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Contact Hours: **1**

West Nile Virus Infection

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COURSE OBJECTIVE: The purpose of this course is to prepare healthcare professionals to recognize the signs and symptoms of West Nile virus fever and diseases and to educate patients and the general public using evidence-based, up-to-date information about its symptoms, treatment, and prevention.

LEARNING OBJECTIVES

Upon completion of this course you will be able to:

- Explain the mechanism of transmission of infections of West Nile virus.
- Describe the signs and symptoms of West Nile virus fever and diseases.
- Discuss the treatment of West Nile virus infections.
- Identify measures for the prevention of West Nile virus infections.

HISTORY AND SPREAD OF WEST NILE VIRUS

In recent years, West Nile virus (WNV) has become a serious threat to human and animal health in temperate regions of Europe and North America. In the United States it is the most common disease spread by mosquitos. The most serious manifestations of a WNV infection are fatal meningitis and encephalitis in people, horses, and birds.

The virus was first isolated from a febrile adult woman in the West Nile District of Uganda in 1937. Its epidemiology and ecology were first described in detail during several outbreaks in the Mediterranean basin in the early 1950s and 1960s. It was recognized as the cause of severe neurologic conditions in elderly patients in Israel in 1957 and described in Africa, Europe, the Middle East, Asia, and Oceania in recent years (Sejvar, 2003).

Infections of West Nile virus first appeared in North America in 1999. WNV is now endemic in the continental United States. According to the CDC (2015f), as of 2014 more than 41,762 illnesses have occurred, including 18,810 neuroinvasive disease cases and 1,765 deaths.

As of yet, there is no specific treatment. The only known way to avoid this potentially dangerous condition is to prevent being bitten by infected mosquitos. For this reason, it is critical that healthcare providers learn about the epidemiology of the disease and educate the public about its prevention.

EPIDEMIOLOGY

Epidemiology is the study of determinants of a disease in a given population. It includes consideration of infectious agents of a disease, hosts and modes of transmission, and risks that increase the likelihood of infection by the causative agents.

Infectious Agent

West Nile virus is a single-stranded RNA virus of the family *Flaviviridae*, genus flavivirus, a member of the Japanese encephalitis antigenic complex. This group of viruses includes several medically important viruses associated with human encephalitis (WHO, 2011).

Host and Mode of Transmission



A single bite by an infected mosquito can transmit West Nile virus. (Source: CDC.)

West Nile virus is most commonly transmitted to humans by mosquitos. Additional routes of human infection, though small in proportion, include organ transplants; blood transfusions; mother to infant during pregnancy, delivery, or breastfeeding; and occupational exposure in laboratory settings (CDC, 2015e).

West Nile viruses follow a transmission cycle involving birds and mosquitos. Mosquitos become infected when they feed on infected birds, which circulate the virus in their blood. Infected mosquitos carry virus particles in their salivary glands and then infect susceptible bird species or other animals (including humans) during subsequent blood-meal feedings.



People, horses, and most other mammals are not known to develop infectious-level viremias and are thus considered “dead-end” hosts that do not transmit the virus to others (CDC, 2015e).

West Nile virus is **not** transmitted:

- From person to person or from animal to person through casual contact. Normal veterinary infection control precautions should be followed when caring for a horse suspected to have this or any viral infection.
- From handling live or dead infected birds. One should avoid bare-handed contact when handling any dead animal. If disposing of a dead bird, use gloves or double plastic bags to place the carcass in a garbage can.
- Through consuming infected birds or animals. In keeping with overall public health practice, and due to the risk of known food-borne pathogens, always follow procedures for fully cooking meat from either birds or mammals.
(CDC, 2015e)

Risk Factors

- **Exposure to mosquitos that carry WNV** is by far the most serious risk factor. Being outside puts one at risk. For this reason it is critical for people to protect themselves from mosquito bites when outdoors.
- **Being an adult over 50 years of age** is the most important risk factor for developing neuroinvasive WNV infections such as meningitis, encephalitis, and poliomyelitis.

Risk through medical procedures is very low. All donated blood is checked for WNV before being used. The risk of getting WNV through blood transfusions and organ transplants is very small and should not prevent people who need surgery from having it. Those with concerns are advised to talk to their primary care provider (CDC, 2015g).

SIGNS AND SYMPTOMS OF WEST NILE VIRUS INFECTIONS

Most persons who become infected with West Nile virus develop no symptoms of illness at all. In previous episodes of WNV in the Northern Hemisphere, an estimated 80% of people who became infected with WNV never developed symptoms attributable to the infection.

Approximately 20% of persons who are infected develop what is called West Nile virus fever. Only a small proportion of these individuals develop what is called West Nile virus severe disease, namely meningitis, encephalitis, and poliomyelitis.



West Nile Virus Fever

The incubation period of West Nile virus fever ranges from 2 to 14 days, although longer periods have been documented in immune-suppressed persons.

Clinical features include:

- Fever
- Headache
- Body aches
- Nausea
- Vomiting
- Fatigue
- Skin rash on the chest, stomach, and back of the body
- Swollen lymph glands

The infected individual gradually recovers from the symptoms within a few days to several weeks and has no further signs or symptoms of the infection.

West Nile Virus Severe Disease

To provide appropriate care for individuals with WNV severe disease, healthcare professionals need to differentiate serious conditions from mild ones, including the following significant factors, clinical features, common laboratory findings, and diagnostic tests.

WNV disease should be seriously considered in any person with a febrile or acute neurologic illness who has had recent exposure to mosquitos, blood transfusion, or organ transplantation, especially during the summer months in areas where virus activity has been reported. The diagnosis should also be considered in any infant born to a mother infected with WNV during pregnancy or while breastfeeding (CDC, 2015b).

Less than 1% of infected persons develop neuroinvasive disease, which typically manifests as meningitis, encephalitis, or acute flaccid paralysis (CDC, 2015b).

SIGNIFICANT FACTORS OF MENINGITIS, ENCEPHALITIS, AND ACUTE FLACCID PARALYSIS

- When the central nervous system is affected, clinical syndromes ranging from febrile headache to aseptic meningitis to encephalitis may occur.
- Headache can be a prominent feature of both WNV fever and severe disease. For this reason, headache is **not** a useful indicator of severe neuroinvasive diseases.
- WNV **meningitis** usually involves fever, headache, and stiff neck. It is clinically indistinguishable from viral meningitis.



- WNV **encephalitis**, the most severe form of neuroinvasive WNV disease, involves fever and global symptoms such as:
 - Altered mental status, from lethargy to confusion or coma
 - Focal neurologic deficits such as limb paralysis and cranial nerve palsies
 - Tremor and movement disorder
- WNV **acute flaccid paralysis** is less common than meningitis or encephalitis. It is usually clinically and pathologically identical to poliovirus-associated poliomyelitis. This syndrome is generally characterized by the acute onset of asymmetric limb weakness or paralysis in the absence of sensory loss. Pain sometimes precedes the paralysis; however, paralysis can occur in the absence of fever, headache, or other common symptoms associated with WNV infections. Involvement of respiratory muscles, leading to acute respiratory failure, can sometimes occur (CDC, 2015b).

SIGNS AND SYMPTOMS OF SEVERE DISEASE

Clinical features include:

- Headache
- High fever
- Neck stiffness
- Stupor
- Disorientation
- Coma
- Tremors
- Convulsions
- Muscle weakness
- Paralysis
- Rarely, cardiac dysrhythmias, myocarditis, rhabdomyolysis, optic neuritis, uveitis, chorioretinitis, orchitis, pancreatitis, and hepatitis have been described in patients with WNV disease
(WHO, 2011; CDC, 2015b)

COMMON LABORATORY FINDINGS

- Routine clinical laboratory studies are generally nonspecific.
- Cerebrospinal fluid (CSF) examination generally shows an increased lymphocyte count, but neutrophils may predominate early in the course of illness.
- Brain magnetic resonance imaging is frequently normal, but signal abnormalities in the basal ganglia, thalamus, and brainstem may be seen in patients with encephalitis, and in the anterior spinal cord in patients with poliomyelitis.
(CDC, 2015b)



DIAGNOSTIC TESTS

A diagnosis of WNV infection relies on clinical symptoms and results of specific laboratory tests. Although infection may be suspected in a person based only on clinical symptoms and patient history, laboratory testing is required to confirm a diagnosis.

WNV-specific **IgM antibodies** are usually detectable 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented. Therefore, positive IgM antibodies occasionally may reflect a past infection. If serum is collected within 8 days of illness onset, the absence of detectable virus-specific IgM does not rule out the diagnosis of WNV infection, and the test may need to be repeated on a later sample.

The presence of WNV-specific IgM in blood or CSF provides good evidence of recent infection but may also result from cross-reactive antibodies after infection with other flaviviruses or from nonspecific reactivity.

WNV IgG antibodies generally are detected shortly after IgM antibodies and persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of IgG 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 (CDC, 2015b).

The **plaque-reduction neutralization test (PRNT)** is the most specific test for the arthropod-borne flaviviruses and can help distinguish false-positive results in an IgM antibody capture enzyme-linked immunosorbent assay or other assays.

Viral cultures and tests to detect viral RNA (e.g., reverse transcriptase-polymerase chain reaction [RT-PCR]) can be performed on serum, CSF, and tissue specimens that are collected early in the course of illness and, if results are positive, can confirm an infection. Immunohistochemistry (IHC) can detect WNV antigen in formalin-fixed tissue. Negative results of these tests do not rule out WNV infection. Viral culture, RT-PCR, and IHC can be requested through state public health laboratories or CDC (CDC, 2015a).

OUTCOMES

Most patients with non-neuroinvasive WNV disease or WNV meningitis recover completely, but fatigue, malaise, and weakness can linger for weeks or months. Patients who recover from WNV encephalitis or poliomyelitis often have residual neurologic deficits. Among patients with neuroinvasive disease, the overall case-fatality ratio is approximately 10%, but it is significantly higher for patients with WNV encephalitis and acute flaccid paralysis than WNV meningitis (CDC, 2015b).



TREATMENT

There is no specific treatment for infections of West Nile virus, though several clinical trials are ongoing. Currently, treatment of severe cases consists of supportive care, namely:

- Hospitalization
- Intravenous fluids
- Respiratory support
- Pain control for headaches
- Antiemetic therapy

REPORTING AND MONITORING

West Nile virus disease and West Nile encephalitis/meningitis are on the list of designated nationally notifiable conditions that must be reported to the CDC. A notifiable disease is one about which timely information on individual cases is considered necessary by CDC to prevent and control the disease.

The list of notifiable infectious diseases varies over time and is reviewed and modified once each year by the Council of State and Territorial Epidemiologists and CDC. Reports are published weekly and annually and are available on the CDC website.

The National Notifiable Diseases Surveillance System (NNDSS) is a multifaceted public health disease surveillance system that gives public health officials capabilities to monitor the occurrence and spread of disease. NNDSS is used to:

- Support reportable disease surveillance by improving information-sharing between healthcare providers and health departments and between states and the CDC
- Support electronic laboratory reporting as part of the Meaningful Use initiative to improve public health disease reporting
- Increase information-sharing and system interoperability between state health departments to improve multi-state disease detection and containment

So, too, is the Arboviral surveillance system (ArboNET), an Internet-based national system developed by state health departments and CDC in 2000. ArboNET collects reports of diseases spread by arthropods (mosquitoes, ticks, sand flies, or midges) and other data (NNDSS, 2015). (See “Resources” at the end of this course.)



PREVENTION AND PUBLIC EDUCATION

Because no human vaccine against West Nile virus is currently available, public education is critical, especially for high-risk individuals, defined as persons who are immunocompromised or aged 50 years or older.

Because mosquitos carry virus particles in their salivary glands, when they bite people, they inject virus into their victim. Thus, **mosquito bite avoidance is crucial to the prevention of West Nile virus infections.**

Prevention control measures include the following:

- Use mosquito repellent when outdoors. Repellent containing DEET (N, N-diethyl-methyltoluamide), picaridin, IR3535, and some oil of lemon eucalyptus and para-menthane-diol products provide longer-lasting protection. Spray exposed skin and clothing.
- Wear protective clothing such as long pants, long sleeves, and socks.
- Stay indoors during primary mosquito-biting hours (i.e., dawn and dusk).
- Install or repair screens on windows and doors to keep mosquitos outside. Use air conditioning if available.
- Remove standing water in places where people live, because mosquitos breed in such water.
- Support community-based mosquito control programs such as insecticide spraying.
- Report dead birds to local authorities; dead birds may be a sign that West Nile virus is in the area.
(CDC, 2015d)

It is the responsibility of:

- Individuals to learn about communicable diseases and their prevention and to apply that information to their lives
- Healthcare providers to communicate and personalize disease prevention measures to their clients
- The Centers for Disease Control and Prevention to educate the public about various diseases that afflict them and measures they can take to prevent the diseases



THE 4 Ds OF PREVENTION

One easy way to avoid mosquito bites and prevent WNV is following these “4 Ds”:

1. **Drain.** Mosquitos lay their eggs in standing water. Eliminate all sources of standing water, including buckets, old car tires, and even pet bowls. In ponds, eliminate mosquito larvae by using mosquito fish, available commercially or from county mosquito abatement districts.
2. **Dress.** Mosquitos bite exposed skin, such as the arms, legs, face, and neck. Donning protective clothing makes it difficult for mosquitos to pierce the skin as they feed and to inject the viral particles harbored in their salivary glands.
3. **Dusk.** Mosquitos that carry West Nile virus bite in the early morning and evening. During these time periods, it is important to use insect repellent and to wear clothing that reduces the risk of skin exposure to mosquito bites. Make sure doors and windows have tight-fitting screens to keep out mosquitos. Repair or replace screens with tears or holes.
4. **DEET.** Use an EPA-registered insect repellent with active ingredients such as DEET, picaridin (KBR 3023), IR3535, oil of lemon eucalyptus or PMD, or Permethrin (on clothing, shoes, bed nets, camping gear but not skin) according to label instructions (CDC, 2015c). Repellents keep the mosquitos from biting you. DEET is approved for use on children, although the American Academy of Pediatrics recommends it not be used on infants under two months of age (AAP, 2015). Some individuals may be allergic to DEET.

Source: SMHS, 2015.

CASE

Sylvia, a nurse in an elementary school, read about the epidemic of West Nile virus infections in her area of the state. She thought about the children in her school and how vulnerable they and their families were to mosquito bites and West Nile virus infections.

She went to the school principal and explained that even though 80% of people who are bitten by infected mosquitos never get sick, those who do get sick may develop severe disease and even die. She told the principal, “Mosquitos spread this terrible disease and they are everywhere! What can we do to prevent West Nile virus infections in our children and their families?”

The principal suggested she present the problem to the faculty at their Thursday afternoon meeting. Sylvia did. Everyone agreed there was a need for action, but they wanted more information about West Nile virus infections. Sylvia offered to send a copy of the CDC fact sheet to every member of the staff. A week later at the regular meeting, the principal and teachers agreed to include the essential information about West Nile virus in the curriculum in an age-appropriate way.



A month later, the principal received a call from the editor of the local newspaper. She had heard about some of the creative ways the children had demonstrated the information in the CDC article about West Nile virus infections and mosquito bite prevention. One of the children drew a picture of a mosquito biting a hand with the caption, "Use DEET, prevent bites." Another made a sign nailed to a stick, which said, "Stay inside at dawn and dusk." And another replaced the picture of a wicked witch on a board game with a picture of a mosquito.

The principal credited Sylvia, the school nurse, for her leadership and referred the reporter to her for more details. At the end of the school year the newspaper published a follow-up story noting that the county health department had not received a single report of a WNV infection.

QUESTIONS PATIENTS MAY ASK ABOUT WEST NILE VIRUS

Q. What is West Nile virus?

A. WNV infection is a potentially serious illness that flares up in the summer and fall.

Q. What are the symptoms of WNV infection?

A.

- **No symptoms in most people;** 70% to 80% of people who are infected show no symptoms at all.
- **Milder symptoms in some people;** up to 20% of infected people develop fever, headache, body aches, joint pains, nausea, vomiting, diarrhea or skin rash. Symptoms last for a few days to several weeks. Most people recover completely from this type of disease but may remain fatigued and weak for weeks or months.
- **Serious symptoms in a few people,** including fever, headache, neck stiffness, disorientation, coma, tremors, seizures, or paralysis. Symptoms may last several weeks, and neurological effects may be permanent. About 10% of people who develop neurologic infection due to West Nile virus will die.

Q. How does WNV spread?

A. Most often WNV is spread by the bite of infected mosquitos that became infected by feeding on birds with WNV. Though rare, WNV can be spread between people through blood by transfusions, transplants, and mother-to-child. WNV is not spread through casual contact such as kissing or touching a person with the virus.

Q. How soon do infected people get sick?

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



Q. How is WNV treated?

A. 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 severe cases, patients often need to be hospitalized to receive supportive treatment, such as intravenous fluids, pain medication, and nursing care.

Q. What should I do if I think I have WNV?

A. Consult a healthcare provider for evaluation and diagnosis.

Q. Who is at risk for infection with WNV?

A. 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 mosquitos. Risk of acquiring WNV through medical procedures is very low. Donated blood is checked for WNV before being used, and the risk of getting WNV should not prevent people from having needed surgery.

Q. What is the CDC doing about WNV?

A. The CDC is working with state and local health departments and other government agencies, as well as private industry, to prepare for and prevent new cases of WNV. Some of the things the CDC is doing include:

- Managing and maintaining ArboNET, a nationwide electronic surveillance system where states share information about WNV and other arboviral diseases
- Supporting states to develop and carry out improved mosquito prevention and control programs
- Developing better, faster tests to detect and diagnose WNV
- Preparing updated prevention and surveillance information for the media, public, and health professionals
- Working with partners to develop vaccines

Q. What else should I know?

A. If you find a dead bird, do not handle the bird with your bare hands. Contact the state health department or state wildlife agency for instructions on reporting and disposing of the body. They may tell you to dispose of the bird after they log your report. Don't handle the body with your bare hands (CDC, 2015c).



RESOURCES

Insect Repellents (EPA)

<http://www2.epa.gov/insect-repellents>

Public response hotlines (CDC)

1-888-246-2675 (English)

1-888-246-2857 (Español)

1-866-874-2646 (TTY)

West Nile Virus: An Historical Overview (U.S. National Library of Medicine)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC311838/>

West Nile Virus disease map (CDC/USGS)

<http://diseasemaps.usgs.gov/mapviewer/>

West Nile Virus fact sheet

http://www.cdc.gov/westnile/resources/pdfs/wnvFactsheet_508.pdf

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TEST

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1. Mosquitos become infected with West Nile virus when they feed on infected:
 - a. Birds.
 - b. Horses.
 - c. Pigs.
 - d. Humans.

2. West Nile virus may spread by which mode of transmission?
 - a. Consumption of fully cooked bird meat
 - b. Casual contact with an infected person
 - c. Garden or sandbox soil
 - d. Human milk via breastfeeding

3. Most patients who develop symptoms of West Nile virus are diagnosed with:
 - a. West Nile virus severe disease.
 - b. West Nile virus chronic syndrome.
 - c. Meningitis and encephalitis.
 - d. West Nile virus fever.

4. Which is a **true** statement about headache in patients infected with West Nile virus?
 - a. Healthcare providers cannot treat headache caused by West Nile virus infection.
 - b. Headache does not help differentiate between mild and severe infection because it may be present in both conditions.
 - c. Headache is omitted from the list of significant clinical features of West Nile virus disease because it is very rare.
 - d. Headache is a symptom of encephalitis but not meningitis in patients with West Nile virus disease.

5. Which symptoms characterize neuroinvasive West Nile virus disease?
 - a. Primary renal hematuric and proteinuric syndrome
 - b. Dysthymic disorder, dissociative fugue, hypochondriasis, and depersonalization disorder
 - c. Endocarditis and peripheral atrial occlusion
 - d. Fever and global symptoms, altered consciousness, and movement disorder



- 6.** A patient with severe West Nile virus disease is hospitalized for supportive care. The nurse caring for the patient anticipates administering which treatment that has shown to be effective in managing patients with WNV?
- Intravenous fluids
 - Anticoagulation therapy
 - Muscle biopsy
 - Antiviral medication
- 7.** Protection against mosquito bites is:
- An impossible dream that is too difficult to take seriously.
 - Accomplished through personal protection, not household, measures.
 - Crucial to the prevention of West Nile virus infection.
 - Desirable, but totally impractical.
- 8.** The “4 Ds” of mosquito bite prevention are “drain,” “dress,” “dusk,” and:
- Defend.
 - DEET.
 - Determinant.
 - Disease.
- 9.** A 74-year-old female patient who is retired visits the local health clinic for a routine physical examination. During the visit, the patient tells the clinician how much she enjoys working in her rose garden. She explains how she tends the garden in the early morning and again in the evening because she has a history of heat stroke. Concerned about recent reports of West Nile virus in the area, the clinician discusses protective measures for WNV. Which statement by the practitioner is the most practical and effective preventative advice for the patient?
- “You should call all your neighbors to determine if they have ponds or other sources of standing water.”
 - “Find an alternate hobby, such as crossword puzzles or knitting, instead of working in your rose garden.”
 - “You must work outside in the garden only in the middle of the day to avoid mosquitos.”
 - “When you’re outdoors, wear long-sleeved shirts and long pants and use an EPA-registered insect repellent on your skin and clothing.”

