

Appendix B: Provincial Case Definitions for Diseases of Public Health Significance

Disease: West Nile Virus Illness

Effective: February 2019

West Nile Virus Illness

1.0 Provincial Reporting

Confirmed and probable cases of disease

2.0 Type of Surveillance

Case-by-case

3.0 Case Classification

3.1 Confirmed West Nile virus Neurological Syndrome (WNNS) Case

Clinical criteria AND AT LEAST ONE of the confirmed case diagnostic test criteria (See Section 4.1.1)

3.2 Probable WNNS Case

Clinical criteria AND AT LEAST ONE of the probable case diagnostic test criteria (See Section 4.1.2)

3.3 Confirmed West Nile virus Non-Neurological Syndrome (WN Non-NS) Case

Clinical criteria AND AT LEAST ONE of the confirmed case diagnostic test criteria (See Section 4.1.1)

3.4 Probable WN Non-NS Case

Clinical criteria AND AT LEAST ONE of the probable case diagnostic test criteria (See Section 4.1.2)

3.5 Confirmed West Nile virus Asymptomatic Infection (WNAI) Case (See Section 7.0, Comment #1)

Confirmed case diagnostic test criteria (See Section 4.1.1) IN THE ABSENCE of clinical criteria

3.6 Probable WNAI Case

Probable case diagnostic test criteria (See Section 4.1.2) IN THE ABSENCE of clinical criteria

4.0 Laboratory Evidence

4.1 Laboratory Confirmation

Any of the following will constitute a confirmed case of West Nile virus (WNV):

- Positive WNV culture
- Positive for WNV antigen in tissue
- Positive for WNV-specific nucleic acid
- Positive for WNV-specific antibody
- Diagnostic rise in WNV antibody titre

4.1.1 Confirmed Case Diagnostic Test Criteria

Confirmed Case Diagnostic Test Criteria (e.g. by Plaque Reduction Neutralization Test [PRNT] on serum or immunoglobulin M [IgM] detection in cerebrospinal fluid [CSF]) should be used to confirm the initial three locally acquired cases within each health region each year. For subsequent cases within that health region, boards of health may use the Probable Case Diagnostic Test Criteria to classify cases in their area as “Confirmed”.

AT LEAST ONE of the following:

- A significant (i.e., fourfold or greater) rise in WNV neutralizing antibody titres (using a PRNT or other kind of neutralization assay) in paired acute and convalescent sera, or CSF (See Section 7.0, Comment #2)

OR

- Isolation of WNV from, or demonstration of WNV antigen or WNV- specific genomic sequences using an assay verified for clinical testing in tissue, blood, CSF or other body fluids

OR

- Demonstration of flavivirus antibodies in a single serum sample using a WNV IgM enzyme-linked immuno-sorbent assay (ELISA), confirmed by the detection of WNV specific antibodies using a PRNT (acute or convalescent serum sample) (See Section 7.0, Comments #3 and #4)

OR

- Demonstration of WNV antibodies in a single CSF sample using a WNV IgM ELISA (See Section 7.0, Comments #2, #3 and #4)

OR

- A significant (i.e., fourfold or greater) rise in flavivirus hemagglutination inhibition (HI) titres in paired acute and convalescent sera or demonstration of a seroconversion using a WNV Immunoglobulin G (IgG) ELISA (See Section 7.0, Comments #3 and #4) AND the detection of WN specific antibodies using a PRNT (acute or convalescent serum sample)

4.1.2 Probable Case Diagnostic Test Criteria

AT LEAST ONE of the following:

- Detection of flavivirus antibodies in a single serum sample using a WNV IgM ELISA without confirmatory neutralization serology (e.g., PRNT) (See Section 7.0, Comment #3)

OR

- A significant (i.e., fourfold or greater) rise in flavivirus HI titres in paired acute and convalescent sera or demonstration of a seroconversion using a WNV IgG ELISA (See Section 7.0, Comment #3)

OR

- A titre of >1:320 in a single WNV HI test, or an elevated titre in a WNV IgG ELISA, with a confirmatory PRNT result

OR

- Demonstration of Japanese encephalitis (JE) serocomplex-specific genomic sequences in blood by nucleic acid amplification test (NAAT) screening on donor blood, by Blood Operators in Canada

4.2 Approved/Validated Tests

- Standard culture for WNV
- NAAT for WNV verified for clinical testing (See Section 7.0, Comment #1)
- WNV antigen detection in tissue
- WNV IgM antibody detection
- WNV HI, PRNT and/or IgG/IgM immunoassays

4.3 Indications and Limitations

- Sensitivity of NAAT testing is approximately 50% when used on plasma / serum samples collected less than 8 days after symptom onset.

5.0 Clinical Evidence

5.1 West Nile virus Neurological Syndrome (WNNS) Clinical Criteria:

- History of exposure in an area where WNV activity is occurring (See Section 7.0, Comment #5)

OR

- History of exposure to an alternative mode of transmission (See Section 7.0, Comment #6)

AND

- Fever
- AND NEW ONSET OF AT LEAST ONE of the following:**
- Encephalitis (acute signs of central or peripheral neurologic dysfunction),
OR
- Viral meningitis (pleocytosis and signs of infection e.g., headache, nuchal rigidity)
OR
- Acute flaccid paralysis (e.g., poliomyelitis-like syndrome or Guillain-Barré-like syndrome) (See Section 7.0, Comment #7)
OR
- Movement disorders (e.g., tremor, myoclonus)
OR
- Parkinsonism or Parkinsonia-like conditions (e.g., cogwheel rigidity, bradykinesia, postural instability)
OR
- Other neurological syndromes (See Section 7.0, Comment #8).

5.2 West Nile virus Non-Neurological Syndrome (WN Non-NS) Clinical Criteria:

- History of exposure in an area where WNV activity is occurring (See Section 7.0, Comment #5)
OR
- History of exposure to an alternative mode of transmission
AND AT LEAST TWO of the following: (See Section 7.0, Comment #8)
 - Fever,
 - Myalgia (See Section 7.0, Comment #9),
 - Arthralgia,
 - Headache,
 - Fatigue,
 - Lymphadenopathy,
 - Maculopapular rash.

6.0 ICD 10 Code(s)

A92.3 West Nile virus infection

7.0 Comments

1. This category includes asymptomatic blood donors whose blood is screened using a NAAT, by Blood Operators (i.e. Canadian Blood Services or Hema-Quebec) and is subsequently brought to the attention of public health officials. The NAAT that is currently used by Blood Operators in Canada is designed to detect all viruses in the Japanese encephalitis (JE) serocomplex. The JE serocomplex includes WN virus and nine other viruses, although from this group only WNV and St. Louis encephalitis virus are currently endemic to parts of North America. The NAAT test used by Blood Operators is not approved for clinical diagnostic testing but can be used for surveillance case classifications, and would result in a classification of a probable case.
2. Whenever submitting a CSF for testing, a serum sample should be submitted for parallel testing. Although PRNT can be performed on CSF, this testing is usually not required, as the presence of IgM in CSF, which has excellent specificity in the acute setting, is sufficient for case confirmation.
3. Both CDC and commercial IgM / IgG ELISAs are now available for front line serological testing. Refer to appropriate assay procedures and kit inserts for the interpretation of test results. Due to high serological cross reactivity among flaviviruses, travel history should be obtained to determine if other flaviviruses should be tested for (e.g. Dengue virus, St. Louis encephalitis and Japanese encephalitis).
4. Early in infection the immune system generates antibodies that bind relatively weakly to viral antigen (low avidity). As the infection proceeds, an increasing percentage of newly generated IgG antibody displays higher binding affinity to virus antigen and thus avidity also rises (Note: avidity is usually measured based upon the ability of IgG to dissociate from antigen preparations after incubation with a solution of urea). As long as high avidity IgG is not yet detected in the serum it can be assumed that the individual was exposed to the viral agent during a recent exposure. With respect to WNV infection it has not been precisely determined when (i.e. post-exposure) high avidity antibodies reach levels in serum that can be accurately detected by serological assays (there may be significant variation depending on the individual). However, it has been shown that > 95% of sera collected from individuals exposed to WNV 6-8 months previously will have IgG antibodies that bind strongly to viral antigen and will give high avidity scores using both indirect fluorescent antibody (IFA) and ELISA testing formats. **Note:** Avidity testing will not replace confirmatory neutralization testing, non-WNV flavivirus IgG antibody (e.g., Dengue, St. Louis encephalitis) may bind to the antigen preparations used in avidity assays.

Note: WNV IgM antibody may persist for more than a year and the demonstration of IgM antibodies in a patient's serum, particularly in residents of endemic areas, may not be diagnostic of an acute WN viral infection. Seroconversion (by hemagglutination inhibition [HI], IgG ELISA or PRNT assays) demonstrates a current WNV infection. Therefore, the collection of acute and

convalescent sera for serologic analysis is particularly important to rule out diagnostic misinterpretation early in the WNV season (e.g. May, June) and to identify initial cases in a specific jurisdiction. However, it should be noted that seroconversions may not always be documented due to timing of acute sample collection (i.e. titres in acute sera may have already peaked). If static titres are observed in acute and convalescent paired sera, it is still possible the case may represent a recent infection. To help resolve this, the use of IgG avidity testing may be considered to distinguish between current and past infection. The presence of both IgM antibody and low avidity IgG in a patient's convalescent serum sample are consistent with current cases of viral associated illness. However, test results that show the presence of IgM and high avidity IgG are indicative of exposures that have occurred in a previous season. Immunocompromised individuals may not be able to mount an immune response necessary for a serological diagnosis. WNV diagnostic test criteria for these individuals should be discussed with a medical microbiologist.

5. History of exposure when and where WNV transmission is present, or could be present, or history of travel to an area with confirmed WNV activity in mosquitoes, birds, horses, other mammals or humans.
6. Alternative modes of transmission, identified to date, include: laboratory-acquired; in utero; receipt of blood components; organ/tissue transplant; and, possibly via breast milk.
7. A person with WNV-associated acute flaccid paralysis may present with or without fever or mental status changes. Altered mental status could range from confusion to coma with or without additional signs of brain dysfunction (e.g. paralysis, cranial nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions and abnormal movements). Acute flaccid paralysis with respiratory failure is also a problem.

Note: A significant feature of WNV neurological illness may be marked muscle weakness that is more frequently unilateral, but could be bilateral. WNV should be considered in the differential diagnosis of all suspected cases of acute flaccid paralysis with or without sensory deficit. WNV-associated weakness typically affects one or more limbs (sometimes affecting one limb only). Muscle weakness may be the sole presenting feature of WNV illness (in the absence of other neurologic features) or may develop in the setting of fever, altered reflexes, meningitis or encephalitis. Weakness typically develops early in the course of clinical infection. Patients should be carefully monitored for evolving weakness and in particular for acute neuromuscular respiratory failure, which is a severe manifestation associated with high morbidity and mortality. For the purpose of WNV Neurological Syndrome Classification, muscle weakness is characterized by severe (polio-like), non-transient and prolonged symptoms. Electromyography (EMG) and lumbar puncture should be performed to differentiate WNV paralysis from the acute demyelinating polyneuropathy (Guillain-Barré syndrome). Lymphocytic pleocytosis (an increase in WBC with a predominance of lymphocytes in the CSF) is commonly seen in acute flaccid paralysis due to WNV.

Other emerging clinical syndromes, identified in 2002 included, but were not limited to the following: myelopathy, rhabdomyolysis (acute destruction of skeletal muscle cells), peripheral neuropathy; polyradiculoneuropathy; optic neuritis; and acute demyelinating encephalomyelitis. Ophthalmologic conditions including chorioretinitis and vitritis were also reported. Facial weakness was also reported. Myocarditis, pancreatitis and fulminant hepatitis have not been identified in North America, but were reported in outbreaks of WNV in South Africa. “Aseptic” meningitis without encephalitis or flaccid paralysis occurring in August and September when WNV is circulating may be due to non-polio enteroviruses circulating at the same time. This should be considered in the differential diagnosis.

8. It is possible that other clinical signs and symptoms could be identified that have not been listed and may accompany probable case or confirmed case diagnostic test criteria. For example, gastrointestinal (GI) symptoms were seen in many WNV patients in Canada and the USA in 2003 and 2004.
9. Muscle weakness may be a presenting feature of WNV illness. For the purpose of WNV Non-Neurological Syndrome classification, muscle weakness or myalgia (muscle aches and pains) is characterized by mild, transient, unlikely prolonged symptoms that are not caused by motor neuropathy.

8.0 Sources

Public Health Agency of Canada. West Nile Virus. In: Case Definitions for Communicable Diseases under National Surveillance. Canada Communicable Disease Report. 2009;35S2.

9.0 Document History

Table 1: History of Revisions

Revision Date	Document Section	Description of Revisions
March 2017	4.1.1 Confirmed Case Diagnostic Test Criteria	1st paragraph updated to clarify which test criteria health units should use to identify ‘Confirmed’ cases. Footnote added to bullet one. “...using an assay verified for clinical testing” added to bullet two. Deleted “...or CSF” from bullet three. Insert a new bullet (four).

Revision Date	Document Section	Description of Revisions
March 2017	4.1.2 Probable Case Diagnostic Test Criteria	Deleted "...or CSF" from bullet one. Update reference to ELISA in bullet 2. Delete "Note" after bullet four regarding PRNT.
March 2017	4.2 Approved/Validated Tests	Added "...verified for clinical testing" to bullet two.
March 2017	5.1 West Nile versus Neurological Syndrome (WNNS) Clinical Criteria	Added "...occurring" to bullet one. Added "...transmission" to bullet two.
March 2017	7.0 Comments	Combined one and two in previous version by deleting "Blood Operators in Canada perform a supplementary WN virus specific antibody (IgM and IgG) testing following any positive donor screen test result" and adding "..., and would result in a classification of probable cases". Inserted a new comment number two regarding CSF for testing.
March 2017	9.0 Document History	Updated.
February 2019	General	Minor revisions were made to support the regulation change to Diseases of Public Health Significance.

