

# Appendix B: Provincial Case Definitions for Reportable Diseases

Disease: West Nile Virus Illness

## 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 WN 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 Suspect WNNS Case

Clinical criteria IN THE ABSENCE OF OR PENDING diagnostic test criteria (See Section 4.1.1) AND IN THE ABSENCE of any other obvious cause.

#### 3.4 Confirmed WN 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)

#### 3.5 Probable WN Non-NS Case

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

#### 3.6 Suspect WN Non-NS Case

Clinical criteria IN THE ABSENCE OF OR PENDING diagnostic test criteria (See Section 4.1.1) AND IN THE ABSENCE of any other obvious cause.

#### 3.7 Confirmed WN virus Asymptomatic Infection (WNAI)<sup>1</sup> Case

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

#### 3.8 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 WN virus:

- Positive West Nile virus culture
- Positive for West Nile virus antigen in tissue
- Positive for West Nile virus-specific nucleic acid

- Positive for West Nile virus-specific antibody
- Diagnostic rise in West Nile virus antibody titre

#### 4.1.1 Confirmed Case Diagnostic Test Criteria

Health units should use the Confirmed Case Diagnostic Test Criteria to confirm initial cases (locally acquired) in their area each year; for subsequent cases, health units may use the Probable Case Diagnostic Test Criteria to classify cases in their area as “confirmed”, **for the purposes of health unit surveillance**. Throughout the remainder of the transmission season health units may wish to document Plaque Reduction Neutralization Test (PRNT) antibody titres to West Nile virus in a proportion of cases, to be determined by that health unit, in order to rule-out the possibility of concurrent activity by other flaviviruses.

##### AT LEAST ONE of the following:

- A significant (i.e., fourfold or greater) rise in WN virus neutralizing antibody titres (using a PRNT or other kind of neutralization assay) in paired acute and convalescent sera, or cerebrospinal fluid (CSF)  
**OR**
- Isolation of WN virus from, or demonstration of WN virus antigen or WN virus-specific genomic sequences in tissue, blood, CSF or other body fluids  
**OR**
- Demonstration of flavivirus antibodies in a single serum or CSF sample using a WN virus Immunoglobulin M (IgM) enzyme-linked immuno-sorbent assay (ELISA)<sup>2,3</sup>, confirmed by the detection of WN virus specific antibodies using a PRNT (acute or convalescent serum sample)  
**OR**
- A significant (i.e., fourfold or greater) rise in flavivirus haemagglutination inhibition (HI) titres in paired acute and convalescent sera or demonstration of a seroconversion using a WN virus Immunoglobulin G (IgG) ELISA<sup>2,3</sup> **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 or CSF sample using a WN virus IgM ELISA<sup>2</sup> without confirmatory neutralization serology (e.g., PRNT)  
**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 WN virus IgG ELISA<sup>2</sup>  
**OR**
- A titre of  $\geq 1:320$  in a single WN virus HI test, or an elevated titre in a WN virus IgG ELISA, with a confirmatory PRNT result  
[Note: A confirmatory PRNT or other kind of neutralization assay is not required in a health jurisdiction/authority where cases have already been confirmed in the current year]  
**OR**

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

#### 4.2 Approved/Validated Tests

- Standard culture for WN virus
- NAT for WN virus
- WN virus antigen detection in tissue
- WN virus IgM antibody detection
- WN virus HI, PRNT and/or IgG/IgM immunoassays

#### 4.3 Indications and Limitations

- Sensitivity of NAT testing is approximately 50% when used on plasma / serum samples collected less than 8 days after symptoms are detected.
- Individuals infected with WN virus display a low level of viremia (on average several thousand genome copies) for approximately one week after symptom onset. The use of NAT testing on acute serum / plasma samples can complement IgM testing when used together to assay "early" acute specimens

### 5.0 Clinical Evidence

#### 5.1 West Nile virus Neurological Syndrome (WNNS)

##### Clinical Criteria:

- History of exposure in an area where WN virus (WNV) activity is occurring<sup>4</sup>  
**OR**
- History of exposure to an alternative mode of transmission<sup>5</sup>  
**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)<sup>6</sup>  
**OR**
- Movement disorders (e.g., tremor, myoclonus)  
**OR**
- Parkinsonism or Parkinsonia-like conditions (e.g., cogwheel rigidity, bradykinesia, postural instability)  
**OR**
- Other neurological syndromes<sup>7</sup>

#### 5.2 West Nile virus Non-Neurological Syndrome (WN Non-NS)

##### Clinical Criteria:

- History of exposure in an area where WN virus (WNV) activity is occurring<sup>4</sup>

OR

- History of exposure to an alternative mode of transmission<sup>5</sup>

AND AT LEAST TWO<sup>7</sup> of the following :

- fever<sup>8</sup>
- myalgia
- arthralgia
- headache
- fatigue
- lymphadenopathy
- maculopapular rash

## 6.0 ICD Code(s)

ICD 10 Code A923

## 7.0 Comments

<sup>1</sup> This category includes asymptomatic blood donors whose blood is screened using a Nucleic Acid Amplification Test (NAT), by Blood Operators (i.e. Canadian Blood Services or Hema-Quebec) and is subsequently brought to the attention of public health officials. The NAT 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 WN virus and St Louis encephalitis virus are currently endemic to parts of North America. Blood Operators in Canada perform a supplementary WN virus-specific NAT and antibody (IgM and IgG) testing following any positive donor screen test result.

<sup>2</sup> 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.

<sup>3</sup> 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 [SLE]) 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 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 the previous season. Immunocompromised individuals may not be able to mount an immune response necessary for a serological diagnosis. West Nile virus diagnostic test criteria for these individuals should be discussed with a medical microbiologist.

<sup>4</sup> History of exposure when and where West Nile virus 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.

<sup>5</sup> Alternative modes of transmission, identified to date, include: laboratory-acquired; in utero; receipt of blood components; organ/tissue transplant; and, possibly via breast milk.

<sup>6</sup> 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 West Nile virus 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 cerebrospinal fluid [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.

<sup>7</sup> 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.

<sup>8</sup> 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 References

- Ministry of Health and Long-Term Care, Public Health Division. iPHIS manual. Toronto, ON: Queen's Printer for Ontario; 2005.
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- Ministry of Health and Long-Term Care. West Nile Virus Preparedness and Prevention Plan Ontario. Toronto, ON: Queen's Printer for Ontario; 2008. Available from [http://www.health.gov.on.ca/english/public/pub/ministry\\_reports/wnv\\_plan\\_2008/wnv\\_plan\\_full.pdf](http://www.health.gov.on.ca/english/public/pub/ministry_reports/wnv_plan_2008/wnv_plan_full.pdf). Retrieved February 3, 2009.

**Date of Last Revision:** November 2008

