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Update on West Nile Virus

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West Nile Virus (WNV) is an arthropod-born Flavivirus that is the most common cause of viral meningoencephalitis in North America. The transmission of WNV to humans is due primarily to inoculation by an infected mosquito, with peak incidence of transmission taking place between July and October. Mosquito exposure is the most important risk factor, with individuals greater than 50 years of age being at a higher risk for developing meningoencephalitis.[1]

Following an incubation period of two to 15 days, the virus migrates to the lymph nodes and spleen eventually spreading to the central nervous system. While the majority of those infected with WNV are asymptomatic (80%), some may demonstrate constitutional symptoms such as fever and fatigue. Clinical signs of meningeal irritation may be observed, whereas those suffering from fulminant encephalitis demonstrate global symptoms including seizures and mental status changes. Finally, cases of poliomyelitis with paralysis have also been documented.[2] Current treatment of WNV infections include supportive care with pain control, antiemetic therapy with rehydration, anticonvulsants, and monitoring for increases in intracranial pressure. [1] Antiviral medications have demonstrated limited utility.

While viral cultures remain the gold standard in diagnosing WNV infections, serological testing of serum and cerebrospinal fluid (CSF) for anti-WNV IgM using enzyme-linked immunosorbent assays (ELISA) is currently the most efficient modality for confirming the presence of WNV.[1] Testing of both serum and CSF determines the extent of infection in WNV, with detection of anti-WNV IgM in the CSF indicating intrathecal synthesis of the virus. The sample should ideally be collected within eight days of symptom onset. Anti-WNV IgM may remain elevated up to six months after an infectious episode. Other testing modalities, including CSF RT-PCR, have demonstrated a limited utility in diagnosis due to low sensitivities and the possibility of transient and low viremia.[1] Additional CSF findings may include pleocytosis with a predominantly lymphocytic infiltrate, high protein, and normal glucose.[3] Brain imaging studies are often not helpful in determining a specific etiology.

The role of the pathologist in WNV infections includes aiding in the diagnosis of the pathogen as well as educating others as to possible causes of serological false positives, which may be observed in those previously vaccinated for or

infected with related Flaviviruses. Some of these include St. Louis encephalitis virus, Japanese B. encephalitis, and Murray Valley encephalitis.[1, 3] Additional neutralization assays including the plaque-reduction neutralization test (PRNT) may help to definitively determine the presence of an arthropod-born Flavivirus infection as well as to assist in distinguishing between the Flaviviruses, although cross reactivity may still be observed.[1]

West Nile Virus is a Flavivirus arthropod-born infection and is the most common cause of meningoencephalitis in North America. Those infected may present with a wide spectrum of symptoms including severe encephalitis with global deficits. Efficient laboratory diagnosis includes ELISA testing of the serum and CSF for the presence of anti-WNV IgM, with the detection of antibody in the CSF indicating central nervous system infection. When the possibility of false positives or other Flavivirus infections are of concern, additional neutralizations assays may be utilized.

Follow Up Questions for Self-Assessment

1. Which of the following symptom(s) do the majority of people infected with WNV display?
    a. Non-specific flu like symptoms—fever and fatigue
    b. Nuchal rigidity and photophobia
    c. New onset seizures and altered mental status
    d. Diffuse rash on the trunk and abdomen
    e. Asymptomatic manifestations

2. What is the most efficient and widely accepted means of diagnosing WNV associated meningoencephalitis?
    a. Culture of a brain biopsy for WNV
    b. RT-PCR
    c. ELISA testing for anti-WNV IgM
    d. Direct immunofluorescence
    e. Electron microscopy

3. Which of the following may cause a false positive test when using ELISA methods for detecting WNV?
    a. Previous vaccination for Flaviviruses
    b. Infection with the St. Louis encephalitis virus
    c. Infection with the Japanese B. encephalitis virus
    d. Infection with the Murray Valley encephalitis virus
    e. All of the above

4. If false positive testing is a concern when conducting ELISA testing for WNV, what additional testing modality should next be considered?

a. ***plaque-reduction neutralization testing (PRNT)***
b. RT-PCR
c. Electron microscopy
d. Viral cultures

References

1. Centers for Disease Control and Prevention. Division of Vector-Borne Infectious Disease. West Nile Virus. www.cdc.gov/ncidod/dvbid/westnile/index.htm. Updated December 16, 2008. Accessed June 22, 2009

2. Glass JD, Samuels O, and Rich MM. Poliomyelitis due to West Nile virus. *N Engl J Med*. 2002;347(16):1280-1281.

3. Petersen LR, Marfin AA. West Nile virus: a primer for the clinician. *Ann Intern Med.* 2002;137(3):173-179.