak Response and Bioterrorism Investigation Team, 246 N. High St., Columbus, OH 43215.
- Additional reporting information, with specifics regarding the key fields for ODRS reporting, can be located in [Section 7](#).

AGENT

West Nile virus is a flavivirus that cross reacts serologically with other flaviviruses (e.g., St. Louis encephalitis virus [SLE], yellow fever virus, dengue virus, Japanese encephalitis virus).

Infectious dose: A single bite of an infectious mosquito.

CASE DEFINITION

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.

Clinical Criteria for Diagnosis

Neuroinvasive disease: A clinically compatible case of neuroinvasive arboviral disease is defined as follows:

- Fever ($\geq 100.4^{\circ}\text{F}$ or 38°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: A clinically compatible case of non-neuroinvasive arboviral disease is defined as follows:

- Fever ($\geq 100.4^{\circ}\text{F}$ or 38°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, cerebrospinal fluid (CSF) or other body fluid *or*
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera *or*
- Virus-specific immunoglobulin M (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

Probable:

- Neuroinvasive case: A case that meets the above clinical criteria for neuroinvasive disease and with virus-specific IgM antibodies in CSF or serum but with no other testing.
- Non-neuroinvasive case: A case that meets the above clinical criteria for non-neuroinvasive disease and with virus-specific IgM antibodies in CSF or serum but with no other testing.

Confirmed:

- Neuroinvasive case: A case that meets the above clinical criteria for neuroinvasive disease and one or more 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*
 - Four-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 case: 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*
 - Four-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.

Comment

The seasonality of West Nile Virus encephalitis is predictable. In Ohio, cases can occur from May to October, when the specific vector mosquito is active.

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 fourfold 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 arboviral-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.

SIGNS AND SYMPTOMS

Two clinical syndromes of WNV are described: (1) "Non-Neuroinvasive Disease" – formerly known as West Nile fever, includes a febrile headache, possibly with nausea and vomiting; (2) "Neuroinvasive Disease" – includes fever and stiff neck, possibly with other symptoms of meningeal irritation, altered level of consciousness (disorientation, lethargy, stupor, coma) and signs of neurological dysfunction (tremor, rigidity, convulsion).

It is estimated that 20% of the people who become infected will develop non-neuroinvasive disease: mild symptoms including fever, headache and body aches, occasionally with a skin rash on the trunk of the body and swollen lymph glands.

The symptoms of severe infection (West Nile neuroinvasive disease) include headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness and paralysis. It is estimated that 1 in 150 persons infected with the West Nile virus will develop a more severe form of disease. Older patients experience a more severe clinical course.

DIAGNOSIS

Preliminary diagnosis is often based on the patient's clinical features, places and dates of travel (if patient is from a non-endemic country or area), activities and epidemiologic history of the location where infection occurred.

Laboratory diagnosis of WNV infections is generally accomplished by testing of serum or CSF to detect virus-specific IgM and neutralizing antibodies.

Four FDA-cleared WNV IgM ELISA kits from different manufacturers are commercially available in the U.S. According to the package inserts, each of these kits is indicated for use on serum to aid in the presumptive laboratory diagnosis of WNV infection in patients with clinical symptoms of meningitis or encephalitis. The package inserts also state that all positive results obtained with any of the commercially-available WNV test kits should be confirmed by additional testing at a state health department laboratory or CDC.

In fatal cases, nucleic acid amplification, histopathology with immunohistochemistry and virus culture of autopsy tissues can also be useful. Only a few state laboratories or other specialized laboratories, including those at CDC, are capable of doing this specialized testing.

EPIDEMIOLOGY

Source

The principle vector in Ohio is the Northern House mosquito, *Culex pipiens*. However, WNV has been detected in many other mosquito species. The role of these other mosquitoes as bridge vectors is under investigation. Birds are the amplification host. Humans are dead-end hosts.

Occurrence

WNV was not known in the western hemisphere until 1999 when it first appeared in New York. Since 1999, widespread epidemics of WNV have occurred in North America. The elderly experience more morbidity and mortality from WNV than children, giving WNV epidemics a distinctive age distribution. However, all age groups are affected. Ohio was hit hardest in 2002 with 441 cases, 31 of which were fatalities. In 2003, CDC reported 9,862 cases from 46 states, including 108 cases from Ohio. Most recently, Ohio reported 5 cases in 2010.

Mode of Transmission

WNV is transmitted to humans through the bite of infected *Culex* or possibly other species of mosquitoes. Spring/Summer amplification of virus occurs in avians. The over-wintering mechanism is not yet known.

Period of Communicability

Humans are dead-end hosts for the virus, i.e., they do not circulate sufficient numbers of the WNV in the blood stream to infect a mosquito, and the disease can not be spread from person to person. However, the disease can be

transmitted via blood transfusions and organ transplants. Since 2003, the blood supply in the USA has been screened for WNV.

Incubation Period

3 to 15 days.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

With serologic identification of WNV infection, a complete travel history for the three weeks prior to onset is obtained. The patient should also be questioned about donating or receiving blood, blood products and organs in the 4 weeks prior to onset of symptoms. Sites of outdoor exposure and activities can be evaluated for the presence of *Culex* mosquitoes by standard collection techniques (shelter collections, light traps, larval samples, bait traps and gravid traps). Mosquitoes collected should be immediately placed on dry ice in sealed air-tight tubes and sent to the Zoonotic Disease Program for arboviral assay. The geographic extent of WNV activity can be estimated by an avian serosurvey.

Treatment

There is no specific treatment for WNV. Supportive therapy is indicated.

Isolation and Follow-up Specimens

Since the diagnosis of WNV is often not known until after patient discharge, enteroviral precautions (i.e. fecal, respiratory) are usually indicated for encephalitis.

Follow-up specimens are not required for cases diagnosed by the presence of WNV in a CSF sample, along with the absence of SLE in the same sample. A plaque-reduction neutralization test is required for confirmatory testing.

Public Health Significance

Significant. Identification of a single case of WNV during the summer months might signify that an outbreak is developing. A statewide epidemic of WNV occurred in 2002.

Contacts

No treatment or prophylaxis of contacts is indicated.

Prevention and Control

Vaccination

There is no vaccine for human use.

Vector Investigation

Likelihood of WNV transmission is reduced if populations of the vector species, *Culex pipiens*, are kept under control by larviciding and control of breeding sites, including catch basins and backyard containers (tires, cans, bottles) in urban areas. Sewage-polluted ditches and stagnant water are more important in the rural setting. Education of the public about backyard breeding sites, screening of windows and personal protection are also recommended as a means of preventing cases. An incidence of 1.5 or more dead birds per square mile per week is an indicator of increased risk of human infection. For advice on vector assessment, contact the Zoonotic Disease Program at 614-752-1029.

Because of the potential for epidemic WNV, the diagnosis of a single human case should be followed by control of adult mosquitoes by aerosol application (ultra-low volume cold fog) of an approved pesticide. This is required to break the transmission cycle.

Special Information

The risk of exposure to WNV is statewide because the northern house mosquito is abundant and has been found in every county.

The Ohio Department of Health, in cooperation with local health departments and mosquito control districts, conducts a program of surveillance for WNV/ flavivirus activity by testing mosquitoes for WNV and flavivirus. Any positive findings will be reported to our cooperators.

What is West Nile Virus?

West Nile virus causes serious illness in humans, horses and birds bitten by infected mosquitoes. Disease has rarely been reported in cats, dogs and other mammals; most mammals are not susceptible even if bitten by an infected mosquito.

West Nile virus has been described in Africa, Europe, the Middle East, Asia and most recently, North America. It first appeared in the United States in 1999, when New York experienced an outbreak affecting 62 people which resulted in 7 deaths. Since then, it has spread rapidly across North America, affecting almost the entire continent.

Nearly 1,000 human cases of West Nile virus are reported annually in the U.S. This is down from the 2003 high of nearly 10,000 cases. Ohio was hit hardest in 2002 with 441 cases, 31 of which were fatalities. As in the rest of the U.S., the number of cases has declined since 2003, and now averages approximately 20 per year. The transmission dynamics of WNV are dependent on short-term weather patterns, such as heat, drought or floods, so future outbreaks involving a large number of cases are possible.

How is West Nile virus spread?

This virus is spread by the bite of a West Nile virus-infected mosquito. Mosquitoes get infected with West Nile virus by feeding on infected birds. Infected mammals do not pass the virus to mosquitoes because there are not enough viruses circulating in their blood. West Nile virus can not be spread directly from one person to another. However, it can be spread through blood transfusions from infected persons. Since, 2003, all donated blood is screened for West Nile virus in the U.S.

Can anyone get West Nile virus?

Yes, anyone can get infected with West Nile virus. More severe infections are seen in the elderly and those with a weakened immune system.

What are the symptoms of a West Nile virus infection?

Approximately 80% of people infected with West Nile virus do not become ill. Most of those who develop symptoms have a mild infection known as West Nile fever, which presents with fever, headache, eye pain, muscle aches, joint pain, a rash on the trunk and swollen lymph nodes. Severe cases involving the central nervous system are called neuroinvasive West Nile virus. This occurs in an estimated 1 in 150 cases. The symptoms may include extreme muscle weakness, inflammation of the brain (encephalitis), confusion, paralysis and coma. In rare cases, the infection may be fatal, particularly in the elderly and people with other medical conditions.

How long after exposure before symptoms appear?

Symptoms usually occur 5 to 15 days after an infected mosquito bites.

How is West Nile virus diagnosed?

Specific antibodies can be detected in blood or spinal fluid. Tests for the actual virus also exist, but these results may take weeks.

Does past infection with this virus make a person immune?

Yes. Prior infection with West Nile virus can provide lifelong immunity to the virus.

What is the treatment for West Nile virus infection?

There is no specific treatment for WNV. Antibiotics are not effective against viruses, and no effective anti-viral drugs have been discovered. Patient care centers on the treatment of symptoms and complications.

Is there a vaccine for West Nile virus?

There is not currently a vaccine available for humans, but they are currently under development. There are vaccines for horses available through veterinarians.

How can I prevent West Nile Virus?

Prevent mosquito bites. It only takes one bite from an infected mosquito to transmit disease.

Avoid mosquito bites.

- Avoid areas where mosquitoes are active.
- Avoid outdoor activities during the peak mosquito biting times of dawn, dusk and early evening.
- When outdoors, apply mosquito repellent as directed to clothing and exposed skin.
- Reapply mosquito repellent as needed, especially if swimming or sweating.
- Clothing will help protect you from mosquito bites. If weather permits, wear long pants, long sleeves and/or socks.
- Install or repair window and door screens to keep mosquitoes outside.

Eliminate mosquito breeding sites.

- At least once or twice a week, empty water from flower pots, pet food and water dishes, birdbaths, swimming pool covers, buckets, barrels and cans.
- Check for clogged rain gutters and clean them out.
- Remove discarded tires and other items that could collect water.
- Be sure to check for containers or trash in places that may be hard to see, such as under bushes or under your home.

For more information, please visit these Web sites:

CDC West Nile Page <http://www.cdc.gov/ncidod/dvbid/westnile/index.htm>

CDC insect repellent use and safety
http://www.cdc.gov/ncidod/dvbid/westnile/ga/insect_repellent.htm

West Nile Facts http://www.cdc.gov/ncidod/dvbid/westnile/wnv_factsheet.htm