WEST NILE VIRUS

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description:

Most WNV infections are asymptomatic. Less severe infections are common and include fever, headache, and body aches, often with a skin rash and swollen lymph glands. More severe infections are often associated with high fever and neurologic involvement including aseptic meningitis (inflammation of the lining of the brain and spinal cord) and encephalitis (inflammation of the brain). WNV encephalitis is not easily distinguished clinically from other causes of encephalitis. Manifestations can include headache, neck stiffness, stupor, disorientation, coma, tremors, convulsions, paralysis, and sometimes, death. The risk of severe illness increases with age.

Causative Agent:

West Nile virus (WNV) is a single-stranded RNA virus of the family Flaviviridae, genus *Flavivirus*, that is spread by mosquitoes. Viruses transmitted by mosquitoes are referred to as arthropod-borne viruses or arboviruses. WNV is one of more than 30 arboviruses that have been identified as human pathogens in the Western Hemisphere.

Differential Diagnosis:

Encephalitis, meningitis, acute flaccid paralysis (AFP), and nonspecific febrile illness.

Laboratory identification:

WNV is usually diagnosed serologically. IgM and IgG specific testing for acute and convalescent sera is available at larger commercial laboratories. Appropriate samples include serum and CSF. RT-PCR is not recommended for patients that are able to mount an immune response, due to the low likelihood of detecting the virus.

> **UPHL:** UPHL performs testing of serum or CSF specimens from patients with signs or symptoms compatible with neurological disease. Requests for testing should be reviewed and approved by a public health epidemiologist familiar with WNV-related disease at the UDOH. Selected patients who are suspected of having WNV infection but do not meet the above criteria will be considered for testing at UPHL when such testing would provide the first evidence of human WNV activity in an area. Use of RT-PCR will be considered for selected immunocompromised patients with symptoms of WNV neuroinvasive disease.

Blood Donor Screening

Public health receives direct notification of WNV detection in blood donations from blood collection agencies (such as Red Cross, ARUP), with applicable information required for case investigations. Testing of donated blood for WNV RNA is being performed at all Utah blood banking systems. Viremic donor surveillance occurs in coordination with the major blood collection agencies servicing Utah.

Treatment:
Treatment of symptoms and supportive care are the only methods of treatment for WNV.

Case fatality:
Case-fatality rates for such WNV disease range from 3–15% of cases with clinical encephalitis.

Reservoir:
Birds are believed to serve as the primary reservoir for WNV. Mosquitoes spread the virus from bird to bird. Some mosquitoes prefer to feed on birds, while others feed on both birds and mammals, such as humans and horses. If a mosquito bites an infected bird and then bites a person, that person may become infected with WNV.

Transmission:
WNV is spread to humans by the bite of an infected mosquito. There is no evidence to suggest that a person can get WNV infection from handling a live or dead infected bird or other animal. Common sense precautions should be followed, including using gloves and/or a plastic bag when handling any dead animal. Current evidence supports the likelihood of direct bird-to-bird transmission.

Additional modes of transmission, including organ transplantation, blood transfusion, breastfeeding, transplacental (mother to infant), and occupational exposures, were recognized during the 2002 WNV epidemic in the U.S. However, these modes of transmission represent a very small percentage of cases. WNV is not spread through casual contact such as touching or kissing a person with the virus.

Susceptibility:
All humans are susceptible to WNV, however, individuals over the age of 50 or immunocompromised individuals are at higher risk for more severe illness.

Incubation period:
The incubation period for WNV infection is generally 3–14 days.

Period of communicability:
WNV infection is not communicable from person to person, other than the rare alternative modes of transmission.

Epidemiology:
WNV was first isolated in the West Nile Province of Uganda in 1937. The first epidemic occurred in Israel during the 1950's. WNV occurs naturally in Africa, India, Australia, the Middle East, Europe, and most recently, North America. Before the fall of 1999, WNV had not been documented in the Western Hemisphere. In 1999, human cases of WNV infection were identified in New York City. By the end of October 1999, WNV had been confirmed in multiple native species of birds from New York City and areas

within a 200-mile radius. Since 1999, WNV infection in humans, birds, other animals and mosquitoes has been reported throughout the U.S. Most cases of WNV infection in North America occur in the summer and early- to mid-fall. People over the age of 50, if they get sick, are more likely to develop serious symptoms from WNV infection.

Utah has not had many seasons of WNV. Human cases have increased from 1 case in 2003 to 158 cases in 2006.

✓ PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms
- Identify sources of infection and work with Mosquito Abatement to eliminate the source.
- Educate the public and clinicians about disease transmission and prevention measures.

Prevention:

Environmental Measures

People should be encouraged to reduce mosquito populations around their homes and neighborhoods by getting rid of any standing water that might support mosquito breeding. Mosquitoes will begin to breed in any puddle or standing water that lasts for more than four days. People should be advised of the following:

- Dispose of, or regularly empty any metal cans, plastic containers, ceramic pots, and other containers (including trash cans) on their property that might hold water.
- Pay special attention to discarded tires. Stagnant water in tires is a common place for mosquitoes to breed.
- Drill holes in the bottom of recycling containers that are left outdoors, so that water can drain out.
- Clean clogged roof gutters; remove leaves and debris that may prevent drainage of rainwater.
- Turn over plastic wading pools and wheelbarrows when not in use.
- Do not allow water to stagnate in birdbaths; aerate ornamental ponds or stock them with fish.
- Keep swimming pools clean and properly chlorinated; remove standing water from pool covers.
- Use landscaping to eliminate standing water.

Personal Preventive Measures/Education

- There is no human vaccine to prevent WNV infection or its consequences. People should be advised to take the following precautions if they live in or visit an area with mosquitoes:

- Avoid outdoor activities between dusk and dawn, if possible, as this is the time of greatest mosquito activity.
- Fix any holes in screens, and make sure they are tightly attached to all doors and windows.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 35%, which is the highest concentration recommended adults. The highest DEET concentration recommended for children 2 months to 12 years of age is 10%. DEET products should not be used on children less than two months of age. Mosquito netting may be used to cover infant carriers or to protect other areas for children less than two months of age. The following precautions should be observed when using DEET products:
    - Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
    - Apply DEET on exposed skin, using only as much as needed.
    - Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and the mouth.
    - Do not use DEET over cuts, wounds, or irritated skin.
    - Wash treated skin with soap and water after returning indoors, and wash treated clothing.
    - Avoid spraying DEET products in enclosed areas.

Picardin (KBR 3023) is a relatively new repellent that is now available in the U.S. Recent studies have shown it to be safe and effective. Picardin-containing repellents should be used according to the manufacturer's recommendations.

A number of plant-derived products are available for use as repellents, but most of these products do not provide the same level or duration of protection as products containing DEET. However, there are studies that show that oil of lemon eucalyptus [p-methane 3,8-diol(PMD)] provides as much protection as low concentrations of DEET when tested against mosquitoes found in the U.S.

Chemoprophylaxis:

None

Vaccine:

Vaccine is available for horses. The FDA is in the process of developing a human vaccine.

Isolation and quarantine requirements:

None

✓ CASE INVESTIGATION

Reporting:

Report all suspect and confirmed cases of WNV.

Case definition:

WNV (2004):

Clinical description

Arboviral infections may be asymptomatic or may result in febrile illnesses of variable severity sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes include aseptic meningitis, myelitis and encephalitis, which are clinically indistinguishable from similar syndromes caused by other viruses. Arboviral meningitis is usually characterized by fever, headache, stiff neck, and pleocytosis in cerebrospinal fluid. Arboviral myelitis is usually characterized by fever and acute bulbar or limb paresis or flaccid paralysis. Arboviral encephalitis is usually characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction. Less common neurological syndromes can include cranial and peripheral neuritis or other neuropathies, including Guillain-Barré syndrome. Non-neuroinvasive syndromes caused by these usually neurotropic arboviruses can rarely include myocarditis, pancreatitis, or hepatitis. In addition, they may cause febrile illnesses (e.g., West Nile fever [WNF]) that are non-localized, self-limited illnesses with headache, myalgias, arthralgias, and sometimes accompanied by skin rash or lymphadenopathy. Laboratory-confirmed arboviral illnesses lacking documented fever can occur, and overlap among the various clinical syndromes is common.

Clinical criteria for diagnosis

Cases of arboviral disease are classified either as neuroinvasive or non-neuroinvasive, according to the following criteria:

Neuroinvasive disease requires the presence of fever and at least one of the following, as documented by a physician and in the absence of a more likely clinical explanation:

- Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma), or
- Other acute signs of central or peripheral neurologic dysfunction (e.g., paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements), or
- Pleocytosis (increased white blood cell concentration in cerebrospinal fluid [CSF]) associated with illness clinically compatible with meningitis (e.g., headache or stiff neck).

Non-neuroinvasive disease requires, at minimum, the presence of documented fever, as measured by the patient or clinician, the absence of neuroinvasive disease (above), and the absence of a more likely clinical explanation for the

illness. Involvement of non-neurological organs (e.g., heart, pancreas, liver) should be documented using standard clinical and laboratory criteria.

Laboratory criteria for diagnosis

Probable case:

- Stable (less than or equal to a two-fold change) but elevated titer of virus-specific serum antibodies, or
- Virus-specific serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.

Confirmed case:

- Four-fold or greater change in virus-specific serum antibody titer, or
- Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, CSF, or other body fluid, or
- Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
- Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Case classification

A case must meet one or more of the above clinical criteria and one or more of the above laboratory criteria.

Comment

Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic tests using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in areas where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization tests using an appropriate battery of closely related viruses. This is essential, for example, in determining that antibodies detected against St. Louis encephalitis virus are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur. Because dengue fever and West Nile fever can be clinically indistinguishable, the importance of a recent travel history and appropriate serologic testing cannot be overemphasized. In some persons, West Nile virus-specific serum IgM antibody can wane slowly and be detectable for more than one year following infection. Therefore, in areas where West Nile virus has circulated in the recent past, the co-existence of West Nile virus-specific IgM antibody and illness in a given case may be coincidental and unrelated. In those areas, the testing of serially collected serum specimens assumes added importance.

Viremic donors identified as having WNV symptoms will be included in case counts. If no WNV symptoms are identified, viremic donors will receive separate classification from human WNV cases for Utah.

Case Investigation Process:

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks:

Multiple human cases in Utah would constitute an outbreak.

Identification of case contacts:

This disease is not spread person to person.

Case contact management:

None

✓ REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l

Control of Communicable Diseases Manual (18th Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Massachusetts Department of Health WNV Disease Plan

Utah Department of Health West Nile Virus Response and Mosquito-Borne Virus Surveillance Plan; Final Draft: August 4, 2004; Updated for 2007 season: June 4, 2007