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# West Nile Virus Infection

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## Disease

The West Nile virus (WNV) is an RNA virus in the Flaviviridae family that is closely related to the Japanese and St. Louis Encephalitis Viruses. Since its discovery in 1937, it has caused sporadic epidemics of a mild febrile illness (West Nile Fever) in areas where it is endemic, primarily Africa, Eastern Europe and the Middle East. However, recent outbreaks of this virus have been more severe with neurological manifestations now being prominent. In New York City during the summer of 1999, an epidemic of unexplained encephalitis with motor weakness coincided with a large epizootic that killed thousands of birds, leading to the identification of the first known appearance of WNV in the Western Hemisphere. The virus has subsequently spread across most of the U.S.

## Pathogenesis

The West Nile virus is primarily a pathogen of birds, chiefly affecting crows where it causes a high level of viremia leading to a fatal meningoencephalitis and myocarditis. Other birds and mammals, particularly horses, can also be infected but are not important reservoirs. *Culex pipiens* and other mosquito species are easily infected after feeding on viremic birds and then serve as efficient vectors transmitting WNV to the next animal or human they bite. After entrance into the blood stream there is a short period of viremia in humans. Symptoms appear after a 2-14 day incubation period in those who develop symptomatic disease. Virulence factors are incompletely understood, but it is known that the virus reaches the central nervous system in the more symptomatic cases with involvement of the meninges and brain parenchyma, particularly the brain stem. Some patients develop a motor axonopathy manifested by progressive muscle weakness that can resemble Guillain-Barre syndrome (GBS).

## Epidemiology

The U.S. epidemic that started in New York with 62 cases continues to spread. As the virus has spread across the country the number of cases has increased, with 9858 reported infections during 2003. Serological surveys suggest up to 140 infections occur for every case of severe disease. The case fatality rate for neuroinvasive infections has remained 10-14% each year. The elderly are disproportionately affected, with most of the deaths and serious cases requiring hospitalization over the age of 65. Underlying diabetes, hypertension and immunosuppression may also be predisposing risk factors. Children rarely develop serious symptomatic disease. In the U.S., the appearance of dead birds is an important sentinel event that has preceded nearly all reported human cases. In addition to dead birds, pooled mosquitoes can be tested for the presence of WNV DNA as another surveillance method to predict periods of high risk for human disease. Transmission to humans is almost exclusively due to the bite of an infected mosquito. Rare cases have occurred following receipt of blood or solid organs from a viremic donor, and from breast-feeding. Up to date surveillance for human cases and WNV activity in animals can be obtained at [www.cdc.gov/ncidod/dvbid/westnile/surv&control.htm](http://www.cdc.gov/ncidod/dvbid/westnile/surv&control.htm).



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## Clinical Features of West Nile Virus Infection

Symptoms of WNV infection are variable and can be considered to fall into a continuous spectrum of disease. Most WNV infections are asymptomatic. Up to 20% may have a mild febrile syndrome with or without a transient maculopapular rash and myalgias (the classic West Nile Fever). Approximately one in 140 infections develop neurological symptoms requiring hospitalization. These include an encephalitis syndrome (with fever, altered level of consciousness, confusion +/- progressive motor weakness resembling GBS), an aseptic meningitis syndrome (with fever, headache, stiff neck, and photophobia) or a combined meningoencephalitis syndrome. GI symptoms such as nausea, vomiting and diarrhea are also very common in severe disease. Rash, myalgias, arthralgias and urinary incontinence or retention are not uncommon. The CSF is abnormal in severe WNV infection requiring hospitalization, with elevated protein and a pleocytosis that is usually lymphocytic. Peripheral lymphopenia is common. Although CT of the brain is usually normal, up to 1/3 of hospitalized WNV cases show evidence of leptomenigeal or periventricular inflammation on MRI.

## Diagnosis

WNV infection should be considered for any person presenting with features of encephalitis, aseptic meningitis or GBS if mosquitoes are active and WNV has been previously detected in a community where the patient lives, works, or has visited. Diagnosis of WNV infection can be confirmed by:

- IgM-capture ELISA on cerebrospinal fluid (CSF) – the most sensitive test
- 4-fold rise in IgG titer from paired acute/convalescent sera (with the acute sample obtained within the first week of symptoms and the convalescent obtained at least 2 weeks later) confirmed by plaque reduction neutralization test (PRNT) that differentiates WNV from other flaviviruses
- Simultaneous presence of IgM and IgG antibodies in serum
- PCR detection of DNA from CSF, blood or tissue – experimental, insensitive
- Isolation of WNV on culture in CSF, blood or tissue

The antibody tests are available at some commercial laboratories, but PCR is rare, and viral isolation can only be attempted in labs with BSL-3 capability. If WNV infection is suspected, CSF and serum (acute and convalescent, if available) samples should be obtained and sent to a laboratory that can reliably perform the testing, such as state or local health departments.

## Treatment

There is no specific antiviral therapy available for WNV infection, however empiric therapy with acyclovir (for HSV encephalitis), and antibiotics (for bacterial meningitis) may be warranted until these two treatable entities have been ruled out by CSF testing. Management consists of supportive therapy, including mechanical ventilation when severe disease leads to flaccid paralysis.

## Prevention

Prevention of human disease relies on avoidance of mosquitoes by vector control methods and personal protective behaviors. Aggressive vector control methods can reduce or stop the spread of human cases, and consists of disrupting standing water pools that are potential breeding grounds, using larvicidal agents in stagnant water sources, and spraying insecticide to kill adult mosquitos during periods of high viral activity. From the time that dead birds are first detected until the time of the first substantial freeze, persons in WNV affected areas should be advised to avoid mosquitoes by the following measures:

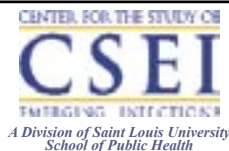
- stay indoors during dusk and dawn, if possible
- wear long-sleeve shirts and pants while outdoors during those hours
- apply insect repellent containing 10-50% DEET to exposed skin and clothing while outdoors during mosquito biting hours according to manufacturer's instructions (not for use with very young children)
- repair any holes in window screens that could allow mosquito entry

These measures should be especially targeted to the elderly, who are most vulnerable.

## Vaccination

Although research is ongoing, there are no currently available human vaccines for West Nile virus.

Additional information and references available at <http://www.emerginginfections.slu.edu>



## Differential Diagnosis

Severe WNV infection with neurological disease can present similarly to other acute viral encephalitides (including Herpes Simplex, Eastern and Western Equine Encephalitis, St. Louis Encephalitis, Japanese Encephalitis), non-infectious encephalitis/encephalopathy (e.g. lupus cerebritis, hepatic, uremic), other causes of meningitis (bacteria, enterovirus, drug-induced) and other causes of progressive weakness (e.g. Guillain-Barre Syndrome). None of the other viral encephalitides are likely to present with the motor weakness resembling GBS that has been reported with WNV. Metabolic encephalopathies and typical GBS would not present with fever in the absence of a concomitant infection.

## Infection Control

Because there is no known human-to-human transmission of West Nile Virus, standard precautions should be followed when contacting patients and handling clinical specimens.

## Reporting

Any suspected cases of WNV infection should be reported to the local health department immediately to allow prompt confirmation, case finding and tracking to aid in the outbreak evaluation.

## Disclaimer

Information contained in this fact sheet was current as of May 2004, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment.

May 2004