COURSE DESCRIPTION

The first cases of West Nile virus were confirmed in New York in 1999 and since then there have been 23,536 reported cases and 904 deaths attributed to the virus. This Continuing Education module will describe West Nile virus, including the

- life cycle,
- diseases,
- United States statistics,
- diagnosis,
- treatment, and
- prevention.
Upon completion of this continuing education module, the professional should be able to:

1. State where and when the first cases of West Nile virus infection were seen in the United States.
2. Identify the most likely manner in which West Nile virus reached the United States.
3. Describe the physical makeup of West Nile virus.
4. Describe the life cycle of West Nile virus including the infection of incidental hosts.
5. Name the two species of mosquitoes most often involved in the transmission of West Nile virus.
6. Identify the season when West Nile virus infections typically peak.
7. Describe the signs and symptoms of human infection with West Nile virus.
8. Identify the methods used to diagnose West Nile virus infection.
9. Describe treatment for infection with West Nile Virus.
10. For the years 1999-2006, state the number of United States infections and deaths resulting from infection with West Nile virus.
11. For the period of 1/1/06 to 11/7/06, list the states that did not report any human cases of West Nile virus.
12. Describe routes of human infection for West Nile virus that do not involve mosquitoes.
13. Describe methods used to prevent human infection with West Nile virus.
14. Describe methods in use by the Centers for Disease Control and other agencies to prevent future outbreaks of West Nile virus.

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INTRODUCTION

In the late summer of 1999, the New York City Department of Health investigated a cluster of encephalitis (inflammation of the brain) cases in Queens County. It was determined that the cause of the encephalitis was West Nile Virus (WNV). Until 1999, WNV was found only in the Eastern hemisphere, with a wide distribution in Africa, Asia, the Middle East, and Europe. Migratory birds are most likely the key manner by which WNV reached the Western hemisphere. Other ways in which the virus could have entered the United States include the importation of infected birds and mosquitoes from areas where WNV is endemic.

West Nile virus was first isolated and identified in 1937 from an infected person in the West Nile district of Uganda. Since 1937, infrequent human outbreaks, mainly associated with mild febrile illness, were reported mostly in groups of solders, children, and healthy adults in Israel and Africa. In 1957, a notable outbreak occurred in an Israeli nursing home that was associated with severe neurological disease and death.

Since the mid-1990s, the frequency and clinical severity of WNV outbreaks have increased. Outbreaks in Romania (1996), Russia (1999), and Israel (2000) have involved hundreds of persons with severe neurological disease. Reasons for the change in severity and frequency are unknown. Differences in the virus’s virulence and changes in the affected population, such as increased age, decreased immunity, or predisposing chronic conditions may be causes.

WEST NILE VIRUS FACTS

Genetically, WNV is a member of the Flavivirus family of viruses. This viral group contains more than 70 viruses including those that cause yellow fever, dengue, St. Louis encephalitis, Japanese encephalitis, and tick-borne encephalitis.

Viruses are classified by shape, nucleic acid content, and presence or absence of an envelope. WNV is an enveloped icosahedral, single stranded RNA virus.

Shape: The shape of an icosahedral is somewhat spherical. The viral icosahedral structure is composed of 60 (or multiples of 60) equal sided triangles. A simple icosahedral shape is illustrated below.
Nucleic Acid Content: Viruses, unlike bacteria and other living cells, contain only DNA or RNA, not both. WNV contains single stranded RNA. In order to multiply, WNV must enter a host cell and utilize the DNA of the host cells.

Envelope: Some viruses, including WNV, are surrounded by an outer layer made up of lipids (fats). The envelope gives the virus an extra layer of protection against enzymes and chemicals of the host, making it more difficult to be killed.

EPIDEMIOLOGY

WNV is primarily a disease that spreads between mosquitos and birds. The virus is transmitted back and forth between birds and mosquitos per the following life cycle:

1. Mosquito #1: A mosquito is infected with WNV. The virus lives in the salivary glands. In parasitology terms, the mosquito is called a vector.
2. Bird #1: An infected mosquito bites a bird. Saliva containing WNV is injected into the bird when the mosquito bites it. The bird develops WNV infection. The virus lives in the blood of the bird. In parasitology terms, the bird is called a host.
3. Mosquito #2: A non-infected mosquito bites a bird that is infected. The virus in the bird’s blood is drawn into the mosquito when the mosquito feeds on the blood. Infection then develops in the mosquito. This mosquito can now transmit WNV to an uninfected bird.

- Most birds infected with the virus do not show symptoms and they develop a life-long immunity to WNV and will not get the disease again. However, birds that are weak may die from the infection.
- In the United States, at least 138 bird species have been reported as positive for a past WNV infection. For unknown reasons, high bird death rates have occurred in both Israel and the United States.
- WNV is primarily transmitted by Culex and Aedes species of mosquitos. However, there may be at least 41 other mosquito species that can transmit WNV.
- The more species of mosquitos that carry WNV and the more species of birds that can become infected, the greater the spread of the disease.
- WNV infections peak when mosquito populations are at their greatest in late summer and early fall.
- Some Culex species may live through the winter in southern states leading to concerns about year-round infections.
**Mammals and WNV**

Humans and other mammals become infected when bitten by mosquitoes that have WNV. However, they are considered “dead end” hosts as mosquitoes cannot become infected with WNV when they bite an infected mammal. In parasitology terms, mammals are called incidental hosts. WNV has infected dogs, cats, horses, raccoons, chipmunks, bats, domestic rabbits and squirrels.

In mammals, serious illness and death are usually seen only in horses. For unknown reasons, the frequency of WNV outbreaks in horses has increased. There is a WNV vaccine for horses.

**West Nile Virus Life Cycle Involving Mammals**

- Mosquito #1 infected with WNV
- Bird becomes infected with WNV when bit by infected mosquito
- Mosquito #2 becomes infected when it bites bird that has WNV
- Infected mammals may become sick when bitten by an infected mosquito. However, mammals are unable to transmit the virus back to a mosquito. Therefore, mammals are considered “dead end” hosts.

**Human Infection with WNV**

The incubation period for human WNV infection is 2-14 days.

- About 80% of people infected with WNV do not have any symptoms.
- About 20% develop “West Nile Fever”.
  - “West Nile Fever” is a sudden mild flu-like illness with fever, headache, and body aches.
  - Occasionally an infected person develops swollen lymph glands and/or a skin rash on the trunk of the body.
  - “West Nile Fever” lasts from 3-6 days.
Less than 1% of people infected with WNV develop central nervous system (CNS) disease, i.e., meningitis, encephalitis, or meningoencephalitis.

- Encephalitis is the most common form of severe WNV infection.
- Symptoms of CNS infection include headache, high fever, neck stiffness, stupor, and disorientation.
- Coma, convulsions, and paralysis may also occur.
- Symptoms of severe disease may last several weeks and neurological effects may be permanent.
- Complete flaccid paralysis (AFP) may result from CNS disease. This is a polio-like syndrome where one side of the body exhibits weakness and paralysis that may last for more than two months.
- Approximately 10% of persons with CNS disease die. The number one factor for death is advanced age.

- Risk factors for becoming sick with WNV include persons over 50 years of age, persons with hematological malignacies (leukemias, lymphomas) or persons taking immunosuppressive drugs or having immunosuppressive diseases (transplant patients, HIV patients).

**DIAGNOSIS**

Diagnosis of WNV infection is made using laboratory tests. In the peripheral blood, individuals with severe WNV disease usually have normal or elevated lymphocytes, slight anemia, and decreased sodium. Increased numbers of white blood cells (usually lymphocytes), increased protein, and normal glucose values are seen in the spinal fluid. These general laboratory findings are insufficient to diagnose WNV infection.

The best method to diagnose WNV infection is a laboratory test called an enzyme linked immunosorbent assay (ELISA) specific for WNV. This test will detect IgM forms of antibodies to WNV. Ninety-five percent of individuals with WNV infections will test positive for these antibodies in both the blood and spinal fluid. Unfortunately, individuals with viral infections similar to WNV can have positive reactions with the WNV ELISA test. Two sophisticated laboratory methods, polymerase chain reaction (PCR) methods and plaque reduction neutralization test (PRNT), can be used to confirm infection a WNV infection.

Radiologic scans such as CT and MRI are generally not effective in identifying specific signs that are unique for WNV. The scans will show the typical signs of encephalitis, meningitis, and meningoencephalitis but the signs are not specific to WNV.

**TREATMENT**

There is no specific treatment for WNV infection. Individuals with mild illness generally recover without treatment. For those with severe illness such as encephalitis, supportive treatment is given. This includes hospitalization, IV fluids/nutrition, pain relief, respiratory support, and prevention of secondary infections. Research is in progress to study the use of interferon, a type of immune cell therapy, as a treatment for encephalitis.
STATISTICS

Following is a table listing the number of WNV infections and deaths since the start of the United States outbreak in 1999.

<table>
<thead>
<tr>
<th>YEAR</th>
<th>NUMBER OF INFECTIONS</th>
<th>NUMBER OF DEATHS</th>
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<td>1999</td>
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<td>7</td>
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<td>2004</td>
<td>2,539</td>
<td>100</td>
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<tr>
<td>2005</td>
<td>3,000</td>
<td>119</td>
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<tr>
<td>2006*</td>
<td>3,830</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>23,536</td>
<td>904</td>
</tr>
</tbody>
</table>

*as of 11/7/06

The map of the United States below shows the distribution of bird, animal, and human WNV infection as of from 1/1/06 to 11/7/06. Only Alaska, Hawaii, and Puerto Rico have not had any WNV activity. Only bird, animal, or mosquito were reported in Delaware, New Hampshire, Maine, North Carolina, Rhode Island, South Carolina, and Vermont.

Map courtesy of CDC
Most public health care experts believe that WNV is now firmly established in the United States and Canada. It is known that WNV has reached as far as Columbia and Venezuela in South America. Public health officials believe that without a doubt, WNV will spread throughout South America. On an interesting note, Mexico has had relatively few human cases of WNV and even fewer individuals who suffer from encephalitis or other severe brain disease. Scientists are at a loss to explain this phenomenon. Some have postulated that there are many related flavivirus infections that occur in Mexico and that as a result, individuals produce antibodies that provide some cross-protection to WNV.

Once established in an area, WNV does not go away. Public health officials warn that having fewer number of WNV cases does not necessarily mean that fewer still cases will be seen in the following year. Depending on the amount of wet weather contributing to the breeding of mosquitos, WNV will continue to cause varying numbers of WNV human infections in the late summer and early fall in the United States. The only way to completely eliminate the virus in the United States is to kill its natural hosts: birds and mosquitos. Even if this were possible, the virus could re-enter the country by a migrating bird or by other means.

**ADDITIONAL ROUTES OF INFECTION**

There have been a very small number of individuals who have contracted WNV by a means other than a mosquito bite.

- Eighty-one cases have been reviewed in which pregnant women became infected with WNV during a pregnancy. Some of the women experienced encephalitis, meningitis, or meningoencephalitis. When born, some babies had various signs and symptoms of WNV disease. Four women miscarried their babies in the first trimester and it is presumed that the miscarriages were due to WNV.

- Two laboratory-acquired cases of WNV have been reported. One case was caused when a microbiologist was performing studies on a dead bird and lacerated his thumb while removing the brain of the bird. The other case occurred when a microbiologist punctured his finger with a needle being used to work with WNV-infected mouse brains. In both cases, the human infections were mild and self-limited.

- Studies have shown that WNV can be transmitted through blood transfusions and organ donations. Since 2003, all blood donation centers in the United States have screened blood donors for WNV. The blood collection centers destroy units of blood that test positive and notify the blood donor of the test results. However, organ donor screening for WNV is not currently required or routinely performed for various reasons, including the following.
  - As of 11/7/06, the current FDA-approved WNV test method is approved only for screening units of blood,
  - The turnaround time to obtain the WNV test results is too long to be practical for organ donation.
  - The WNV test performance is unproven for the organ donation setting.
In a few instances, mothers have transmitted WNV to their infants through breast feeding. CDC cautions that this is a very rare occurrence and should not affect a woman's decision to breast feed her baby.

**PREVENTION**

At the present time, there is no human vaccine for WNV. The best method to prevent infection by WNV is to avoid exposure to mosquitoes and eliminate mosquito breeding sites. The following recommendations are made to minimize exposure to mosquitoes and WNV.

- Empty standing water in old tires, cemetery urns, buckets, plastic covers, toys, etc.
- Empty and change water in bird baths, fountains, wading pools, rain barrels, and potted plant trays at least once a week.
- Drain or fill temporary pools with dirt.
- Keep swimming pools treated and and assure the water is circulating.
- Keep rain gutters unclogged.
- Wear head nets, shoes, socks, long sleeves, and long pants if you venture into areas with high mosquito populations.
- Make sure window and door screens are “bug tight”.
- Replace your outdoor lights with yellow “bug” lights.
- If there is a mosquito-borne disease warning in effect, stay inside during dawn, dusk, and evening when mosquitoes are most active.
- Wear mosquito repellent with a 10% to 30% concentration of DEET on skin and clothing. NOTE: DEET cannot be used on the hands of young children or on infants under 2 months of age. To protect infants, the stroller or playpen should be covered with mosquito netting when outside. According to the CDC, oil of lemon eucalyptus offers the same protection as DEET when used in similar concentrations.

The CDC has been working with the Environmental Protection Agency and other federal, state, and local agencies, to prevent future outbreaks of WNV. Efforts to detect and contain the virus include the following:

- Sampling of mosquito and bird populations for WNV
- Increased observation of animals and humans for infection
- Eliminating mosquito breeding areas
- Increasing physician awareness and reporting of WNV
- Conducting public awareness campaigns to let people know how to reduce the risk of exposure to WNV
References

West Nile Virus.  [www.mayoclinic.com/print/west-nile-virus](http://www.mayoclinic.com/print/west-nile-virus)

West Nile Virus.  [www.cdc.gov/ncidod/dvbid/westnile](http://www.cdc.gov/ncidod/dvbid/westnile)


The Buzz on West Nile Virus.  [www.fda.gov/oc/opacom/hottopics/westnile.htm](http://www.fda.gov/oc/opacom/hottopics/westnile.htm)


TEST QUESTIONS
West Nile Virus #1225714

Directions:
- Before taking this test, read the instructions on how to correctly complete the answer sheet.
- Select the response that best completes each sentence or answers each question from the information presented in the module.
- If you are having great difficulty answering a question, go to [www.ncctinc.com](http://www.ncctinc.com) and select CE/Renewals, then select CE Update to see if course content and/or a test question have been revised.

1. West Nile virus was first isolated in:
   
   a. Egypt in 1939  
   b. Israel in 2000  
   c. Romania in 1996  
   d. Uganda in 1937

2. West Nile virus is in the same family of viruses that cause:
   
   a. Indian encephalitis  
   b. Rocky Mountain Spotted Fever  
   c. typhoid fever  
   d. yellow fever

3. West Nile virus most likely entered the United States by:
   
   a. exotic South American birds transported to pet shops  
   b. infected horses  
   c. infected migratory birds  
   d. infected turtles from Mexico
4. Which one of the following is NOT associated with the structure of West Nile virus?
   a. DNA
   b. enveloped
   c. icosahedral
   d. RNA

5. The normal life cycle of West Nile virus involves the transmission of the virus back and forth from:
   a. mosquito to bird
   b. mosquito to horse
   c. mosquito to human
   d. mosquito to mammals other than humans

6. In mammals other than humans, WNV usually causes serious illness and death in:
   a. cats
   b. dogs
   c. horses
   d. squirrels

7. Which one of the following statements is FALSE?
   a. Approximately 80% of people infected with WNV have no symptoms.
   b. Approximately 20% of people infected with WNV develop “West Nile Fever”.
   c. Less than 1% of people infected with WNV develop CNS disease.
   d. The majority of people who develop WNV CNS disease die.

8. Symptoms of West Nile Fever include:
   a. body aches
   b. fever
   c. headache
   d. all answers are correct

9. West Nile Fever lasts from about:
   a. 1 - 2 days
   b. 2 – 14 days
   c. 3 – 6 days
   d. 4 – 8 days
10. The most common form of CNS disease caused by WNV is:
   a. encephalitis
   b. meningitis
   c. meningoencephalitis
   d. West Nile Fever

11. Patients who develop encephalitis from WNV may develop:
   a. complete flaccid paralysis
   b. polio
   c. renal failure
   d. sepsis

12. The number one risk factor associated with death from WNV CNS disease is:
   a. advanced age
   b. HIV
   c. leukemia
   d. organ transplant

13. Which one of the following is TRUE regarding laboratory findings in patients with WNV CNS disease?
   a. Patients usually have decreased numbers of white blood cells in the spinal fluid.
   b. Patients usually have slight anemia and increased sodium in the peripheral blood.
   c. A polymerase chain reaction (PCR) test can be used to confirm a WNV infection.
   d. all answers are correct

14. Supportive treatment for serious WNV infection includes hospitalization, IV fluids, pain relief, respiratory support, and prevention of secondary infections.
   a. True
   b. False

15. From 1999 to 11/7/06, the number of reported deaths in the United States due to WNV was:
   a. 119
   b. 264
   c. 904
   d. 3,000
16. Which one of the following states did not report any WNV human infections from 1/1/06 to 11/7/06?
   a. Connecticut
   b. Kansas
   c. Maryland
   d. Rhode Island

17. WNV has been shown to be transmitted by all of the following EXCEPT:
   a. blood transfusion
   b. laboratory worker to laboratory worker
   c. mother to unborn baby
   d. organ donation

18. Which one of the following is a TRUE statement regarding prevention of WNV?
   a. Avoid being outside for extended periods of time during daylight hours.
   b. Bird baths, fountains, wading pools, rain barrels, and similar items should be emptied of water at least once a week.
   c. Insect repellent with a 10% - 30% concentration of DEET should be liberally applied to the bodies and hands of young children before they go outside.
   d. Wear tank tops, shorts, and sandals without socks when outside during the early evening hours.

*End of Test*