



Colorado Department
of Public Health
and Environment

WEST NILE VIRUS

Guidelines for Emergency Departments and Health Care Providers

Updated July 13, 2007

These guidelines are provided to assist emergency department and other health care providers with the recognition and diagnosis of illness due to West Nile virus (WNV).

For up-to-date results on WNV surveillance data in Colorado, please visit CDPHE's Zoonotic Diseases web site at: <http://www.cdphe.state.co.us/dc/zoonosis/wnv/wnvhom.html> . For general prevention information and educational materials refer patients to <http://www.FightTheBiteColorado.com>.

Clinical Features

- Incubation period: probably 3- 14 days
- Most human infections (~80%) are not clinically apparent
- Approx. 1 in 5 infected persons develops febrile illness
- Approx. 1 in 150 infected persons develops neuroinvasive disease.
- The full clinical spectrum of WNV has not been determined
- Older age (>50 yrs.) is the most significant risk factor for severe neurological disease and death
- Case fatality rate is approximately 8% for neuroinvasive disease (2% in 2003 for all cases).

West Nile Fever

The less severe form of WNV infection has been described as a febrile illness of sudden onset. IgM positive Colorado patients interviewed in 2003 (n=2100) reported the following symptoms: malaise (85%), headache (85%), myalgia (77%), fever (75%), muscle weakness (72%), chills (66%), anorexia (68%), rash (63%), eye pain (49%) and lymphadenopathy (39%). Some patients have developed transient muscle tremors, fasciculation or flaccid paralysis following an otherwise mild febrile illness. The acute febrile period generally lasts three to six days, although patients report that extreme fatigue, malaise and weakness have persisted for several weeks.

Neuroinvasive Infections

- Neuroinvasive disease due to WNV infection has occurred in patients of all ages although it is most commonly reported in persons > 50 years of age.
- Neurological presentations have included:
 - severe muscle weakness
 - acute flaccid paralysis
 - ataxia and extrapyramidal signs
 - cranial nerve abnormalities
 - myelitis
 - optic neuritis
 - Guillain-barre' syndrome
 - respiratory paralysis

Acute Flaccid Paralysis (poliomyelitis)

- Presents as a polio-like syndrome
 - Asymmetric weakness or paralysis without pain or sensory loss
 - CSF pleocytosis
 - Electromyography and nerve-conduction studies are indicative of a severe asymmetric process involving anterior horn cells of the spinal cord and their axons
 - Onset of dysarthria and dysphagia early in the clinical course was predictive of subsequent respiratory failure requiring mechanical ventilation
- Must differentiate from Guillain-Barre' Syndrome
 - GBS treatment modalities are not effective for WNV infections and are associated with significant potential morbidity

Clinical Suspicion

Diagnosis of WNV infection is based on a high index of clinical suspicion during the transmission season and obtaining specific laboratory tests.

- In Colorado, human WNV infections are most likely to occur from June through October with peak activity from August through mid-September.
- WNV, or other arboviral diseases such as St. Louis encephalitis, should be considered in patients with unexplained encephalitis, meningitis or acute flaccid paralysis.
- The local presence of WNV positive animal or human cases should raise suspicion.
- Obtaining a recent travel and mosquito exposure history is important. Year-round transmission is possible in some areas, particularly southern states.
- Acute febrile illness or encephalitis within two weeks of receiving blood products.
- WNV season coincides with peak enteroviral meningitis activity.

Treatment

Treatment is supportive, often involving hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections for patients with severe disease. Clinical trials on immune globulins, ribavirin, interferon alpha-2b and other compounds are being evaluated but no controlled studies have been completed on the use of these or other medications, including steroids, anti-seizure drugs, or osmotic agents, in the management of WNV encephalitis.

Atypical Modes of Transmission

The majority of patients will be exposed to WNV via the bite of an infected mosquito. However, several new modes of WNV transmission have been described: organ transplant, receipt of blood products, breastfeeding and intrauterine transmission. These atypical modes of transmission are expected to occur infrequently. Details of these investigations are available at: <http://www.cdc.gov/ncidod/dvbid/westnile/publications.htm>.

Blood transfusion

- Transmission has been documented via whole blood, packed RBCs, platelets and plasma.
- In July, 2003 FDA and blood banks instituted screening procedures for blood products. In 2003, over 1,000 units of infected blood were identified and removed. Six cases of WNV transmission via blood were documented in 2003, compared to 23 such cases in 2002.
- WNV testing is indicated for patients with encephalitis, flaccid paralysis or a febrile illness with neurological manifestations within 2 weeks of receiving any blood products.

- Patients with laboratory diagnosed WNV infection should be questioned about blood donation within the preceding 14 days and any donated units should be withdrawn.

Intrauterine

- During the 2002 season, five pregnant women were identified with WNV infection. Four of these women gave birth to healthy, uninfected infants. One birth had an adverse outcome. The infant was found to be infected with WNV although correlation to the adverse outcome could not be established.
- A case series of 72 pregnant women infected in 2003 is underway. Preliminary results have documented probable *in utero* infection in 4 infants including one with neonatal neuroinvasive disease.
- Women who are pregnant should take precautions to prevent mosquito bites.
- There is **no** indication to screen asymptomatic, pregnant women for WNV infection.
- New recommendations for management of infants born to mothers infected with WNV during pregnancy are available at :
<http://www.cdc.gov/ncidod/dvbid/westnile/congenitalinterimguidelines.htm>

Breast-feeding /Organ Donation/Occupational Exposure

- A single case of transmission via breast-feeding was reported in 2002 in a woman who developed an acute febrile illness 15 days post-delivery. Cerebrospinal fluid and a sample of breast milk were positive for WNV-specific IgM. The infant remained afebrile and healthy, although a serum sample collected at 25 days of age was WNV-specific IgM positive
- Because of the well established benefits from breast-feeding, and the unknown level of risk of WNV transmission, no change in breast-feeding recommendations are being made.
- There is **no** indication to screen asymptomatic, breast-feeding women for WNV infection.
- A single case in which four organ recipients developed illness after receiving organs from a single donor (two kidneys, heart, liver). The organ donor was determined to have been infected by blood products received during resuscitation efforts.
- Three laboratory workers were infected via accidental percutaneous exposures while handling WNV infected birds.

Laboratory Diagnosis

Diagnosis is based on clinical suspicion and WNV antibody testing of CSF and serum. Testing is conducted at commercial labs and the state health department lab.

Laboratory Findings

- Total leukocyte counts in peripheral blood were mostly normal or elevated, with lymphocytopenia and anemia also occurring.
- Hyponatremia was sometimes present, particularly among patients with encephalitis.
- Examination of the cerebrospinal fluid (CSF) showed pleocytosis, usually with a predominance of lymphocytes.
- Protein was universally elevated; glucose was normal.
- Computed tomographic scans of the brain mostly did not show evidence of acute disease, but in about one-third of patients, magnetic resonance imaging showed enhancement of the leptomeninges, the periventricular areas, or both.

Diagnostic Testing

- The most efficient diagnostic method is detection of IgM antibody to WNV in serum or cerebrospinal fluid (CSF).
- In neuroinvasive disease, specimens collected within 7 days of onset are usually positive. However seroconversion may take up to 2 weeks or longer in some patients. If specimens collected within a week of onset are negative, but the diagnosis of WNV infection is still being considered, a second serum sample collected 3-4 weeks post-onset should be tested.
- Since IgM antibody does not cross the blood-brain barrier, demonstration of WNV IgM antibody in CSF is considered diagnostic (confirmation) of WNV infection and strongly suggests central nervous system infection.
- Demonstration of WNV IgM antibody in serum is diagnostic, however, false positives and cross-reactions with related flaviviruses, especially St. Louis encephalitis virus, can occur.
- Patients recently vaccinated against or recently infected with related flaviviruses (e.g yellow fever, Japanese encephalitis, dengue) may have positive WNV results.
- WNV-specific IgM has persisted in patients for >500 days. Positive serologic tests must be correlated with clinical presentation, season and potential exposure to WNV.
- A positive IgG antibody test from a single sample is **not** diagnostic for acute infection.

Indications for Testing

- Clinically compatible illness during transmission season.
- Providers should consider if there is any clinical value in testing patients with mild fevers of unknown origin in the absence of neurological signs.
- Encephalitis cases of unknown etiology.
- Aseptic meningitis cases, although at this time of year, the majority of such cases may be caused by enteroviruses; CSF testing by PCR for enterovirus is recommended.
- Patients with flaccid paralysis or neurological symptoms following a febrile illness.
- Pregnant or breast-feeding women with a compatible febrile illness and exposure history.
- Patients with onset of compatible illness within 2 weeks of receiving blood products or having donated blood.

WNV Specimen Testing (call for shipping address and lab forms)

State Health Department Laboratory: (303) 692-3485

Weld County Health Department Laboratory: (970) 304-6415 x2273

- Submit acute CSF and/or serum sample (collected within seven days of illness onset)
- A convalescent sample, 3-4 weeks post-onset, may be necessary
- Specimens should be sent refrigerated (i.e. with cold packs) via your hospital/clinical lab
- ****The public health lab charge for WNV testing is \$75 per specimen (CSF or serum)****

REPORT cases of WNV infection to the local or state health department

Communicable Disease Epidemiology Program

(303) 692-2700 After hours (303) 370-9395

References:

- Peterson LR, Marfin AA. West Nile Virus: A Primer for the Clinician. Ann Intern Med 2002;137:173-9.
- Nash D et al. The outbreak of West Nile Virus infection in the New York City area in 1999. NEJM 2001;344:1807-14.
- Weiss D et al. Clinical findings of West Nile Virus infection in hospitalized patients, New York and New Jersey, 2000. Emerg Infect Dis 2000;7:654-8.
- Sejvar, J, et al. Neurologic manifestations and outcome of West Nile virus infection. JAMA. 2003; 290:511-15.