

## **West Nile Virus Summary**

### **Introduction**

West Nile Virus (WNV) is a mosquito-borne formerly old-world Flavivirus with a rapidly expanding geographic distribution, first isolated in the West Nile district of Uganda in 1937. Up until the appearance of WNV in the New York City area in 1999, the virus was found only in the Eastern Hemisphere, specifically in Asia, Africa, the Middle East, and Europe. In 1999 this zoonosis emerged in the New York City area, first recognized as a cause of mortality in several bird species, then as a cause of illness and mortality in humans. Since that time, WNV has firmly established itself in a large portion of the United States, and was the cause of the largest human West Nile epidemic and animal epizootic ever reported in 2002 (4,156 human cases of WN disease, with 284 deaths, 16,741 dead birds, 6,604 infected mosquito pools, and 14,571 equine cases). However, cases in the U.S. in 2003 eclipsed those reported in 2002 by greater than 100 percent: in 2003, 9858 human cases and 258 deaths were reported to CDC. Cases have also been documented in Canada, the Caribbean, and in Mexico. Human disease has been acquired in every state in the contiguous United States except Oregon and Washington, and is expected to occur in every state in 2004. The lone case in 2004 thus far has been reported in New Mexico. In addition to mosquito-borne disease, blood transfusion, transplacental transmission, organ transplantation, and breast-feeding associated cases have all been documented.

Migratory birds are thought to be the major introductory hosts of West Nile virus to new geographic areas. This virus causes subclinical illness in a large proportion of those infected, a mild febrile illness in 20%, and a severe neurological illness (encephalitis, meningitis, or both) in 1 in 150 patients. Older patients are at greatest risk for severe illness, which can cause permanent neurological sequelae or death. There is currently no specific treatment for WNV infection, and prevention is based on limiting mosquito exposure in enzootic and epidemic areas.

### **Clinical Features**

Most infections in humans are clinically unapparent, however about 20% of those infected will develop a mild illness (known as West Nile fever). The incubation period ranges from 3 to 14 days, and clinical manifestations usually last 3 to 6 days. The illness is characterized by sudden onset of fever; signs and symptoms may include malaise, nausea and vomiting, headache and eye pain, rash, myalgia, and lymphadenopathy.

Severe infections are most often characterized by encephalitis or meningitis. The single most important risk factor for severe disease is advanced age, although severe WNV infections can occur in patients at any age. The risk of neurological disease is reportedly 10-fold greater for persons over age 50 years, and increases to approximately 50-fold greater for persons over age 80 years. Defining clinical characteristics of severe cases are

mainly neurological, and may include weakness, deteriorating mental status, flaccid paralysis, ataxia and extrapyramidal signs, cranial nerve palsies, myelitis or optic neuritis, polyradiculitis, seizures, and/or obtundation. Other organ systems may also be affected: hepatitis, myocarditis, and pancreatitis have all been reported. Hospitalized WNV victims have an approximately 10 percent risk of death. In patients with severe disease who recover, significant neurological sequelae may unfortunately be present. Over 50% of cases in the initial New York City experience had serious prolonged disability (cognitive dysfunction, muscle weakness and inability to ambulate, depression, memory loss, other sequelae).

**Reservoir and Spread:** The primary reservoir of WNV in nature appears to be in numerous species of birds. The virus has an enzootic cycle in culicine mosquitoes and bird populations, and domestic avian, equine, and human infections occur via “bridge vector” mosquitoes such as *Culex pipiens*, *Culex restuans*, and *Culex quinquefasciatus*. The virus becomes amplified in bird and mosquito populations until late summer in temperate climates, when infections begin to show up in accidental hosts such as humans. Bird die-offs such as occurred in the first U.S. outbreak (predominately but not limited to crows) may precede or coincide with human illness, although this has not been a consistent feature in old world outbreaks, where adult birds may have high levels of immunity. Cases in the United States have occurred mainly in July through December, with a peak in late summer and early fall. In more tropical climates, year-round transmission is possible. West Nile virus is now considered permanently established in North America.

## **Diagnosis and Treatment**

Diagnosis of WNV infection is based on a high index of clinical suspicion and on specific laboratory tests. Severe West Nile disease, or other arboviral diseases such as St. Louis encephalitis or eastern equine encephalitis, should be strongly considered in adults older than 50 who develop unexplained encephalitis or meningitis in summer or early fall. The local presence of WNV enzootic activity in bird populations, or the presence other human WNV cases should further raise suspicion. Obtaining a recent travel history is also important. Laboratory findings may include normal or elevated total leukocyte counts, lymphopenia and anemia, hyponatremia, CSF lymphocytic pleocytosis with elevated protein and normal glucose, and in patients with neurologic disease, enhancement of the leptomeninges and periventricular areas on MRI in about 30 percent.

### **Presenting Symptoms (Clinical Diagnosis)**

- Fever
- Malaise
- Rash
- Headache
- Eye Pain
- Myalgias

- Nausea and Vomiting
- Neurological Signs

**Laboratory Clinical Diagnostic Testing:** CBC with Differential, Electrolytes and Glucose, BUN and Creatinine, Lumbar Puncture with testing of CSF for cell count and differential, glucose and protein, and for specific infectious agents, serum for serologic diagnosis.

**Specific Diagnostic Testing** (available through local and state health departments): The most efficient diagnostic method is detection of IgM antibody to WNV in serum or cerebral spinal fluid (CSF), collected within 8 days of illness onset using the IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA). Detection of IgM in serum may also indicate prior infection, since IgM may persist in serum as long as one year. Since IgM antibody does not cross the blood-brain barrier, IgM antibody in CSF strongly suggests current central nervous system infection. Patients who have been recently vaccinated against or who have been recently infected with related flaviviruses (e.g., yellow fever, Japanese encephalitis, St. Louis encephalitis, dengue) may have positive WNV MAC-ELISA results. PRNT testing may help distinguish WNV from other cross-reacting flaviviruses, and a rise in WNV-specific neutralizing antibody titers in acute and convalescent serum specimens confirms WNV infection.

**Differential Diagnosis:** Other arboviral illnesses such as St. Louis encephalitis, many other causes of bacterial and aseptic meningitis and encephalitis, Rocky Mountain Spotted Fever, other viral febrile illnesses. Probably most important is ruling out treatable bacterial, fungal, or mycobacterial meningitis in cases with CNS involvement.

**Reporting:** West Nile virus encephalitis is a reportable disease nationally. State and local reporting requirements, which may vary, are listed online at:

[www.cdc.gov/ncidod/dvbid/westnile/city\\_states.htm](http://www.cdc.gov/ncidod/dvbid/westnile/city_states.htm)

**Prevention:** Prevention of West Nile disease revolves around reducing mosquito exposure. Emptying containers that capture water around the home where mosquitoes may breed, avoiding areas where mosquitoes are biting, using barrier methods such as screening or long-sleeve clothing, and wearing appropriate mosquito repellents such as DEET are all important measures. There is no vaccine yet for prevention of human infection, although there are candidate vaccines under development. An equine vaccine is available for horses. Excellent information on prevention can be found at CDC's West Nile website at:

<http://www.cdc.gov/ncidod/dvbid/westnile/qa/prevention.htm>

**Treatment:** Treatment is supportive; hospitalization and intensive supportive care including mechanical ventilation may be required for those most severely affected. Antiviral drugs such as ribavirin have not been proven to improve survival or outcome.