CASE DEFINITION FOR WEST NILE VIRUS

1. **General disease/pathogen information:** West Nile virus (WNV) is a mosquito-borne viral disease resulting in an encephalomyelitis characterized by central and peripheral nervous system dysfunction. Many vertebrate species are susceptible to natural WNV infection; however, fatal neurological outbreaks have only been documented in equids, humans, geese, wild birds (particularly corvids), squirrels, farmed alligators, and dogs. Birds serve as the natural host reservoir of WNV. Many birds do not develop clinical infections, but fatal disease occurs in some birds, especially if naïve to the virus.
   - **1.1.** *Etiologic agent:* WNV is a *Flavivirus* of the family Flaviviridae. It is related to the St. Louis encephalitis, Japanese encephalitis, yellow fever, and Murray Valley encephalitis viruses.
   - ***1.1*** *Distribution:* WNV is distributed worldwide. It is endemic in parts of Africa, Asia, the Middle East, Europe, North America, Central America, Caribbean Islands, and South America. WNV was first identified in the United States in 1999 in New York State and is currently endemic across the entire continental United States.
   - ***1.2*** *Clinical signs:* 10-39 percent of unvaccinated horses infected with WNV will develop clinical signs. Most clinically affected horses exhibit neurological signs such as ataxia (including stumbling, staggering, wobbly gait, or incoordination) or at least two of the following: circling, hind limb weakness, recumbency or inability to stand (or both), multiple limb paralysis, muscle fasciculation, proprioceptive deficits, altered mental status, blindness, lip droop/paralysis, teeth grinding. Behavioral changes including somnolence, listlessness, apprehension, or periods of hyperexcitability may occur. Other common clinical signs include colic, lameness, anorexia, and fever.
   - **1.2.** *Incubation period***:** Estimated at 3-15 days in horses
   - **1.3.** *Differential diagnosis:* Diagnosis of WNV cannot be based on clinical signs alone because of its clinical similarity to many neurological disease/disorders of equids including other arboviruses (Eastern and Western encephalomyelitis and Highlands J virus), other infectious diseases (equine protozoal myeloencephalitis, bacterial meningitis, equine herpesvirus myeloencephalopathy, rabies) and noninfectious diseases (hypocalcemia, tremorigenic toxicities, hepatoencephalopathy, leukoencephalomalacia, and trauma).
   - **1.4.** *Transmission and reservoir:* WNV is maintained in an enzootic transmission cycle between birds and mosquitoes. Equids are dead-end hosts. Mosquito vectors, primarily *Culex* species, acquire the virus from viremic birds and transmit it to susceptible equids, humans, and other animals. Cats can acquire the virus from eating infected mice. There also appears to be the possibility of oral and vertical transmission in people and birds, but the importance of these transmission methods is unknown. WNV has been transmitted through blood transfusion in humans and would likely be feasible if equine blood donors were viremic at the time of blood collection for transfusion. The level of WNV activity depends heavily upon vector and host competence. WNV has been detected in over 150 species of birds in the United States, many of which do not

develop clinical signs. Many species of mosquitoes and birds can support virus replication. *Culex pipiens* is a major vector in the Eastern and Midwestern United States and *Culex tarsalis* in the Western States. Corvids such as the American crow and blue jays along with other birds such as the house finch are suspected to be very efficient host reservoirs. Migratory birds may be responsible for introducing the virus into new regions from endemic regions. Immunity to WNV likely develops in regional bird populations resulting in reduced viral activity after initial outbreaks when bird populations are naïve. WNV has been isolated from 10 different species of ticks in the United States; however, the role of ticks in the natural transmission cycle is unclear. Viral transmission corresponds with the mosquito feeding and life cycle and is at its peak from mid-July to October in temperate regions. Transmission may be sustained year-round in semi-tropical regions of the country.

1.5. *Epidemiology:* Equids are particularly susceptible, developing encephalomyelitis due to WNV infection. Outbreaks involving equine WNV cases may occur following a noticeable bird die-off in the same region if the regional birds are susceptible to fatal WNV infections. Clinical disease develops in 10-39 percent of infected equids (in United States.), and there is a case-fatality rate of 30-40 percent (in United States). Horses that become recumbent and unable to rise have much higher case-fatality rates of 60-80 percent. Most of these deaths are from humane euthanasia or sequelae to the neurological dysfunction; however, spontaneous death from WNV infection can occur. Recovery from infection typically occurs within 7 days of onset of clinical signs. To diagnose WNV, one must consider geographic region, mosquito activity, and previous cases of WNV infection in that area in birds, humans, and equids. Vaccination status of the equid should also be considered in the diagnosis as it can affect diagnostic test interpretation. Laboratory testing will provide definitive diagnoses.

2. Laboratory criteria

2.1. *Agent identification:* Virus identification can be performed by culture, immunohistochemistry, or reverse transcriptase polymerase chain reaction (RT-PCR). Preferred diagnostic tissues from equids for virus isolation are brain or spinal cord; isolation of WNV or detection of WN viral nucleic acid sequences in equine blood or CSF are infrequent.

2.2. *Serological tests:* Antibody titers can be identified in paired serum samples by IgG ELISA, plaque reduction neutralization test (PRNT), and hemagglutination inhibition (HI). Only a single serum sample is required for IgM capture enzyme linked immunosorbent assay (ELISA). For paired serum samples, the first serum should be drawn as soon as possible after onset of clinical signs and the second drawn at least 14 days post-onset. WNV vaccination history must be considered in interpretation of serology results.

2.2.1. Assumptions:

2.2.1.1. IgM antibody in equine serum is relatively short-lived. A positive IgM-capture ELISA means infection with WNV or a closely related flavivirus has occurred, probably within the last 3 months.

2.2.1.2. Neutralizing antibody detected in serum by PRNT indicates past infection with WNV or vaccination with WNV vaccine; equines exposed to WNV in prior years may test positive by PRNT.

3. Case definition

3.1. *Suspect equine case:* A susceptible animal with neurological signs consistent with West Nile encephalomyelitis and is located in or has recently visited an area with the appropriate climate with active hematophagous insects.

3.2 *Presumptive positive equine case:* A suspect case that has neutralizing serum antibodies as detected by PRNT without history of prior WNV vaccination.

3.3 *Confirmed positive equine case:*

3.3.1 Compatible clinical signs; ***AND***

3.3.2 Isolation of WNV from or demonstration of specific viral antigen or genomic sequences in tissue, blood cerebrospinal fluid, or other body fluid; ***OR***

3.3.3 Detection of IgM antibody against WNV by IgM-capture ELISA in serum (dilution dependent upon specific test used) or cerebrospinal fluid (at 1:2 or greater dilution); ***OR***

3.3.4 An associated fourfold or greater change in IgG-capture ELISA* or plaque-reduction neutralization test (PRNT) antibody titer to WNV in appropriately timed, paired serum specimens from an equid that is unvaccinated against WNV; ***OR,***

3.3.5 Positive immunohistochemistry for WN viral antigen in tissue.

**Controlled studies support WNV IgM at the confirmed positive level of certainty*

4. Reporting criteria:

4.1. Suspect cases are reported according to individual State procedure, typically by notification of State West Nile virus official or State animal health official.

4.2. Positive cases are to be reported to CDC's ArboNET by the State's chief animal health officer or appointed arboviral coordinators. Public distribution of this information is provided at:

4.2.1. USDA's National Animal Health Surveillance System (NAHSS) Equine West Nile virus information page
http://www.aphis.usda.gov/vs/nahss/equine/wnv/index.htm

4.2.2. U.S. Department of the Interior's USGS Disease Maps information page
http://diseasemaps.usgs.gov/wnv_us_veterinary.html

4.3. National Animal Health Reportable System (NAHRS) disease reporting of confirmed case occurrence. If a case meets the presumptive level of diagnostics only, animal health officials must use their discretion to decide if the case is valid. If considered valid, the case should be reported to NAHRS

5. Control and surveillance procedures

5.1. Annual vaccination of horses is recommended. Detailed vaccination guidelines are available from the American Association of Equine Practitioners (AAEP) at: http://www.aaep.org/vaccination_guidelines.htm

5.2 Reduce exposure to potentially WNV-infected mosquitoes by use of insect repellants, fans and screens in shelters

5.3 Insect vector control by eliminating mosquito habitat (stagnant water sources), regular removal of manure, and weed control.

5.4 Active surveillance in equids and wild birds is conducted by the USDA's Veterinary Services (VS), Centers for Disease Control and Prevention (CDC), U.S. Geological Survey, State wildlife agencies, and State and local health and vector control agencies.

References

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8. U.S. Department of Health and Human Services. Public Health Service. Centers for Disease Control and Prevention. *Epidemic/Epizootic West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control.* Produced by the National Center for Infectious Diseases, Division of Vector Borne Infectious Diseases, Fort Collins CO, 3rd Revision, 2003
9. United States Department of the Interior, U.S. Geologic Survey (USGS) Disease Map 2008. http://diseasemaps.usgs.gov/index.html Accessed March 7, 2009.