

West Nile Virus Disease

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To identify areas in which West Nile virus (WNV) is being transmitted.
2. To target public education about reducing mosquito habitats and preventing mosquito bites.
3. To provide information for mosquito control and environmental health initiatives.
4. To identify periods of time when WNV poses a significant risk to the blood supply.
5. To identify new routes of exposure.

B. Legal Reporting Requirements

1. Health care providers: Notifiable to local health jurisdiction within 3 work days.
2. Hospitals: Notifiable to local health jurisdiction within 3 work days.
3. Laboratories: Isolation of WNV or detection of virus specific antibody or viral nucleic acid notifiable to local health jurisdiction of the patient's residence within 2 work days.
4. Local health jurisdictions: Notifiable to Washington State Department of Health Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days.
5. Veterinarians: Notifiable to the local health jurisdiction or to Washington State Department of Agriculture.

C. Local Health Jurisdiction Investigation Responsibilities

1. Through investigation, identify unusual exposures and transmission routes other than vector-borne (i.e., donor or recipient of blood products, tissue or organs) within 24 hours of the initial report.
2. Facilitate transport of specimens (e.g., serum or cerebrospinal fluid [CSF]) to the Washington State Public Health Laboratories (PHL) if initial testing or confirmatory testing is needed. Please call CDES prior to submitting specimens (206-418-5500).
3. Report all *confirmed* and *probable* cases to DOH CDES (see definitions below). Complete the West Nile virus case report form (<http://www.doh.wa.gov/notify/forms/wnv.pdf>) and enter the data into the Public Health Issues Management System (PHIMS) as "West Nile Virus Disease" (*Note*: not "Arboviral Disease"). The revised form (August 2009) includes questions for Centers for Disease Control and Prevention WNV enhanced surveillance form.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Background

West Nile virus (WNV) was first isolated in 1937 from a febrile woman in the West Nile District of Uganda. WNV was first recognized as a cause of severe meningoencephalitis

in elderly patients during an outbreak in Israel in 1957. It was first introduced to North America in 1999 in New York City. Since then, WNV has spread across the United States, first reaching Washington in 2002.

A. Etiologic Agent

West Nile virus is a single-stranded RNA virus of the family Flaviviridae, genus Flavivirus. It is a member of the Japanese encephalitis virus serocomplex, which contains several medically important viruses that cause encephalitis in humans: Japanese encephalitis, St. Louis encephalitis, Murray Valley encephalitis, and Kunjin (an Australian subtype of West Nile virus). The close antigenic relationship of the flaviviruses, particularly those belonging to the Japanese encephalitis complex, accounts for the serologic cross-reactions observed in the diagnostic laboratory.

B. Description of Illness

Serosurveys have shown that less than 1% of WNV-infected persons develop serious **WNV neuroinvasive disease (WNND)** which includes encephalitis, meningitis, acute flaccid paralysis (“WNV poliomyelitis”), optic neuritis, and cranial nerve abnormalities. Approximately 20% of infected individuals develop **WN fever (WNF)** and about 80% remain asymptomatic.

The incidence and case-fatality rate of WNND increase with age, with the greatest risk occurring in persons over 50 years old. Among those with severe illness due to West Nile virus, case-fatality rates range from 3% to 15% and are highest among the elderly. However, this differs by clinical syndrome: WN encephalitis has been associated with 10-15% mortality, and WN “poliomyelitis” may have a case-fatality rate exceeding 50%.

WNF is a febrile illness of sudden onset, often accompanied by headache, myalgias, fatigue, and malaise. Gastrointestinal symptoms, rash, and lymphadenopathy occasionally occur. Symptoms generally last 3 to 6 days but may last for weeks. WNF rarely results in fatality.

C. West Nile Virus Infections in Washington State

Washington State agencies conduct surveillance for WNV infections in humans, birds, mosquitoes, horses and other animals. The first detections of the virus in Washington occurred in 2002; the first locally acquired human infections were reported in 2006 from Pierce and Clark counties. As of June 2009, only 6 locally acquired cases have been reported; 19 travel-related cases have also been reported among Washington residents. For current or historical information about WNV in Washington, visit: <http://www.doh.wa.gov/ehp/ts/Zoo/WNV/WNV.html>

D. Vectors and Reservoirs

WNV is maintained in an enzootic cycle involving vector mosquitoes and many bird reservoir species. Although corvids (crows, ravens, magpies, jays) infected with WNV often become ill and die, many infected birds survive and do not have any symptoms. More than 300 native and exotic bird species have been found to be infected with WNV in the United States. Competent bird reservoirs may have virus circulating in their bloodstream for 1 to 4 days after contracting WNV. Mosquitoes that feed on them during that period can become infected.

WNV is transmitted mainly by mosquitoes in the *Culex* subgenus, which occur in Washington State, though many other mosquito species are also known to become infected. Humans, horses, and most other mammals do not develop the high-level viremia that infect mosquitoes, and are considered "dead-end" or incidental hosts.

E. Modes of Transmission

The main route of transmission is through the bite of an infected mosquito. In very rare cases, WNV also has been transmitted through blood transfusions, organ transplants, percutaneous injuries in the laboratory, the placenta, and possibly breast milk.

F. Incubation Period

Usually 2 to 14 days.

G. Period of Communicability

Infected people may develop a short lived (2–3 day) low-level viremia that can contaminate donated blood units; blood collection centers screen donated units to prevent this from occurring. Transmission through organ transplantation, transplacentally, and via breast milk are very rare. WNV is not spread through casual contact such as touching or kissing a person with the virus.

H. Treatment

In the absence of an effective antiviral agent, treatment for WNV infection is supportive. Treatment for WNV often involves hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections.

Controlled trials investigating specific antiviral treatments are ongoing.

3. CASE DEFINITION

A. Clinical Description

Illnesses are classified as either neuroinvasive or non-neuroinvasive, according to the following criteria:

Neuroinvasive disease requires the presence of fever and at least one of the following, as documented by a physician and in the absence of a more likely clinical explanation:

- Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma); or
- Other acute signs of central or peripheral neurologic dysfunction (e.g., paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements); or
- Pleocytosis (increased white blood cell concentration in cerebrospinal fluid [CSF]) associated with illness clinically compatible with meningitis (e.g., headache or stiff neck).

Non-neuroinvasive disease requires, at minimum, all of the following:

- Presence of documented fever, as measured by the patient or clinician; and
- Absence of neuroinvasive disease (as described above); and

- Absence of a more likely clinical explanation for the illness.

Note: involvement of non-neurological organs (e.g., heart, pancreas, liver) can occur and should be documented using standard clinical and laboratory criteria.

B. Laboratory Criteria for Diagnosis

Presumptive:

1. A stable elevated titer (\leq two-fold change) of virus-specific serum antibodies in paired sera; or
2. Serum immunoglobulin M (IgM) antibodies detected by antibody-capture EIA without a confirmatory test for virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen.

Confirmatory:

1. Fourfold or greater change in virus-specific serum antibody titer in paired sera; or
2. Isolation of virus from or demonstration of viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid; or
3. Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA); or
4. Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific IgG antibodies in the same or a later specimen by another serologic method (e.g., plaque reduction neutralization or hemagglutination inhibition).

Note: See “Specimen Collection” section for appropriate timing of specimen collection.

C. Case Classification (2004)

Probable: A clinically compatible case meeting one or more of the presumptive laboratory criteria.

Confirmed: A clinically compatible case meeting one or more of the confirmatory laboratory criteria.

Comment: Asymptomatic presumptive viremic blood donors should be entered into PHIMS, classified as “Suspect” and manually reported. If WNV illness develops after the PVD is first reported, reclassify the report as a case.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

The most efficient diagnostic method for West Nile virus (WNV) infection is detection of virus using the IgM antibody-capture enzyme immunoassay (MAC-EIA) or microsphere immunoassay (MIA) of IgM antibody to WNV in serum collected 8 to 14 days after onset or CSF collected within 8 days of illness onset. More than 90% of those infected have detectible serum IgM 8 days after onset. The EIA can exhibit serologic cross-reactivity in patients who have been recently vaccinated against or recently infected with related

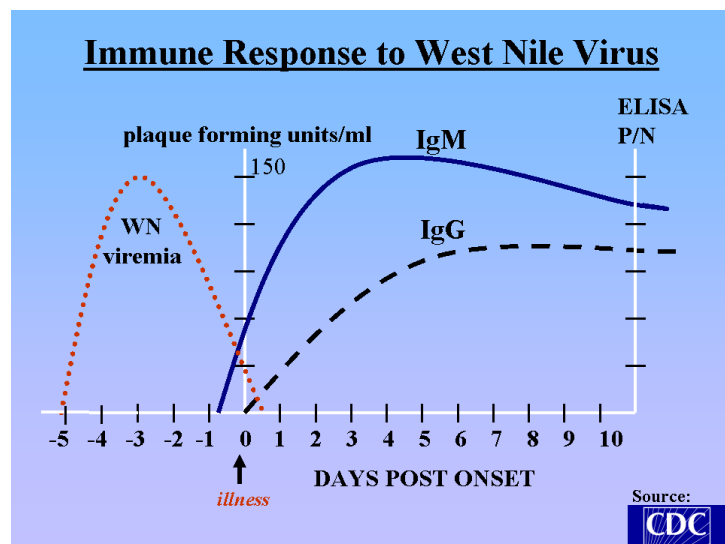
flaviviruses (e.g., Japanese encephalitis, as well as yellow fever and dengue). In addition, since most WNV infections are asymptomatic and IgM can persist in the serum for 12 months or longer, the presence of IgM in residents from an endemic area may indicate a previous rather than current infection.

The diagnosis can also be confirmed by demonstrating a four-fold rise in antibody titer between acute and convalescent (14-21 days after acute) serum specimens. Since serum IgM does not cross the blood-brain barrier, IgM in the CSF strongly suggests central nervous system infection.

The plaque-reduction neutralization test (PRNT) is the most specific test for the arthropod-borne flaviviruses and can be used to help distinguish false-positive results from the MAC-EIA or EIA test.

Reverse transcription polymerase chain reaction (RT-PCR) assay to detect WNV nucleic acid in serum or CSF is useful for evaluation of patients with immune dysfunction, but is not recommended for routine diagnosis of WNV disease.

Other antibody detecting diagnostic assays, such as hemagglutination inhibition and indirect fluorescent antibody tests, may be available at commercial laboratories.



B. Services Available at the Washington State Public Health Laboratories (PHL)

The following WNV tests at PHL can be requested by local health jurisdictions:

1. Enzyme immunoassay (EIA) for IgM antibody in serum or CSF.
2. Microsphere immunoassay (MIA) for IgM antibody in serum or CSF. This assay is more rapid and specific than the EIA.

Until the disease is established in Washington State, PHL will send all positive specimens to the CDC for confirmatory testing by plaque reduction neutralization test (PRNT).

C. Criteria for Testing WNV Specimens at PHL*

All specimens need to be approved by Communicable Disease Epidemiology Section prior to submission. Testing at PHL is appropriate for:

1. Patients with suspected WNV neuroinvasive disease (i.e., fever and change in mental status, CSF pleocytosis, or other acute central or peripheral neurologic dysfunction) when there is no other likely diagnosis.
2. Pregnant or breastfeeding women symptomatic with suspected WNV infection and their neonates or breastfeeding infants.
3. Recent blood, tissue, or organ donors or recipients suspected to have WNV infection.
4. Persons with commercial laboratory evidence of WNV infection to confirm the diagnosis (until human WNV disease is established in Washington State).

* Initial testing should be performed at a commercial laboratory for persons who do not fit in these four categories (i.e., person with West Nile non-neuroinvasive disease).

D. Specimen Collection and Shipping

1. Submit ≥ 2 cc of CSF and/or ≥ 1 cc serum (separated serum, not whole blood or plasma) for EIA/MIA.
 - a. Serum should ideally be obtained ≥ 8 days after onset of symptoms. A second serum specimen will be requested if the first is non-reactive or indeterminate and was obtained less than 8 days after onset of symptoms. Convalescent serum should be drawn 14-21 days after the acute specimen. To confirm the infection, a four-fold rise in antibody titer should be demonstrated between an acute and convalescent serum specimen.
 - b. CSF should ideally be collected 3-8 days after onset. CSF obtained less than 3 days after onset of symptoms will be accepted, however, if non-reactive, the test does not rule out WNV infection and a serum specimen obtained 8 days after onset will be requested.
2. Specimens should be refrigerated and transported cold. Frozen CSF is acceptable. Avoid repeated freeze-thaw cycles. If the specimen is already frozen, ship it frozen (on dry ice). Specimens should be submitted with a completed PHL Virus Examinations form (<http://www.doh.wa.gov/EHSPHL/PHL/Forms/SerVirHIV.pdf>).

5. ROUTINE CASE INVESTIGATIONS

Interview the case or others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Review the laboratory report, clinical description, and epidemiologic factors such as season and known West Nile virus (WNV) activity in the area. If laboratory testing is positive for immunoglobulin M (IgM) and was done at a laboratory other than Washington State Public Health Laboratories (PHL), Communicable Disease Epidemiology Section (CDES) may request facilitating transport of that or another specimen to PHL for further testing.

B. Identify Potential Sources of Infection

Obtain a complete travel history and history of mosquito bites during the 15 day period prior to symptom onset. Ascertain whether the case received blood products, tissues or

organs within 30 days of their WNV infection, and if so, contact CDES immediately and inform the blood or tissue bank of the potential source.

C. Identify Potentially Exposed Persons

Determine if the patient donated blood, tissues or organs, breastfed, or gave birth during the communicable period. If the patient donated blood, tissues or organs in the 30 days prior to onset, contact CDES immediately and inform the blood or tissue bank of the potential blood contamination. In cases of potential mother-to-infant transmission, notify CDES and monitor the infant for compatible signs and symptoms for 14 days after last possible exposure.

D. Environmental Evaluation

Notify local environmental health program and/or vector control of locally acquired cases. In outbreak settings, an investigation may assist in identifying and controlling factors favoring transmission.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations / Case Management

1. Hospitalized patients should be treated with standard precautions.
2. Cases do not require isolation.
3. Infected persons should be advised not to donate blood, tissues or organs.
4. Infected lactating women should discuss with their medical care provider the risks and benefits of breast-feeding.

If the patient received blood products, organs, or tissues in the 30 days prior to onset, contact Communicable Disease Epidemiology Section (CDES) immediately and inform the blood or tissue bank of the potential source.

B. Contact Management

No follow up is needed for household and other close contacts since West Nile virus is not transmitted by close contact. In cases of potential mother-to-infant transmission, notify CDES and monitor the infant for compatible signs and symptoms for 14 days after last possible exposure. Additional testing may be requested to confirm the WNV transmission. If the patient donated blood products, organs or tissues in the 30 days prior to onset, contact CDES immediately and inform the blood or tissue bank of the potential exposure.

C. Management of Other Exposed Persons

People with recent mosquito bites in areas where WNV is circulating should report symptoms of fever, headache, loss of appetite, rash, or stiff neck to their health care provider.

D. Environmental Measures

Environmental measures to reduce WNV transmission may include the elimination of mosquito breeding habitats and the use of chemical (i.e., pesticides) and biological

controls. Consult with local environmental health or vector/mosquito control programs to determine appropriate intervention measures.

7. MANAGING SPECIAL SITUATIONS

A. Presumptive Viremic Donor (PVD)

1. Blood collection agencies routinely screen blood products for West Nile virus (WNV) using nucleic acid-amplification tests (NAT) during months when there is WNV activity.
2. Blood collection agencies report persons whose blood screens positive to Communicable Disease Epidemiology Section (CDES) which, in turn, reports the person to the local health jurisdiction. Local public health professionals should initiate an investigation using the WNV Case Report Form.
3. Persons whose blood donation screens positive for WNV, with either a) a single reactive NAT with a signal-to-cutoff value ≥ 17 or b) two reactive NATs using two different primers/methods, are considered PVDs and no further testing is indicated.
4. If a person's blood donation screens positive for WNV using a less stringent method, the LHJ should assist in obtaining a serum sample drawn 8-14 days after the date of the donation to test for IgM. If IgM is detected and the person remains asymptomatic, the person is a PVD. If IgM is not detected, the NAT should be considered a false positive and the case should be closed.

Note: Clinical Syndrome and Case Classification: All PVDs should be entered into PHIMS, classified as "Suspect" and manually reported to CDES unless WNV illness is documented. If WNV illness develops after the PVD is first reported, please revisit PHIMS to reclassify the patient as a case (see Part 3. Case Definition).

8. ROUTINE PREVENTION

A. Immunization Recommendations

Currently there is no human West Nile virus vaccine available.

B. Prevention Recommendations

1. Reduce exposure to mosquitoes.
 - Make sure windows and doors are "bug tight." Repair or replace screens.
 - Stay indoors at dawn and dusk, if possible, when mosquitoes are most active.
 - Wear a long sleeve shirt, long pants, and a hat when going into mosquito-infested areas, such as wetlands or woods.
 - Use mosquito repellent when necessary. The most effective mosquito repellents contain the EPA approved active ingredients DEET (N, N-diethyl-m-toluamide), Picaridin, oil of lemon eucalyptus, or IR3535. Read and follow instructions on the label. Permethrin is another long-lasting repellent that is intended for application to clothing and gear, but not directly to skin. In general, the more active ingredient (higher concentration) a repellent contains, the longer time it protects against

- mosquito bites. Do not over use repellents. Take special care when using repellents on children.
- Additional information regarding the use of mosquito repellents can be found on the CDC website at: <http://www.cdc.gov/ncidod/dvbid/westnile/RepellentUpdates.htm> and http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm
2. Reduce the number of mosquitoes in breeding sites outdoors by draining sources of standing water.
- Empty anything that holds standing water—old tires, buckets, plastic covers, and toys.
 - Change water in your birdbaths, fountains, wading pools, pet bowls, and animal troughs at least twice week.
 - Recycle unused containers that may collect water—bottles, cans, and buckets.
 - Make sure roof gutters drain properly and clean clogged gutters in the spring and fall.
 - Fix leaky outdoor faucets and sprinklers.

C. Prevention of Laboratory-Associated Infections

Laboratory-associated infections have been reported, attributed to both aerosol and parenteral inoculations. Biosafety Level 2 practices are recommended for testing human diagnostic specimens. Biosafety Level 3 practices are recommended for WNV cultures and PRNT.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

March 2008: In Section 1C, the guideline for timeliness of initiating an investigation was removed.

July 2008: In Section 1C, the CDC WNV Enhanced surveillance form was added.

In Section 4A, additional information was added regarding laboratory tests.

In Section 8B, IR3535 was added as an EPA approved effective mosquito repellent.

June 2009: In section 2B, case-fatality rates and new terminology for clinical syndromes were updated.

In section 3C, case classification for presumptive viremic donors was updated.

In section 4B, the change in laboratory tests available at PHL were noted.

In section 4D, information about the timing of specimen collection was clarified.

In section 8C, prevention of lab-associated infections was moved from section 4.

August 2009: In section 1C, request to complete a separate CDC enhanced surveillance form was removed.