

West Nile Virus

Includes West Nile Neurological Syndrome (WNNS), West Nile Non-Neurological Syndrome (WN Non-NS) and West Nile Asymptomatic Infection (WNAI)

Case Definition

West Nile Neurological Syndrome (WNNS)

Confirmed Case

Clinical criteria^[1] and laboratory confirmation of infection:

- Isolation of West Nile virus (WNV) from, or demonstration of WNV-specific genomic sequences in tissue, blood, CSF and other body fluids by PCR

OR

- Demonstration of WNV antigen in tissue.

Probable Case

Clinical criteria^[1] and ONE of the following:

- WNV IgM positive and WNV IgG negative, in a single serum or CSF sample

OR

- WNV IgM positive and WNV IgG positive (low avidity), in a single serum or CSF sample

OR

- WNV IgM positive and significant rise in WNV IgG, in paired acute and convalescent sera by EIA

OR

- WNV IgM positive and fourfold or greater rise in WNV Hemagglutination Inhibition (HI) titre in paired acute and convalescent sera.

The following suspect case definition is provided as a guideline to assist with case finding and public health management, and should not be reported to AHW.

Suspect Case

Clinical criteria^[1] and ONE of the following:

- WNV IgM positive and WNV IgG positive (medium or high avidity)

OR

- The pending or absence of laboratory results in the absence of any other cause.

^[1] Clinical criteria for WNNS:

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 birds, horses, other mammals, sentinel chickens, mosquitoes, or humans.

OR

History of exposure to an alternate mode of transmission (laboratory-acquired; in utero; receipt of blood components; organ/tissue transplant; and possibly via breast milk).

AND

Onset of 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),^[2,3] or
- Movement disorders (e.g., tremor, myoclonus), or
- Parkinsonism or Parkinson like conditions (e.g., cogwheel rigidity, bradykinesia, postural instability), or
- Other neurological syndromes as defined below.[4]

^[2] A significant feature of WNNS may be marked muscle weakness that is more frequently unilateral, but can 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 WNNS 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-associated paralysis from acute demyelinating polyneuropathy (e.g., 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 whereas pleocytosis is not a seen feature of Guillain-Barré Syndrome.

^[3] 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 may result in respiratory failure.

^[4] Other emerging clinical syndromes identified during 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 (ADEM). 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 acute 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. [Sejvar J., et al. (2003). JAMA, 290(4) :511-515, Sejvar J., et al. (2003) Emerg Infect Dis, 9(7) :788-93, and Burton, JM, et al. (2004). Can. J. Neurol. Sci., 31(2):185-193.]

West Nile Non-Neurological Syndrome (WN Non-NS)

Confirmed Case

Clinical criteria^[5] and laboratory confirmation of infection:

- Isolation of West Nile virus (WNV) from, or demonstration of WNV-specific genomic sequences in tissue, blood, CSF and other body fluids by PCR

OR

- Demonstration of WNV antigen in tissue.

Probable Case

Clinical criteria^[5] and the following serology results:

- WNV IgM positive and WNV IgG negative in a single serum or CSF sample

OR

- WNV IgM positive and WNV IgG positive (low avidity) in a single serum or CSF sample

OR

- WNV IgM positive and significant rise in WNV IgG in paired acute and convalescent sera using EIA

OR

- WNV IgM positive and fourfold or greater rise in WNV HI titre in paired acute and convalescent sera.

The following suspect case definition is provided as a guideline to assist with case finding and public health management, and should not be reported to AHW.

Suspect Case

Clinical criteria^[5] with:

- WNV IgM positive and WNV IgG positive (medium or high avidity)

OR

- The pending or absence of laboratory results in the absence of any other cause.

^[5] Clinical Criteria for WN Non-NS:

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 birds, horses, other mammals, sentinel chickens, mosquitoes, or humans.

OR

History of exposure to an alternate mode of transmission (e.g., laboratory-acquired, in utero, receipt of blood components, organ/tissue transplant, and possibly via breast milk).

AND

At least **TWO** of the following:

- Fever
- Myalgia^[6]
- Arthralgia
- Headache
- Fatigue
- Lymphadenopathy
- Maculopapular rash
- Other (e.g., gastrointestinal)

^[6] For the purpose of WN Non-NS classification, muscle weakness or myalgia (muscle aches and pains) is characterized by mild, transient, unlikely prolonged symptoms that are not associated with motor neuropathy.

West Nile Asymptomatic Infection (WNAI)

Confirmed

Absence of clinical criteria and laboratory confirmation of infection:

- Isolation of West Nile virus (WNV) from, or demonstration of WNV-specific genomic sequences in tissue, blood, CSF and other body fluids by PCR

OR

- Demonstration of WNV antigen in tissue.

Probable

Absence of clinical criteria and ONE the following laboratory results:

- WNV IgM positive and WNV IgG negative in a single serum or CSF sample

OR

- WNV IgM positive and WNV IgG positive (low avidity) in a single serum or CSF sample

OR

- WNV IgM positive and significant rise in WNV IgG in paired acute and convalescent sera using EIA

OR

- WNV IgM positive and fourfold or greater rise in WNV HI titre in paired acute and convalescent sera.

OR

- Positive Canadian Blood Services NAT Screening Test ^[7]

^[7]This category could include 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 assay that is used by Blood Operators in Canada is designed to detect all viruses in the Japanese encephalitis (JE) serocomplex. The JE serocomplex includes WNV and 9 other viruses, although from this group only WNV and St Louis encephalitis virus are currently endemic to parts of North America. Blood operators in Canada perform supplementary WN virus-specific NAT following any positive donor screen test result.

Reporting Requirements

1. Physicians/Health Practitioners and others

Physicians, health practitioners and others listed in Section 22 of the *Public Health Act* shall notify the Medical Officer of Health (MOH) (or designate) of all confirmed and probable WNNS, WN Non-NS and WNAI cases by mail, fax or electronic transfer within 48 hours (two days).

2. Laboratories

All laboratories, including regional laboratories and the Provincial Laboratory of Public Health (PLPH), shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two days) to the:

- CMOH (or designate),
- MOH (or designate) and
- Attending/ordering physician.
- The PLPH shall report to Canadian Blood Services (CBS) on a daily basis the following information:
 - Names of individuals who have blood samples submitted for WNV testing, and
 - Names of individuals who have tested positive for WNV.

3. Alberta Health Services (AHS)

- The MOH (or designate) shall forward the preliminary NDR and the *Alberta Enhanced Surveillance Report* forms to the CMOH (or designate) within two weeks and the final report forms within four weeks of notification of all confirmed and probable WNNS, WN Non-NS and WNAI cases.
- The MOH (or designate) will report, as soon as possible, all cases of WNNS (suspect – with pending labs only) and confirmed and probable WNNS and WN Non-NS to the nearest CBS Centre using the *Public Health West Nile Virus Notification to Canadian Blood Services* form who have been:
 - Recipients of blood components with the onset of illness within 8 weeks of receiving blood
 - Blood donors with the onset of illness within 8 weeks of donating blood.
- For out-of-zone reports, the MOH (or designate) first notified shall notify the MOH (or designate) where the client resides by mail, fax or electronic transfer and fax a copy of the positive laboratory report within 48 hours (two days).
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two days) including:
 - name,
 - date of birth,
 - out-of-province health care number,
 - out-of-province/country address and phone number,
 - attending physician (locally and out-of-province) and
 - positive laboratory report.

4. Canadian Blood Services (CBS)

Positive screening tests of donors are immediately reportable to the:

- CMOH
- MOH (where the donor resides)
- Individual donor
- Attending physician (with donor consent)

CBS has agreed to forward weekly surveillance of West Nile virus donor testing for Alberta (number tested and number positive).

5. Organ and Tissue Transplant Organization.

Any organization detecting WNV infection in donors or recipients should immediately notify the:

- CMOH
- MOH (where the donor/recipient resides)
- Ordering physician
- Individual donor or recipient (where applicable).

Etiology

WNV belongs to a family of viruses called *Flaviviridae*.⁽¹⁾ Serologically, it is a member of the Japanese encephalitis (JE) virus complex that includes St. Louis encephalitis (SLE), Kunjin, and Murray Valley encephalitis viruses. Other flaviviruses include Dengue, Yellow fever and tickborne encephalitis.

WNV usually cycles between mosquitoes and birds.⁽¹⁾ Infectious mosquitoes carry WNV in their salivary glands, and this is transmitted to susceptible bird species during a blood meal. Birds will be viremic for 1–4 days after exposure, after which the birds will develop life long immunity or die. A sufficient number of mosquitoes must bite the viremic birds to ensure continued survival of the virus. Humans and animals are accidental, dead-end hosts.

Clinical Presentation

An incubation period typically of 2 to 6 days occurs following exposure but can be as long as 14 days.⁽²⁾ Most WNV infections are clinically inapparent. Approximately 20% will develop WN Non-NS and approximately 1:150 infections (less than 1%) will result in severe neurological disease. Case fatality rates for WNNS have varied from 4 to 18%.

The symptoms of WN Non-NS may include fever, myalgia, arthralgia, headache, fatigue, lymphadenopathy and/or maculopapular rash (mainly on the chest, back, abdomen and/or arms). Persistent fatigue is common and may continue for months, even among otherwise healthy individuals.^(3;4)

There are three main presentations of WNNS: meningitis, encephalitis and acute flaccid paralysis. Symptoms may include headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis.⁽⁵⁾ Other rare presentations include cranial nerve palsies, optic neuritis and ataxia. Long-term sequelae such as muscle weakness, fatigue, headache, and effects on cognitive function (e.g., confusion, depression, and memory loss) can occur, lasting for years, or permanently.⁽⁶⁾ For other diagnostic findings refer to [Annex 1: West Nile Neurological Syndrome: Diagnostic Findings](#).

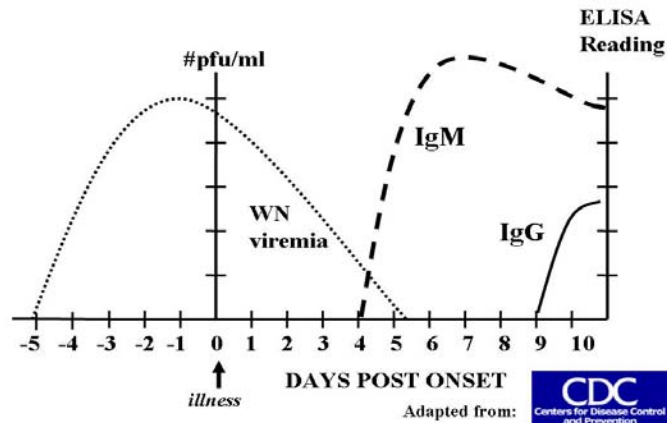
Diagnosis

The diagnosis of WNV is often based on a high index of suspicion and obtaining the results of specific laboratory tests. The presence of WNV enzootic activity or human cases increases the likelihood of infection in the population. A diagnosis of West Nile infection should be considered in the following:

- living in or travel to an area where WNV transmission is present (endemic);
- individuals and symptoms suggestive of WNNS and WN Non-NS during the summer months and early fall;
- individuals with unexplained fever beginning > 3 days and < 8 weeks (56 days) after blood transfusion;
- fever in persons with a history of having received organs or tissue donation within previous 8 weeks;
- pregnant women with unexplained febrile illnesses during WNV season; and
- immunocompromised individuals with a fever not yet diagnosed.

The virus has come and gone in about half of cases who present during the first week of illness, as shown in Figure 1 below:

Figure 1: West Nile Virus: Viral Markers in Blood During Infection



The following tests are used in the diagnosis of WNV:

WNV Nucleic Acid Testing (PCR, NAT or NASBA)

- Detects RNA in plasma in about 40% of cases during the first week of illness. Rarely positive after 8 days of illness or when IgM appears.
- No cross-reactivity with other flaviviruses.
- Low sensitivity in CSF, probably <20%.
- A positive NAT test is always confirmed by a second NAT test targeting a different gene (confirmed WNV case).

WNV IgM

- Only positive in about 50% of cases during the first week of illness (NAT testing detects most of the other 50%). WNV IgM is nearly always positive in cases after the first week of illness.
- Little cross-reactivity with other flaviviruses.
- WNV IgM antibody persists for >9 months in at least two thirds of cases. For this reason the presence of IgM antibody is not necessarily diagnostic of acute infection, particularly in areas where WNV was known to have circulated previously.

WNV IgG

- Cross reacts extensively with other flaviviruses, such as St. Louis encephalitis, dengue fever, Japanese encephalitis and yellow fever, including vaccination.
- Negative IgG, in the presence of WNV IgM, likely indicates recent WNV infection (probable WNV case).
- NOT recommended for asymptomatic individuals. Not a reliable marker of immunity to WNV.
- Useful to show rising IgG levels in acute and convalescent sera, which are strongly suggestive of recent flavivirus infection or vaccination.

WNV IgG avidity

- Low avidity antibodies indicate recent (<4 months) infection or vaccination with a flavivirus. In combination with a positive WNV IgM result, indicates a probable WNV case.

- Medium and high avidity antibody indicates a mature response and exposure to a flavivirus at least 6 months previously. Some WNV cases have high avidity IgG early in infection, possibly due to previous exposure to other flaviviruses, therefore high/medium avidity IgG does not rule out recent WNV infection (suspect WNV case).

For more guidance on the interpretation of WNV laboratory results go to the Provincial Laboratory for Public Health website at: www.provlab.ab.ca/education.htm.

Results from a study confirmed the persistence of WNV IgM antibody among residents in the south eastern Alberta. Seventy-two per cent of people previously diagnosed with WNV infection in the summer of 2003, tested positive for IgM in the summer of 2004.(7) For this reason, the detection of WNV specific genomic sequences by PCR will be increasingly important for the diagnosis of acute infection during the subsequent years of WNV infection in Albertans. In some instances, when the patient is WNV-PCR negative, a rising IgG titre or presence of low avidity IgG may support the diagnosis of acute infection.

Epidemiology

Reservoir

Birds,(8) people, horses, and most other mammals are not known to develop infectious-level viremia, and are incidental, dead-end hosts.

Transmission

The most common mode of transmission is through the bite of an infected mosquito (night-time feeder). Other means of WNV transmission include contact with infected blood transfusion or transplanted organs. There also have been reports of in utero infection,(9) through breast milk,(10) and workers who handle infected tissue or specimens.(11)

Incubation Period

Symptoms usually develop two to 15 days after exposure.(2) The incubation period may be longer for immunocompromised individuals. The period of viremia begins 6–7 days prior to symptom onset and ends within a week of symptom onset.(12)

Period of Communicability

Humans infected with WNV can transmit virus to others during the viremic phase of infection via blood including transfusion, transplantation of organs/tissue, in utero and breast milk.(2) The duration and magnitude of viremia in people with the varying categories of disease over the clinical spectrum is not known.

Host Susceptibility

WNV has been the cause of infection in humans across the age spectrum and susceptibility is likely universal.(2;5) Advancing age is the most important risk factor for serious neurological disease and deaths. Pre-existing conditions such as immunosuppression, diabetes and heart disease may be independent risk factors.(6)

Occurrence

Worldwide

WNV was first isolated in Uganda in 1937. WNV epidemics have occurred in Asia, Europe, Israel, Africa and Russia. The virus was first detected in North America in 1999. New York was the first US area to report WNV.

Canada

In 2001, the first positive bird was detected in Ontario. WNV was first reported in humans in Canada in 2002 in Ontario and Quebec; 414 cases were reported.(2) The majority of cases (95%) occurred in Ontario. Since then the number of WNV cases reported in Canada each year has ranged from 25 to more than 2200 cases. The number of WNV-related deaths reported each year has ranged from 0 to 14 cases.

For up-to-date national surveillance data visit the Public Health Agency of Canada website at: www.phac-aspc.gc.ca/WNV-vwn/index.html.

Alberta

Geographically, WNV cases in Alberta are predominantly reported in the Grassland and Parkland natural regions in the south east area of the province.

The seroprevalence of WNV is estimated to be 0.3% in Alberta, with 6900 seropositive healthy individuals in the province at any given point in time. Approximately 94% of cases are asymptomatic and seniors (65 years and older) are at greatest risk of disease.(13)

The first two cases of WNV in Alberta were reported in 2002 and were related to travel to areas of Canada and the US where human WNV cases were also being reported at that time.

Year	WNNS	WN Non-NS	WNAI	Total
2003	48	224	3	0
2004	0	1	0	1
2005	2	8	0	10
2006	1	38	1	40
2007	21*	296	3	320
2008	0	1	0	1
2009	2	1	0	2

**2 cases in 2007 died due to WNV.*

For up-to-date WNV information for Alberta visit the AHW website at: www.health.alberta.ca/health-info/west-nile-virus.html

Key Investigation

Assess potential risk factors and likely mode of transmission for the acquisition of WNV within 3 weeks prior to onset of symptoms, as well as other considerations:

- living in an area where WNV transmission is present (endemic),
- travel to an out-of-province area where WNV transmission is present,
- travel to an area outside of local community (e.g. elsewhere in Alberta) where WNV transmission is present,
- recall of being bitten by mosquitoes,
- blood/blood component recipient (within the past 8 weeks prior to onset of symptoms),
- organ/tissue transplant recipient (within the past 8 weeks prior to onset of symptoms),
- handling of sick or dead birds or animals,
- occupational unprotected exposure to the blood or body fluids of humans, animals, or birds containing WNV, e.g., laboratory worker, outdoor worker, bird/animal handler, health care worker, and/or
- if an infant, assess for possible transmission in utero or through breast milk.

Control

Management of a Case

- In collaboration with the client and the attending physician, determine if the clinical picture meets the clinical criteria as per the WNNS, WN Non-NS, or WNAI Case Definitions.
- The laboratory result will determine how the case should be classified (e.g., confirmed, probable, or suspect).
- All cases reported as WNV positive (WNAI) by the CBS screening of donors require follow-up blood specimens obtained in the community to verify acute WNV infection.
- It is recommended that infants born to mothers with WNV during pregnancy, as well as infants with positive WN laboratory tests, undergo clinical evaluation for WNV infection.(14) A medical infectious disease specialist should be involved in the assessment. (See [Annex 2 - Alberta Pregnancy Algorithm for WNV and Pre & Post-Natal Assessment and Investigations for WNV](#)).
 - The health benefits of breastfeeding are well established, and the risk for West Nile virus transmission through breastfeeding is unknown, therefore breastfeeding is NOT contraindicated. Lactating women who are ill or who are having difficulty breastfeeding for any reason should consult their health care practitioner.(15)

Treatment of a Case

- There is no specific treatment, medication or cure for WNV. Treatment for WNV is supportive and in those with severe disease may involve intravenous fluids, respiratory support, and the prevention and management of secondary infection.

Management of Contacts

- Prophylactic antiviral medications are not known to be effective in the prevention of WNV infection.
- There is no evidence to suggest that WNV can be transmitted to household contacts of persons infected with WNV.
- Workers exposed to WNV infected material (e.g., dead birds) should:(11)
 - cleanse any wound or cleanse exposed skin immediately and receive first aid;
 - report the incident to the supervisor;
 - submit blood specimens for serologic and virologic analysis that are taken at the time of the injury and 2 weeks later; and
 - report any illness within 2 weeks of exposure to Occupational Health and their health care practitioner.

Preventive Measures

In Alberta, the primary transmitter of WNV to humans is the *Culex tarsalis*. However, only a small number of people bitten by infected mosquitoes will develop illness. Preventing mosquito bites is considered the best measure to avoid the low risk of contracting WNV infection.

Workplace health and safety:

- Outdoor worker: Occupational groups at risk for WNV exposure and infection should receive training about potential WNV hazards. Workers are at low risk of WNV infection through normal contact with WNV-infected animals. Outdoor workers, where mosquitoes are actively biting, are at increased risk for exposure to WNV. Public Health Agency of Canada has developed a national *Occupational Health Advisory* for outdoor workers and those handling dead birds or animals at:
www.phac-aspc.gc.ca/ols-bsl/wnvbio-eng.php

- Workers in laboratories and others handling potentially infectious specimens: Precautions for handling clinical specimens potentially containing WNV are contained in the Health Canada WN *Biosafety Advisory* at: www.phac-aspc.gc.ca/ols-bsl/wnvbio-eng.php

Canadian Blood Services:

Since July 1, 2003 all blood donations in Canada have been routinely tested for WNV using a pooled NAT¹ Test. The key components of the CBS WNV plan are:

- Screening of blood donors for illness and symptoms such as fever. Donors are counselled to contact the CBS clinic immediately if they become ill within a few days of their blood donation.
- All donated blood is tested for WNV by NAT testing of pooled samples from 6 donations (mini-pool testing or MPT). If the pooled testing is positive, testing of each individual donation contributing to the pool is done. If a positive donor is found, the blood donation is discarded, the donor is notified and postponed from donating for 56 days, and public health is informed so that follow-up can be initiated.
- CBS collates and analyzes public health surveillance data, donor testing information, as well as donor and donor clinic demographic information to assess WNV risk levels in each health region across the country. Where the risk exceeds a predetermined threshold, single donor/unit testing (SUT) is initiated without preceding MPT.
- Blood donations from individuals with *probable* or *confirmed* cases of WNV that are reported to the CBS by public health authorities are discarded. If any of the blood was delivered to hospitals, the hospital will be instructed to discard it. If the blood was transfused, CBS will recommend that hospitals advise the recipient's physician.
- If CBS is notified that a blood recipient has been diagnosed with probable or confirmed WNV infection and has received a blood transfusion within the past 8 weeks, other individuals receiving a blood product donated by the same donor(s) are identified and followed up for possible WNV infection. Un-transfused blood products from the blood donor(s) will be discarded. CBS only requires notification if the recipient is suspected to have transfusion-transmitted WNV infection.
- There have been no cases of transfusion-transmitted WNV infection reported in Canada since CBS began screening in 2003.

For more information on WNV surveillance at CBS visit their website at: www.bloodservices.ca.

Organ/tissue donors are tested for WNV by the PLPH. Between 500 and 600 organs/tissue specimens are tested each year in Alberta and none have tested positive. It is anticipated that the risk of WNV infection through organs/tissue will be very low.

Resources

Alberta Health and Wellness. West Nile virus website.
www.health.alberta.ca/health-info/west-nile-virus.html

O'Leary DR, Kuhn S, Kniss KL, Hinckley AF, Pape WJ, Kightlinger LK, Beecham BD, Miller TK, Neitzel DF, Michaels SR, Campbell GL, Rasmussen SA, Hayes EB. (2006). Birth outcomes following West Nile virus infection of pregnant women, United States, 2003–2004. *Pediatrics*, 117(3), e537–45.

Public Health Agency of Canada, West Nile virus website.
www.phac-aspc.gc.ca/wn-no/index_e.html

¹ The NAT assay that is used by Blood Operators in Canada is designed to detect all viruses in the Japanese encephalitis (JE) serocomplex. The JE serocomplex includes WNV and 9 other viruses

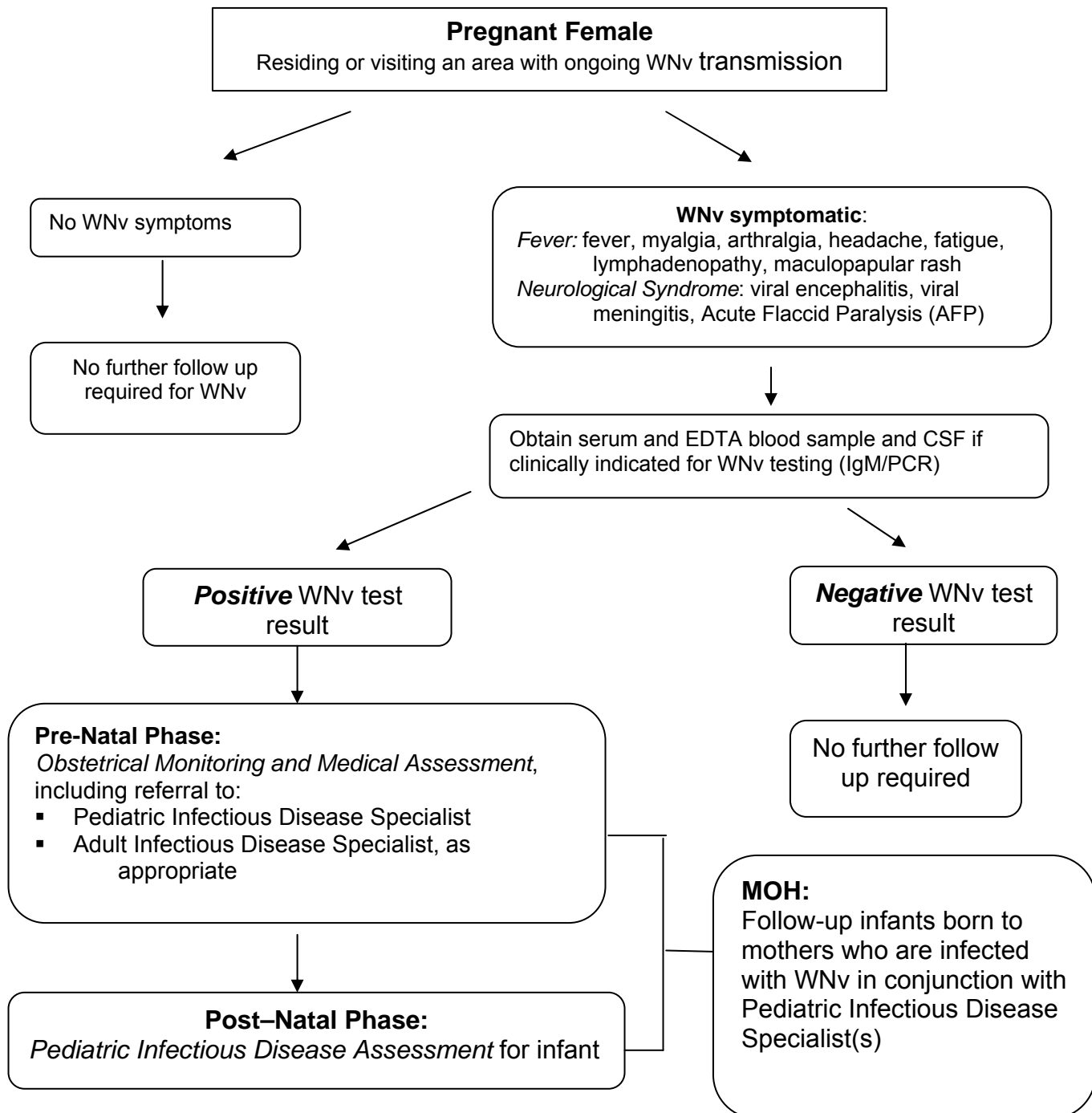
ANNEX 1: West Nile Neurological Syndrome: Diagnostic Findings

Diagnosis	Clinical Presentation
West Nile Meningitis (35–40% of cases)	<p>Clinical signs of meningeal inflammation (nuchal rigidity, Kernig or Brudzinski sign, or photo- or phonophobia)</p> <p>AND</p> <p>Additional evidence of one or more of the following:</p> <ul style="list-style-type: none"> • Fever (> 38°C) or hypothermia (< 35 °C) • Peripheral leukocyte count > 10,000/mm³ • CSF pleocytosis (≥ 5 leukocytes/mm³) • Evidence of acute meningeal inflammation
West Nile Encephalitis (55–60% of cases)	<p>Signs of encephalopathy (depressed or altered level of consciousness, lethargy or personality change lasting ≥24 hours)</p> <p>AND</p> <p>Additional evidence of two or more of the following:</p> <ul style="list-style-type: none"> • Fever (> 38°C) or hypothermia (< 35 °C) • Peripheral leukocyte count > 10,000/mm³ • CSF pleocytosis (≥ 5 leukocytes/mm³) • Evidence of acute inflammation (with or without involvement of the meninges) OR acute demyelination • Presence of focal neurologic deficit (weakness, cranial nerve palsies) – movement disorders including tremor, parkinsonism and ataxia, may be frequent) • Clinical signs of meningeal inflammation • EEG findings consistent with encephalitis • Seizures (new onset or exacerbation of previously controlled)
West Nile Acute Flaccid Paralysis (unknown but may be 5–10% of cases)	<p>Acute onset of limb weakness with marked progression over 48 hours</p> <p>AND</p> <p>At least two of the following:</p> <ul style="list-style-type: none"> • Asymmetrical weakness • Areflexia/hyporeflexia of affected limb(s) • Absence of pain, paresthesia, or numbness in affected limb(s) • CSF pleocytosis (≥ 5 leukocytes/mm³) AND elevated protein levels (≥ 0.45g/dL) • Electrodiagnostic studies (EMG, nerve conduction) consistent with an anterior horn cell process • Spinal cord MRI documenting abnormal increased signal in anterior gray matter

Source: Sejvar JJ, Haddad M, Tierney B et al. *JAMA* 2003; 290:511-15

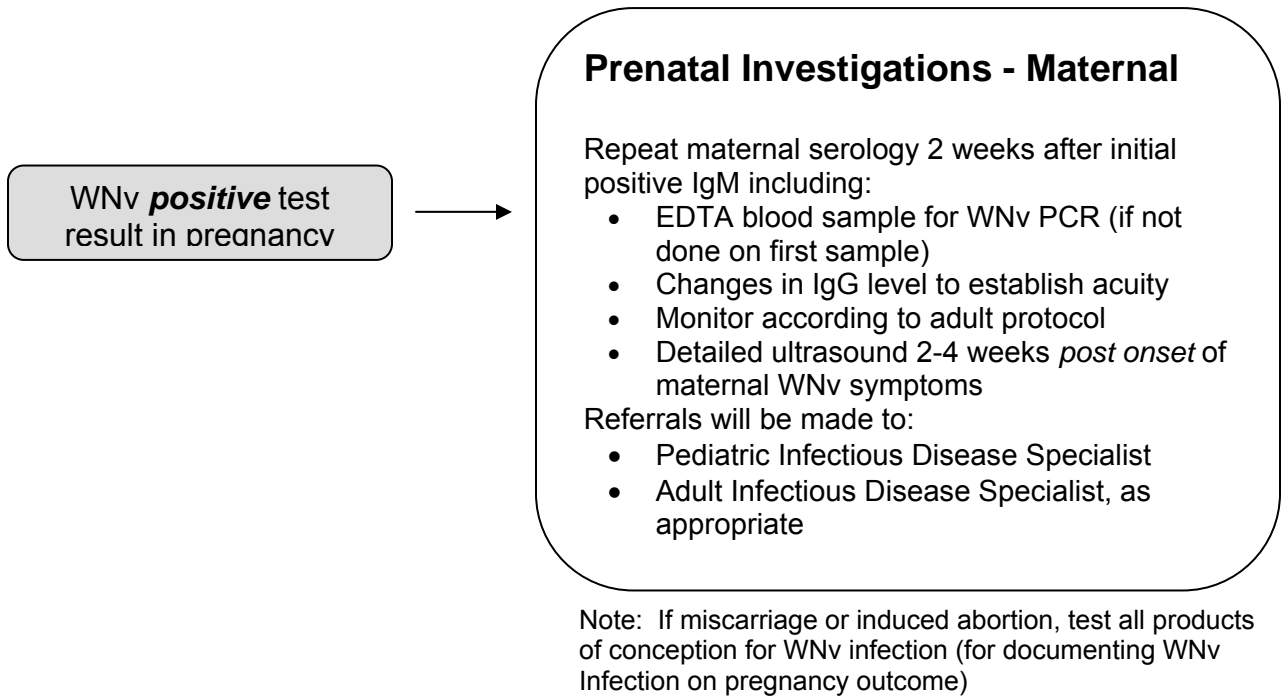
ANNEX 2: Prenatal and Post-Partum WNV Follow-up

Pregnancy Algorithm West Nile virus (WNV)



Source: Adapted from MMWR. June 2004

Prenatal Assessment and Investigations for WNV - Maternal



Post - Natal Assessment and Investigations for WNV – Infant

Infants born to mothers infected with WNV during pregnancy

Clinical Exam	Investigations	Pathology
<p>Thorough physical exam of newborn, including:</p> <ul style="list-style-type: none"> Careful measurement of the infant's head circumference, length, weight Assessment of gestational age Neurological exam for abnormalities Examination for dysmorphic features Abdominal exam for splenomegaly and hepatomegaly Examination for rash or other skin lesions <p>N.B.</p> <ol style="list-style-type: none"> Photograph dysmorphic features and skin abnormalities. If an abnormality is noted, consultation with an appropriate specialist is recommended. 	<p><u>Serology:</u> Within 2 days of birth and at age 8 weeks: IgM and IgG antibody to WNV</p> <p><u>Newborn hearing screen:</u></p> <ul style="list-style-type: none"> Before discharge or within 1 month after birth by evoked otoacoustic emissions testing or auditory brainstem response testing Referral to audiologist if infant failed the initial screening test 	<p>Initial examination of placenta by a pathologist is recommended.</p> <p>If congenital WNV infection is identified or strongly suspected, retain:</p> <ul style="list-style-type: none"> Placenta (freeze a section, preserve remainder in formalin) Sample of umbilical cord tissue (freeze) Sample of neonatal blood (centrifuge sample of blood, refrigerate/freeze serum) <p>Caution: Wharton's Jelly can cause a very high incidence of false positive WNV serology from cord blood.</p>

**Infants with clinical or laboratory evidence of possible congenital WNV infection:
(in addition to the investigations above)**

Clinical Exam	Investigations	Pathology
<ul style="list-style-type: none"> Evaluation by a dysmorphologist or clinical geneticist. Further evaluation to determine alternative causes of congenital abnormalities including: <ul style="list-style-type: none"> Genetic Infectious Other teratogenic causes Careful evaluation of head circumference, physical characteristics, and developmental milestones for first year of life Ophthalmologic evaluation including examination of the retina. 	<p><u>Blood/Serology:</u></p> <ul style="list-style-type: none"> CBC, platelets, liver function tests (including ALT and AST) PCR for WNV on EDTA blood Repeat IgM and IgG to WNV at age 6 months <p><u>CT scan:</u></p> <ul style="list-style-type: none"> If abnormal, a pediatric neurologist should be consulted <p><u>CSF:</u></p> <ul style="list-style-type: none"> Consider, and if done, should include testing for PCR to WNV <p><u>Hearing Test:</u> Repeat at 6 months</p>	<p>Placenta and Umbilical Cord tissue:</p> <ul style="list-style-type: none"> Histopathologic examination Testing of frozen tissue for WNV nucleic acid <p>Neonatal blood</p> <ul style="list-style-type: none"> IgM and IgG antibody to WNV. WNV PCR (investigational) <p>Caution: Wharton's Jelly can cause a very high incidence of false positive WNV serology from cord blood.</p>

Source: Adapted from MMWR Interim guidelines for the evaluation of infants born to mothers infected with West Nile Virus during pregnancy. 53, 154-157

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