

WEST NILE VIRUS DISEASE

(West Nile Virus Encephalitis, WNV)

REPORTING INFORMATION

- **Class B:** Report by the end of the next business day after 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)
 - Via the Ohio Disease Reporting System (ODRS) or telephone
 - The Ohio Department of Health (ODH) [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 and not sent to ODH, unless otherwise requested. If requested, the form can be faxed to ODH at 614-564-2456.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset and all the fields in the Epidemiology module.

AGENT

West Nile virus is an RNA virus belonging to the genus *Flavivirus* of the family *Flaviviridae*. There is substantial serologic cross reaction with other flaviviruses (e.g., St. Louis encephalitis, yellow fever, dengue, Powassan, Japanese encephalitis viruses).

Infectious dose: A single bite from 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.

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 headache, myalgia, stiff neck, altered mental status, seizures, limb weakness or CSF pleocytosis. AFP may result from anterior ("polio") myelitis, peripheral neuritis or post-infectious peripheral demyelinating neuropathy (i.e. Guillain-Barre 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, rash or gastrointestinal symptoms. Other physical complaints include vertigo, stiff neck or muscle weakness without progression to more clinically apparent neurological involvement.

Clinical Criteria for Diagnosis

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

Neuroinvasive disease:

- 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 or chills as reported by the patient or a healthcare 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 or serum.

Case Classification

Probable:

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

Confirmed:

- Neuroinvasive disease: 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 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 or other body fluid excluding CSF 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.

Comments

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

Imported arboviral diseases: Human disease cases due to dengue or yellow fever are nationally notifiable to CDC using specific case definitions. However, many other exotic arboviruses (e.g. chikungunya, Japanese encephalitis, tick-borne encephalitis, Venezuelan equine encephalitis and Rift Valley fever viruses) important public health risks for the United States as competent vectors exist that could allow for sustained transmission upon establishment of imported arboviral pathogens. Healthcare providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual arboviral etiology, particularly in international travelers. If a suspected case occurs, it should be reported to the appropriate local/state health agencies and CDC.

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 West Nile virus 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 with mild symptoms including fever, headache and body aches, occasionally with a skin rash on the trunk of the body, gastrointestinal symptoms 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% of persons infected with the West Nile virus will develop a more severe form of disease (e.g. meningitis, encephalitis, acute flaccid paralysis). Older patients experience a more severe clinical course. West Nile virus meningitis is clinically indistinguishable from aseptic meningitis caused by other viruses. Patients with West Nile virus encephalitis usually experience seizures, mental status changes, focal neurologic deficits or movement disorders. Acute flaccid paralysis from West Nile virus is often identical to poliovirus-associated poliomyelitis with damage of anterior horn cells and may progress to respiratory paralysis requiring mechanical ventilation. Other rare severe manifestations of West Nile virus have been reported and include cardiac dysrhythmias, myocarditis, rhabdomyolysis, optic neuritis, uveitis, chorioretinitis, orchitis, pancreatitis and hepatitis.

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. In addition to other more common causes of encephalitis and aseptic meningitis (e.g., herpes simplex virus and enteroviruses), arboviruses such as LaCrosse, St. Louis encephalitis, Eastern equine encephalitis, Western equine encephalitis, Powassan and West Nile viruses should also be considered in the differential etiology.

Laboratory diagnosis of West Nile virus infections is generally accomplished by testing of serum or CSF to detect virus-specific IgM and neutralizing antibodies. The presence of West Nile virus IgM antibodies is usually good evidence of recent West Nile virus infection, but may indicate infection with another closely related flavivirus (e.g. St. Louis encephalitis). For a West Nile virus case to be considered confirmed, serum samples that are antibody-positive on the initial screening should be evaluated by a more specific test; currently, the plaque reduction neutralization test (PRNT) is recommended for differentiating between flavivirus infections. Because West Nile virus IgM antibodies can remain detectable in some patients for >1 year, a

positive IgM antibody test result occasionally may reflect past infection unrelated to the current illness. Serum collected within 8 days of illness onset may lack detectable IgM, so the test should be repeated on a convalescent phase serum. West Nile virus IgG antibodies are generally detectable shortly after the appearance of IgM and persist for years.

Four FDA-cleared West Nile virus IgM ELISA kits from different manufacturers are commercially available in the U.S. There is also a microsphere-based immunoassay (MIA) available that can detect IgM antibodies and differentiate between West Nile and St. Louis encephalitis viruses.

Several tests have been developed to detect viable West Nile virus, West Nile virus antigen or West Nile virus RNA. These tests vary in sensitivity, specificity and the time required to conduct the test. Among the most sensitive tests are those using real-time PCR (RT-PCR) to detect West Nile virus RNA in human cerebrospinal fluid, serum and other tissues. Despite the sensitivity of the RT-PCR test, it is limited in its ability to diagnose human West Nile virus neuroinvasive disease because of the low level viremia present in most cases at the time of clinical presentation. However, nucleic acid amplification tests (NAAT) may be useful for diagnosing immunocompromised patients, who may have a delayed or absent antibody development.

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.

EPIDEMIOLGY

Source

The principle vector in Ohio is the Northern House mosquito, *Culex pipiens*. However, West Nile virus 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

West Nile virus was not known in the western hemisphere until 1999 when it first appeared in New York. Since 1999, widespread epidemics of West Nile virus disease have occurred in North America. The elderly experience more morbidity and mortality from West Nile virus than children, giving West Nile virus 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, CDC reported 5,674 cases including 286 deaths from 48 states, and Ohio reported 122 cases including 7 deaths in 2012.

Mode of Transmission

West Nile virus is primarily 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. Although rare, person-to-person transmission can occur through transfusion of infected blood products, transplantation of infected organs, intrauterinely to infants and through human milk. Percutaneous and aerosol infection have also

occurred in laboratory workers. Since 2003, the blood supply in the USA has been screened for West Nile virus.

Period of Communicability

Humans are dead-end hosts for the virus (i.e. they do not circulate sufficient numbers of the virus in the blood stream to infect a mosquito). The disease cannot be spread from person to person.

Incubation Period

2 to 14 days.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

With serologic identification of West Nile virus 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. Female patients should be asked whether they were pregnant at the time of infection, and infants should be checked whether they were breastfed before illness onset. 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).

Treatment

There is no specific treatment for West Nile virus disease. Supportive therapy is indicated.

Isolation and Follow-up Specimens

Since the diagnosis of West Nile virus 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 West Nile virus in a CSF sample, along with the absence of St. Louis encephalitis virus in the same sample. A plaque reduction neutralization test (PRNT) is required for confirmatory testing.

Public Health Significance

Significant. Identification of a single case of West Nile virus during the summer months might signify that an outbreak is developing. Statewide epidemics of West Nile virus occurred in 2002 and 2012.

Contacts

No treatment or prophylaxis of contacts is indicated.

Blood, Tissue and Organ Donors

Since 2003, the U.S. blood supply has been routinely screened for West Nile virus RNA, usually with nucleic acid amplification tests (NAAT). These tests are very sensitive, but not very specific. Blood banks usually re-test after a first positive with either an antibody test (IgM or IgG) or an ultra-sensitive PCR test. The initial NAAT screening tests may pick up on a West Nile virus infection before an appropriate antibody response develops.

Donors who test positive for West Nile virus screening tests should be asked whether they developed any symptoms, particularly a fever, after or at the time of their donation. Those meeting the clinical case definition are reported as West Nile virus cases. Those who do not meet the clinical case definition are not counted as cases but are reported to the CDC as asymptomatic viremic donors.

Whether symptomatic or not, all donors positive for West Nile virus or reported cases who donated blood, tissue or organs in the four weeks prior to illness onset warrant follow-up with the blood or tissue bank. The donor's blood or tissue products should be destroyed or quarantined, and any recipients of products should be identified so they can be managed appropriately.

Prevention and Control

Vaccination

There is no vaccine for human use.

Vector Investigation

Likelihood of West Nile virus 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 ODH Zoonotic Disease Program (ZDP) at 614-752-1029.

Because of the potential for epidemic West Nile virus disease, 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. For health jurisdictions utilizing mosquito control programs outside their own agency, the Ohio Revised Code allows for the sharing of protected health information to mitigate a threat to the public's health.

Ohio Revised Code 3701.17 (B4) states,

"The director determines the release of the information is necessary, based on an evaluation of relevant information, to avert or mitigate a clear threat to an individual or to the public health. Information may be released pursuant to this division only to those persons or entities necessary to control, prevent, or mitigate disease."

Special Information

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

What is West Nile virus?

West Nile virus is an arthropod-borne virus (arbovirus) most commonly spread by infected mosquitoes. West Nile virus can cause febrile illness, encephalitis (inflammation of the brain) or meningitis (inflammation of the lining of the brain and spinal cord).

West Nile virus transmission has been documented in Europe and the Middle East, Africa, India, parts of Asia and Australia. It was first detected in the United States in 1999, and has since spread across the continental United States and Canada.

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 declined in Ohio 2003-2011, averaging approximately 20 per year. However, 2012 was another epidemic year with 5,674 cases and 286 deaths from 48 states; Ohio reported 122 cases and 7 deaths in 2012. The transmission dynamics of West Nile virus 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 do people get infected with West Nile virus?

Most people get infected with West Nile virus by the bite of an infected mosquito. Mosquitoes become infected when they feed on infected birds. Infected mosquitoes can then spread the virus to humans and other animals

In a very small number of cases, West Nile has been spread through blood transfusions, organ transplants and from mother to baby during pregnancy, delivery or breastfeeding. Since 2003, all donated blood is screened for West Nile virus in the United States.

Who is at risk for infection with West Nile virus?

Anyone living in an area where West Nile virus is present in mosquitoes can get infected. West Nile virus has been detected in all lower 48 states (not in Hawaii or Alaska). Outbreaks have been occurring every summer since 1999. The risk of infection is highest for people who work outside or participate in outdoor activities because of greater exposure to mosquitoes.

Is there a vaccine available to protect people from West Nile virus?

No. Currently, there is no West Nile virus vaccine available for people. Many scientists are working on this issue, and there is hope that a vaccine will become available in the future. There are vaccines for horses available through veterinarians.

How soon do people get sick after getting bitten by an infected mosquito?

The incubation period is usually 2 to 6 days but ranges 2 to 14 days. This period can be longer in people with certain medical conditions that affect the immune system.

What are the symptoms of a West Nile virus disease?

No symptoms in most people. Most people (70%-80%) who become infected with West Nile virus do not develop any symptoms.

Febrile illness in some people. About 1 in 5 people who are infected will develop a fever with other symptoms such as headache, body aches, joint pains, vomiting, diarrhea or rash. Most people with this type of West Nile virus disease recover completely, but fatigue and weakness can last for weeks or months.

Severe symptoms in a few people. Less than 1% of people who are infected will develop a serious neurologic illness such as encephalitis or meningitis (inflammation of the brain or surrounding tissues). The symptoms of neurologic illness can include headache, high fever, neck stiffness, disorientation, coma, tremors, seizures or paralysis. Recovery from severe disease may take several weeks or months. Some of the neurologic effects may be permanent. About 10% of people who develop neurologic infection due to West Nile virus will die.

Who is at risk for serious illness if infected with West Nile virus?

People with certain medical conditions such as cancer, diabetes, hypertension and kidney disease are also at greater risk for serious illness.

What should I do if I think a family member might have West Nile virus disease?

Consult a healthcare provider for evaluation and diagnosis.

How is West Nile virus diagnosed?

Diagnosis is based on a combination of clinical signs and symptoms and specialized laboratory tests of blood or spinal fluid. These tests typically detect antibodies that the immune system makes against the viral infection.

What is the treatment for West Nile virus disease?

There are no medications to treat or vaccines to prevent West Nile virus infection. Over-the-counter pain relievers can be used to reduce fever and relieve some symptoms. People with milder symptoms typically recover on their own, although some symptoms may last for several weeks. In more serious cases, patients often need to be hospitalized to receive supportive treatment such as intravenous fluids, pain medications and nursing care.

When do most cases of West Nile virus disease occur?

Most people are infected from June through September.

Where do most cases of West Nile virus disease occur?

West Nile virus disease cases have been reported from all 48 lower states. The only states that have not reported cases are Alaska and Hawaii. Seasonal outbreaks often occur in local areas that can vary from year to year. The weather, number of birds that maintain the virus, numbers of mosquitoes that spread the virus and human behavior are all factors that can influence when and where outbreaks occur.

How do people reduce the chance of getting infected?

The most effective way to avoid West Nile virus disease is to prevent mosquito bites. It only takes one bite from an infected mosquito to transmit disease.

- Use mosquito repellent when you go outdoors. Repellents containing DEET, picaridin, IR3535 and some oil of lemon eucalyptus and para-methane-diol products provide longer-lasting protection.
- Wear long sleeves and pants from dusk through dawn when many mosquitoes are most active.

- Install or repair screens on windows and doors. If you have it, use your air conditioning.
- Help reduce the number of mosquitoes around your home. Empty standing water from containers such as flower pots, gutters, buckets, pool covers, pet water dishes, discarded tires and birdbaths.

For more information, please visit these websites:

CDC West Nile Information <http://www.cdc.gov/westnile/index.htm>

CDC Insect Repellant Use and Safety <http://www.cdc.gov/westnile/faq/repellent.html>

U.S. Geological Survey West Nile Virus Human Case Maps

http://diseasemaps.usgs.gov/wnv_us_human.html