West Nile Virus in Humans

Public Health Guidelines
(June 2006)

Alberta Health and Wellness
Edmonton, Alberta
June 8, 2006

West Nile Virus - Public Health Guidelines (2006)

Table of Contents

List of Acronyms

AHW	Alberta Health & Wellness
CBS	Canadian Blood Services
CMOH	Chief Medical Officer of Health
ESR	Enhanced Surveillance Report
FMP	Fastest Means Possible
JE	Japanese Encephalitis
MOH	Medical Officer of Health
NAT	Nucleic Acid Amplification Test
NDR	Notifiable Disease Report
PCR	Polymerase Chain Reaction
PHAC	Public Health Agency of Canada
PHO	Provincial Health Office
PRNT	Plaque Reduction Neutralization Titre
RHA	Regional Health Authority
WN	West Nile
WNAI	West Nile Asymptomatic Infection
WN Non-NS	West Nile Non-Neurological Syndrome
WNNS	West Nile Neurological Syndrome
WNV	West Nile Virus

Alberta Case Definitions for West Nile (WN)

Note: *The current Case Definitions were drafted with available information at the time of writing. Case Definitions and Diagnostic Test Criteria are subject to change as new information becomes available.*

West Nile Neurological Syndrome (WNNS)

Disease Case Classification	
Confirmed Case (FMP)	**Clinical Criteria:** ▪ History of exposure in an area where WN virus (WNv) activity is occurring[1] **OR** ▪ History of exposure to an alternate mode of transmission[2] **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),[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 in the note** below. **AND** ▪ Laboratory confirmation of infection of one of the following: ▪ WNv NAT positive, blood, or CSF, **OR** ▪ WNv IgM positive, low avidity antibody, WNv PRNT positive, **OR** ▪ Significant rise in WNv IgG, WNv PRNT positive, **OR** ▪ Fourfold or greater rise in WNv HI titre, WNv PRNT positive.
Probable Case (FMP)	**Clinical Criteria: as per confirmed case** **AND the following serology result:** ▪ WNv IgM positive, low avidity antibody, **OR** ▪ WNv IgM positive, significant rise in WNv IgG, **OR** ▪ WNv IgM positive, fourfold or greater rise in WNv HI titre.
Suspect Case (FMP)	**Clinical Criteria: as per confirmed case in:** ▪ The absence of or pending laboratory results **AND** ▪ The absence of any other cause.

West Nile Neurological Syndrome (WNNS)

Disease Case Classification	
National Surveillance	Confirmed Cases
Provincial Surveillance	Confirmed and Probable Cases
Type of Surveillance	Case-by-Case
Comments	Refer to Appendix A - *West Nile Virus Testing in 2006* .
Date of Development	Adopted from *National Surveillance for West Nile Virus Case Definition* May 2006 and WNv diagnostic testing and interpretation prepared by Dr. Peter Tilley, Medical Microbiologist, Provincial Laboratory for Public Health, June 2005.

**** Note:**
A significant feature of West Nile neurological illness 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 WNV Neurologic 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- 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.

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. JAMA (2003) Vol.290 (4) p. 511-515, Sejvar, J. et al. Emerg Infect Dis (2003) Vol 9 (7) p.788-93 and Burton, JM et al Can. J. Neurol. Sci. (2004) Vol.31 (2) p.185-193]

[1]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.

[2]Alternate modes of transmission identified to date include: laboratory-acquired; in utero; receipt of blood components; organ/tissue transplant; and possibly via breast milk.

[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.

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

Disease Case Classification	
Confirmed Case	**Clinical Criteria:** ▪ History of exposure in an area where WN virus (WNv) activity is occurring[1] **OR** ▪ History of exposure to an alternate mode of transmission[2] **AND AT LEAST TWO** of the following[3]: ▪ Fever ▪ Myalgia[4] ▪ Arthralgia ▪ Headache ▪ Fatigue ▪ Lymphadenopathy ▪ Maculopapular rash **AND** ▪ Laboratory confirmation of infection of one of the following: ▪ WNv NAT positive, blood, or CSF, **OR** ▪ WNv IgM positive, low avidity antibody, WNv PRNT positive, **OR** ▪ Significant rise in WNv IgG, WNv PRNT positive, **OR** ▪ Fourfold or greater rise in WNv HI titre, WNv PRNT positive.
Probable Case	**Clinical Criteria: as per confirmed case** **AND the following serology result:** ▪ WNv IgM positive, low avidity antibody, **OR** ▪ WNv IgM positive, significant rise in WNv IgG, **OR** ▪ WNv IgM positive, fourfold or greater rise in WNv HI titre.
Suspect Case	**Clinical Criteria: as per confirmed case in:** ▪ The absence of any other cause **AND** ▪ The absence of or pending laboratory results.
National Surveillance	Confirmed Cases
Provincial Surveillance	Confirmed and Probable Cases
Type of Surveillance	Case-by-Case
Comments	Refer to Appendix A - *West Nile Virus Testing in 2006.*
Date of Development	Adopted from *National Surveillance for West Nile Virus Case Definition* May 2006 and WNv diagnostic testing and interpretation prepared by Dr. Peter Tilley, Medical Microbiologist, Provincial Laboratory for Public Health, June 2005.

[1]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 WN virus activity in birds, horses, other mammals, sentinel chickens, mosquitoes, or humans.

[2]Alternate modes of transmission identified to date include: laboratory-acquired; in utero; receipt of blood components; organ/tissue transplant; and possibly via breast milk.

[3]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 case-patients in Canada and the USA in 2003 and 2004.

[4] 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 a mild, transient, unlikely prolonged symptoms that are not associated with motor neuropathy.**

West Nile Asymptomatic Infection (WNAI)**

Disease Case Classification	
Confirmed Case	The absence of clinical criteria **AND** Laboratory confirmation of infection by one of the following: ▪ WNv NAT positive, blood, or CSF, **OR** ▪ WNv IgM positive, low avidity antibody, WNv PRNT positive, **OR** ▪ Significant rise in WNv IgG, WNv PRNT positive **OR** ▪ Fourfold or greater rise in WNv HI titre, WNv PRNT positive.
Probable Case	The absence of clinical criteria **AND** the following serology result: ▪ Positive Canadian Blood Services NAT screening test.
National Surveillance	Confirmed Cases
Provincial Surveillance	Confirmed and Probable Cases
Type of Surveillance	Case-by-Case
Comments	Refer to Appendix A - *West Nile Virus Testing in 2006.*
Date of Development	Adopted from *National Surveillance for West Nile Virus Case Definition* May 2006 and WNv diagnostic testing and interpretation prepared by Dr. Peter Tilley, Medical Microbiologist, Provincial Laboratory for Public Health, June 2005.

**** Note:** 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 WN virus and 9 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 supplementary WN virus- specific NAT following any positive donor screen test result.

REPORTING REQUIREMENTS

West Nile infection was added to Schedule 4 of the Communicable Disease Regulation in 2005. Notification of WNv to Alberta Health and Wellness (AHW) is to occur by the fastest means possible (FMP) by direct voice communication for WNNS. WN Non-NS and WNAI notification is Non FMP. (See Appendix B *Algorithm for Reporting WNv to Alberta Health and Wellness*). Additional information after the first phone contact may be faxed, or e-mailed, as necessary. The following groups or organizations are required to report WNv infection:

1. **Physicians/Health Practitioners and Others**
   The following are reportable to the Medical Officer of Health (MOH):
   - WNNS (FMP): Confirmed and probable cases as well of cases of viral encephalitis or viral meningitis of unknown etiology (suspect cases) during the WNv season.
   - WN Non-NS (within 48 hours): Confirmed and probable cases.
   - WNAI (within 48 hours): Confirmed and probable cases.
   - *The Arbovirus Patient History Form – ProvLab* (Appendix C) must accompany WNv diagnostic specimens sent to the ProvLab.

   See Appendix D - *Reporting Algorithm for WNNS and WN Non-NS*

2. **Laboratories**
   A positive test for WNv is immediately reportable by the Provincial Laboratory for Public Health (ProvLab) to the:
   - CMOH
   - MOH (Region)
   - Ordering physician

   The Arbovirus Patient History Form – ProvLab (Appendix C) must accompany positive WNv laboratory report to the MOH and CMOH, when available.

   See Appendix D - *Reporting Algorithm for WNNS and WN Non-NS* and Appendix E - *Laboratory Confirmation for Case Definitions for WNv*

3. **Canadian Blood Services (CBS)** (See Appendix F - *Canadian Blood Services Responsibilities* and Appendix G - *Reporting Algorithm for WNAI – Canadian Blood Services*)
   Positive screening tests of donors are immediately reportable to the:
   - CMOH
   - MOH (where the donor resides) (See Appendix H - *Canadian Blood Services Notification to Public Health of West Nile Virus*)
   - Attending physician (with donor consent)
   - Individual donor

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

4. **Organ and Tissue Transplant Organization**.
   Any organization detecting WNv infection in donors or recipients should immediately notify:
   - CMOH
   - MOH (where the donor/recipient resides)
   - Ordering physician
   - Individual donor or recipient (where applicable)

5. **Regional Health Authority (RHA)**
   The MOH (or designate) will notify the CMOH as per Appendix B - *Algorithm for Reporting WNv to Alberta Health and Wellness* of:
   - WNNS (FMP): Confirmed and probable cases
   - WN Non-NS: Confirmed and probable cases
   - WNAI: Confirmed cases

In addition to RHAs notifying the CMOH of the above, other public health reporting requirements include the following:

1. Investigation and follow-up all **lab** reported WNv cases.

2. Notification to AHW:
   - The MOH will ensure completion of the *Notifiable Disease Report (NDR)* for confirmed and probable WN cases and submit to the PHO, by Wednesday noon, all reports of cases reported in the week prior (Sunday to Saturday). [See Appendix B *Algorithm for Reporting WNv to Alberta Health and Wellness*]
   - The *Alberta Enhanced Surveillance Report (ESR)* is to be forwarded as soon as client contact is made:
     - WNNS (within 7 days)
     - WN Non-NS and WNAI (within 14 days)

3. Notification to Canadian Blood Services (CBS)
   - The MOH will report, as soon as possible, all confirmed and probable cases of WNNS and WN Non-NS cases to the nearest Canadian Blood Service (CBS) Centre using *Public Health West Nile Virus Notification to Canadian Blood Services form* (see Appendix I) who have been:

     i. recipients of blood components with the onset of illness within 8 weeks of receiving blood
        or
     ii. blood donors with the onset of illness within 8 weeks of donating blood.

The ProvLab will report to CBS on a daily basis the following information:

i. Names of individuals who have blood samples submitted for WNv testing, and
ii. Names of individuals who have tested positive for WNv.

Reporting Forms: *The Arbovirus – Patient History Form*, (Appendix C) and the *Enhanced Surveillance Report (ESR) West Nile Virus Infection* (Appendix J) are utilized for interpretation and classification.

ETIOLOGY

WNv belongs to a family of viruses called *Flaviviridae*. Serologically it is a member of the Japanese encephalitis (JE) virus complex that includes St. Louis encephalitis (SLE), JE, Kunjin, and Murray valley encephalitis viruses. Other flaviviruses include dengue, yellow fever and tick borne encephalitis.

The WNv usually cycles between mosquitoes and birds. Infectious mosquitoes carry WNv in their salivary glands, which 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.

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 +) are at greatest risk of disease. [(1)]

CLINCIAL PRESENTATION

Most WNv infections are mild and 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% - 18%.

West Nile Non-Neurological Syndrome (WN Non-NS)
The symptoms of WN Non-NS usually begin abruptly as a febrile flu-like illness usually resolving within 3 to 6 days.[2] Symptoms include headache, and body aches, occasionally with a skin rash on the trunk of the body and swollen lymph glands. Fever has not always accompanied the symptoms, hence the change in terminology from West Nile Fever to West Nile Non-Neurological Syndrome.

West Nile Neurological Syndrome (WNNS)
The symptoms of severe infection (encephalitis or meningitis) include headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis.[3]

Advancing age is the most important risk factor for serious neurological disease and deaths. Pre-existing conditions such as immunosuppression may be independent risk factors.

Please refer to note on page 2 under WNNS Case definition for more information.

See also Appendix K, West Nile virus Notes for Clinicians.

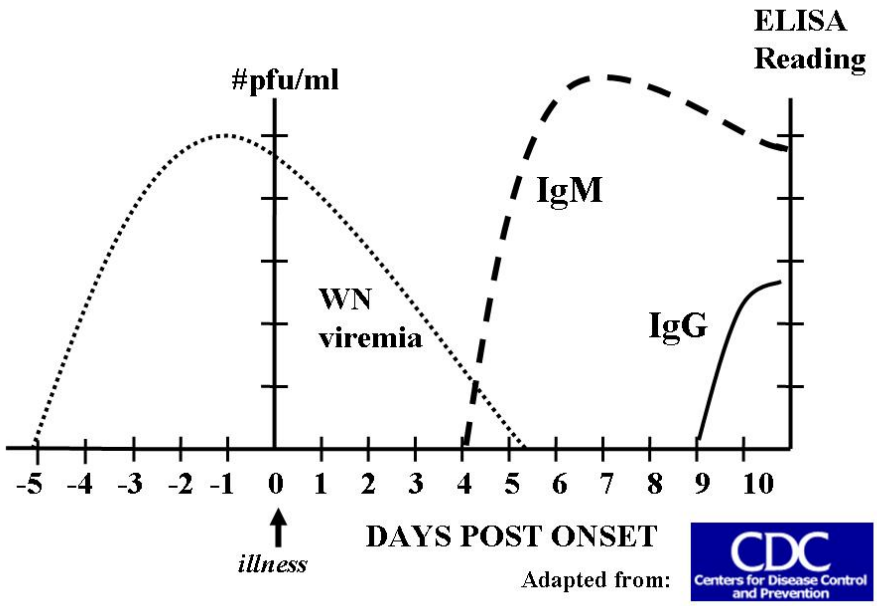
DIAGNOSIS

The diagnosis of WNv is often based on a high index of suspicion and obtaining the results of specific laboratory tests (Refer to Appendix A – *West Nile Virus Testing in 2006*). 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:

- Travel to an area affected by WNv.
- 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.
- 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



A common WNv diagnostic method is the detection of IgM and IgG antibody in serum. Factors for consideration when interpreting results include:[5][6]

- IgM appears during the first week of illness in about 50% of cases. WNv PCR on blood will detect another 45%.
- Serum of people recently infected with or vaccinated for yellow fever, JE, or dengue may contain IgM antibody. IgG antibody cross reacts extensively between flaviviruses.
- Studies of WNv cases have demonstrated that IgM antibody may persist for 12 months or longer. 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.
- Rising titres of IgG antibody indicate recent flaviviral infection. Low avidity IgG antibody also indicates recent flaviviral infection.

Results from an Alberta study confirmed the persistence of WNv IgM antibody among Palliser Health Region residents. Seventy-two percent of people previously diagnosed with WNv infection in the summer of 2003, tested positive for IgM in the summer of 2004 (P. Tilley, Emerg Infect Dis 11;1154-5, 2005). 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 may support the diagnosis.

EPIDEMIOLOGY

Transmission

The most common mode of transmission is through the bite of an infected mosquito. Other means of WNv transmission include: contact with infected blood transfusion or transplanted organs.[7] There also have been reports of in utero infection, [8] through breast milk, [9] and workers who handle infected tissue or specimens.[10]

Incubation Period & Period of Viremia

Symptoms usually develop in 2 to 15 days after exposure.[2] The incubation period may be longer for immunocompromised individuals. Symptoms for WNv generally last 3 to 6 days although severe disease may last several weeks and neurological effects may be permanent. The period of viremia begins 6-7 days prior to symptom onset and ends within a week of symptom onset.[11]

Period of Communicability

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

Susceptibility and Resistance

WNv has been the cause of infection in humans across the age spectrum and susceptibility is likely universal. Most cases of WNNS are in people > 50 years of age.[6]

OCCURRENCE

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. In 2001 the first positive bird was detected in Ontario. The first positive human cases were reported in 2002 in Ontario and Quebec.[2]

Canada

In 2002, 398 probable and confirmed cases were reported. Ontario reported 389/398 (96%) of the cases. During 2003 Health Canada has reported 1388 cases, with 14 deaths. The highest number of cases was reported in Saskatchewan (848) followed by Alberta (275). In 2004, Health Canada reported 25 cases, with no deaths. The highest number of cases (13) was reported in Ontario. In 2005, 239 cases of WNv infection were reported with 12 deaths reported (8 from Ontario). The highest number of cases (101) was reported in Ontario.

The national WNv Monitor posts surveillance data at:
http://www.phac-aspc.gc.ca/wnv-vwn/index.html

Alberta

- The first two cases of WNv in Alberta were reported in 2002 and were related to travel to areas of Canada and the US that were reporting human WN cases.
- In 2003, 275 cases of WNv infections were reported to AHW (223 WN Non-NS, 48 WNNS, 48 WNAI, 1 unknown). Geographically, WNv cases were predominantly reported from the Grassland and Parkland natural regions in the south east area of the province. Palliser Health Region reported the highest number of cases (N=131) and the highest rate of disease.
- In 2004, one case of WNv, related to foreign travel, was reported from the Northern Lights Health Region.
- In 2005, there were 10 cases infections were reported to AHW, 2 WNNS and 8 WN Non-NS. Three out of the ten cases were travel related (travel outside of RHA).

- For up-to-date WNv information visit the AHW website at: http://www.health.gov.ab.ca/public/wnv.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:

- 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).
- Recall of being bitten by mosquitoes.
- Blood/blood component recipient (8 weeks prior to onset of symptoms).
- Organ/tissue transplant recipient (8 weeks prior to onset of symptoms).
- Pregnant.
- 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.
- If an infant, assess for possible transmission in utero or through breast milk.

CONTROL

Management of Case

1. Clinical presentation and Case Definition.
   In collaboration with the client and the attending physician, determine the clinical presentation as per WNNS, WN Non-NS, or WNAI Case Definition (i.e. confirmed, probable, or suspect).

2. Diagnostic tests and follow-up specimens.
   - Review laboratory results and obtain follow-up specimens (e.g. convalescent blood sample) when required (See Appendix A - *West Nile Virus Testing in 2006).*
   - All specimens for WNv analysis are submitted to ProvLab.
   - All cases reported as WNv positive by the CBS screening of donors require a follow-up blood specimen obtained in the community to verify acute WNv infection.
   - The routine ProvLab requisition and the *Arbovirus - Patient History Form* (Appendix H - *Canadian Blood Services Notification to Public Health of West Nile Virus*), should accompany all specimens submitted by public health professionals.

3. Environmental sampling and public health investigation of human WNv infection.
   The mosquito and bird surveillance program will continue in the southeast portion of the province. Additional environmental sampling, e.g. mosquitoes or birds, in other geographic areas where a human case has been reported is not warranted.

4. Follow up of infants born to mothers infected with WNv.
   Based on a February 2004 CDC publication in MMWR,[12] Alberta WNv Public Health Guidelines recommends that infants born to mothers with WNv during pregnancy, as well as infants with positive WN laboratory tests, undergo clinical evaluation for WNv infection. A medical infectious disease specialist should be involved in the assessment. (See Appendix L - *Alberta Pregnancy Algorithm for WNv and Pre & Post-Natal Assessment and Investigations for WNv*).

Treatment of 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

1. Household and other close contacts. There is *no evidence* to suggest that WNv can be transmitted to human contacts of persons infected with WNv.

2. Occupational exposure to WNv containing materials (e.g. dead birds):

   Workers exposed to WNv infected material should:[10]
   - 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.
   - Report any illness within 2 weeks of exposure to the Occupational Health Service and the personal physician.

No prophylactic antiviral medications are known to be effective in the prevention of WNv infection.

PREVENTIVE MEASURES

1. **Preventing vector mosquitoes from biting humans**. 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 still considered the best measure to avoid the low risk of contracting WNv infection. Refer to *Fight the Bite* website http://www.health.gov.ab.ca/public/WNv/Index.html

2. **Surveillance and monitoring for WNv in Alberta**.
   Surveillance activities for 2006 focus on the detection of WNv in mosquitoes, birds, horses and humans. Refer to the 2006 public *Fight the Bite* website developed by AHW: http://www.health.gov.ab.ca/public/WNv/Index.html

3. **Blood safety measures.** See Appendix M - *Role of Canadian Blood Services* for complete details.

   In addition, ensure that patients are informed of the risks of WNv infection through blood transfusion and non-fractionated blood products, and the potential alternatives where medically appropriate. Transfusion-transmitted WNv infection has serious outcomes for some patients and should be considered a material risk of blood transfusion. During WNv season this should be part of the informed consent for transfusion.

4. **Workplace health and safety.**

- Outdoor workers.

  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 national *Occupational Health Advisory* for outdoor workers and those handling dead birds or animals at:
  http://www.phac-aspc.gc.ca/wnv-vwn/work_wnv_e.html

- 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:
  http://www.phac-aspc.gc.ca/ols-bsl/wnvbio_e.html

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Resources

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APPENDICES

APPENDIX A

West Nile Virus Testing in 2006

West Nile Virus Testing in 2006

West Nile virus testing for mild uncomplicated febrile illness is not required for public health purposes and is generally not indicated unless, in the physician's opinion, the results will influence clinical management. Testing is recommended for the following patients during West Nile season (June – Oct):

- Meningitis, encephalitis, acute flaccid paralysis or other neurological symptoms,
- Patients with unexplained fever occurring more than 3 days and less than 8 weeks after a blood transfusion,
- Febrile patients with a history of blood, organ or tissue donation within 8 weeks,
- Transplant or other immunocompromised patients with unexplained fever and possible exposure to mosquitoes,
- Pregnant women with unexplained febrile illnesses during WNv season
- Healthy blood donors with positive WNv screening tests at Canadian Blood Services.

Please submit to ProvLab the following specimens, with the requisition and **Arboviral History Form** (available at www.provlab.ab.ca):

Specimen:	**Transport:**	**Please specify on requisition:**	**Comment:**
Acute serum (All patients)	7-10 mL in gold top serum separator tube(s)	"WNv - acute"	WNv IgM will be performed within 3 days.
Acute whole blood (All patients)	7-10 mL in purple top EDTA tube(s)	"WNv PCR"	Detects about 40% of cases during 1st week of illness, prior to antibody.
CSF	1 mL in dedicated sterile tube, if possible	"WNv PCR" or "HSV PCR"	Testing for Enterovirus will be done automatically if WNv PCR ordered.
Convalescent serum (>10 days after acute, critical cases only)	7-10 mL in gold top serum separator tube(s)	"WNv-convalescent"	WNv IgM will be repeated, and IgG will be tested to detect seroconversion.

- IgM on serum, and PCR on EDTA blood together detect >95% of cases on the first blood sample. Convalescent serology may be useful for rare critical cases where IgM and PCR are both initially negative.
- Many patients remain IgM-positive for > 1 yr, so a convalescent serum is recommended to demonstrate changing IgG titres in IgM-positive patients.
- WNv PCR can detect viral RNA in CSF, but has low sensitivity (10-20%). Many CSF specimens are positive for enterovirus.

Please call if you have questions or comments
Peter Tilley MD FRCPC (403) 944-1203, p.tilley@provlab.ab.ca

How to Interpret Acute West Nile Virus Test Results

Acute WNv tests:

IgM	IgG	EDTA blood WNv NASBA/PCR	CSF WNv PCR	Interpretation
any	Any	POSITIVE		This patient is viremic, and is a confirmed case of West Nile virus infection. There is no cross-reactivity with other flaviviruses in the Provincial Lab WNv NASBA/PCR
			POSITIVE	Viral RNA present in the CSF. This is a confirmed case of West Nile virus infection. There is no cross-reactivity with other flaviviruses in the Provincial Lab WNv PCR
			negative	Viral RNA not detected in the CSF. This test has very low sensitivity and does not rule out WNv infection. Please refer to blood tests.
POSITIVE	Negative	negative or not submitted		Possible acute West Nile virus infection, but IgM persists at low levels for 1 year in 60% of patients, and this may be a previous season's infection. Possible non-specific IgM reaction. A follow-up serum in two weeks is recommended to demonstrate rising IgG titres and low avidity IgG. There is very little cross-reactivity with other flaviviruses in IgM tests.
POSITIVE	POSITIVE, high avidity	negative or not submitted		Past West Nile virus infection. IgG antibody takes 3-6 months to mature to the high avidity level. IgM persists into the following season in 60% of patients, and this likely a previous season's infection. A follow-up serum in two weeks is recommended to demonstrate stable titres.
POSITIVE	POSITIVE, low avidity	negative or not submitted		Probable acute West Nile virus infection. IgG antibody takes 3-6 months to mature to the high avidity level. A follow-up serum in two weeks is recommended to demonstrate changing titres and confirm infection
negative	POSITIVE	negative or not submitted		Past flavivirus exposure. IgG assays cannot differentiate WNv from dengue, St Louis encephalitis, Japanese encephalitis or yellow fever. Could be due to vaccination. IgG does not reliably indicate immunity to WNv.
negative		negative		Not a WNv case. Data from 2003 show that an IgM test and blood NASBA, performed together on the initial blood sample, detect >95% of cases. Follow-up serology is recommended only for critical cases.

PCR: polymerase chain reaction, NASBA: nucleic acid sequence based amplification. (Both are DNA or RNA amplification tests with similar clinical roles)

How to Interpret Acute and Convalescent West Nile Virus Serology Results

Acute and Convalescent WNv tests:

Acute	Convalescent	Interpretation
IgM negative	IgM POSITIVE	Probable WNv case. IgM is relatively specific for WNv, and a seroconversion indicates that infection is recent (<3 weeks).
IgM POSITIVE IgG negative	IgM POSITIVE IgG POSITIVE, significant rise in IgG level	Probable WNv case. Rising IgG levels, or rising WNv HI titres, or low avidity IgG indicate recent flavivirus exposure. WNv IgM is relatively specific for WNv, indicating recent infection is WNv. First 5 cases in Alberta will be submitted to the National Microbiology Lab for confirmation by PRNT.
IgM POSITIVE IgG POSITIVE	IgM POSITIVE IgG POSITIVE, significant rise in IgG level	
IgM POSITIVE IgG negative	IgM POSITIVE IgG POSITIVE, Fourfold rise in WNv HI titre	
IgM POSITIVE IgG POSITIVE	IgM POSITIVE IgG POSITIVE, Low avidity IgG	
IgM POSITIVE IgG negative	IgM POSITIVE IgG POSITIVE, Fourfold rise in WNv HI titre, WNv PRNT POSITIVE, titre ≥80	Confirmed WNv case. WNv PRNT test is highly specific for WNv, indicating definite WNv exposure. Rising HI titre (or rising IgG level, or low avidity IgG) indicate recent infection.
IgM POSITIVE IgG POSITIVE	IgM POSITIVE IgG POSITIVE, Stable IgG level, High avidity IgG	Past WNv infection. IgM persists into the following summer in 60% of patients.
IgM negative IgG negative	IgM negative IgG POSITIVE, significant rise in IgG level	Acute flavivirus infection, probably not WNv. IgG and WNv HI tests also detect St Louis encephalitis, Japanese encephalitis, dengue and yellow fever, including vaccine responses. Needs neutralization titres at National Lab.
IgM negative IgG POSITIVE	IgM negative IgG POSITIVE, Stable IgG level, High avidity IgG	Past flavivirus exposure. IgG and WNv HI tests also detect St Louis encephalitis, Japanese encephalitis, dengue and yellow fever, including vaccine responses. Not a reliable indicator of WNv immunity.
IgM negative IgG negative	IgM negative IgG negative	Not WNv. Lack of antibody to WNv by 21 days after onset of illness is extremely unusual.

PRNT: plaque reduction neutralization titres, HI: Hemagglutination inhibition assay

PROVLAB ALBERTA

West Nile Virus Test Summary for Public Health Practitioners

Test Name	Test Format	Test Performance and Interpretation
WNv Nucleic acid testing (NAT)	Also known as polymerase chain reaction (PCR), or NASBA. Detects presence of viral RNA by an amplification method in plasma or CSF.	• 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. • Low sensitivity in CSF, probably <20%. • A positive NAT test is always confirmed by a second NAT test targeting a different gene. • A positive NAT test indicates a CONFIRMED CASE of WNv infection.
WNv IgM	A high volume enzyme immunoassay test (EIA) which detects WNv-specific IgM in serum	• 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. A patient with a positive WNv IgM result may have had the infection last season!
WNv IgG	EIA for WNv IgG in serum.	• Cross reacts extensively with other flaviviruses, such as St. Louis Encephalitis, Dengue, Japanese Encephalitis and Yellow Fever, including vaccination. • NOT recommended for asymptomatic persons. NOT a reliable marker of immunity to WNv. • Useful to show rising IgG levels in acute and convalescent sera, which

Test Name	Test Format	Test Performance and Interpretation
		are strongly suggestive of recent flavivirus infection or vaccination.
WNv IgG Avidity	Measures strength of antibody binding to WNv.	• 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. • High avidity antibody indicates a mature response, and exposure to a flavivirus at least 6 months previously.
WNv Hemagglutination Inhibition Titre	Measures ability of patient's antibodies to block binding of WNv to goose red blood cells! Provides a quantitative measure of antibody level (titre). Performed at the National Microbiology Lab in Winnipeg.	• Detects both IgM and IgG. • Cross reacts extensively with other flaviviruses, such as St. Louis Encephalitis, Dengue, Japanese Encephalitis and Yellow Fever, including vaccination. • Useful to show rising antibody levels in acute and convalescent sera, which is strongly suggestive of recent flavivirus infection or vaccination
WNv Plaque Reduction Neutralization Titre (PRNT)	Measures ability of patient serum to block live WNv infection in a cell line. Performed in the Containment Level-3 Lab at the National Microbiology Lab in Winnipeg.	• Highly specific for WNv. "Gold standard" serologic test. • Indicates CONFIRMED previous WNv infection. • Hazardous and laborious. Not a rapid test. Results takes 4-8 weeks.

P. Tilley MD FRCPC
403-944-1203
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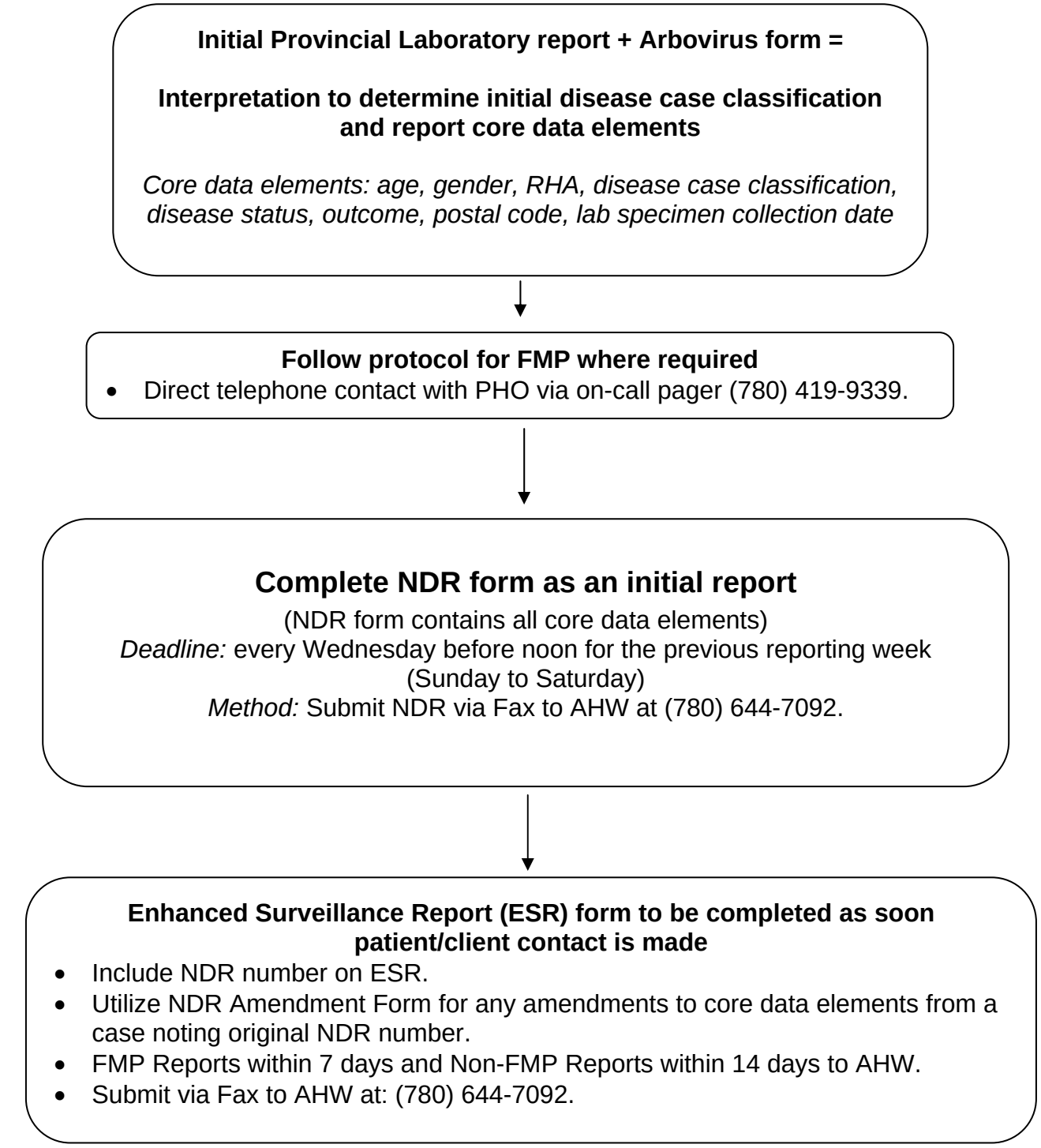
APPENDIX B

Algorithm for Reporting WNv to Alberta Health and Wellness

Algorithm for Reporting WNv to Alberta Health and Wellness



APPENDIX C

Arbovirus Patient History Form - ProvLab

PROVINCIAL LABORATORY FOR PUBLIC HEALTH

Calgary Telephone: (403) 944-1200
Calgary Fax: (403) 270-2216
Edmonton Telephone: (780) 407-7121
Forms available at www.provlab.ab.ca

ARBOVIRUS - PATIENT HISTORY FORM

Patient Name: _____ **DOB:** _____ **Sex**: ____

PHN:

_____

Submitting Physician:

_____

Physician Phone No: _____ **Fax No:** _____ **Pager:** _____

Date of onset of symptoms: _____ (*very important*)

Acute clinical features (P*lease circle all that apply*)**:**

Fever (120)	**Rash** (254)	**Generalized lymphadenopathy** (184)	**Altered mental status (785)**
Cranial nerve palsy (789)	**MuscleWeakness** (786)	**Flaccid paralysis** (787)	**Tremor** (791)
Seizures (268)	**Sensory deficits**(794)	**SIADH** (793)	

Other relevant symptomatology:

_____

CSF WBC count: _____ **predominantly** □ **Neutrophils** □ **Lymphs**

□ **Blood transfusion within 8 weeks of onset** (783) Date: _____

□ **Blood donation within 8 weeks of onset** (796) Date _____

□ **Organ/tissue donation within 8 weeks of onset** (446) Date: _____

□ **Pregnant** (238)Due Date: _____

Immunocompromised:

□ **Transplant (465)** □ **Leukemia (386)** □ **Other** □ **Steroids (797)** □ **Lymphoma (388)**

History of travel within 3 weeks before onset (*please specify*):

_____

History of vaccination for: □ **Yellow Fever** Approx. date: _____
□ **Japanese encephalitis** Approx. date _____

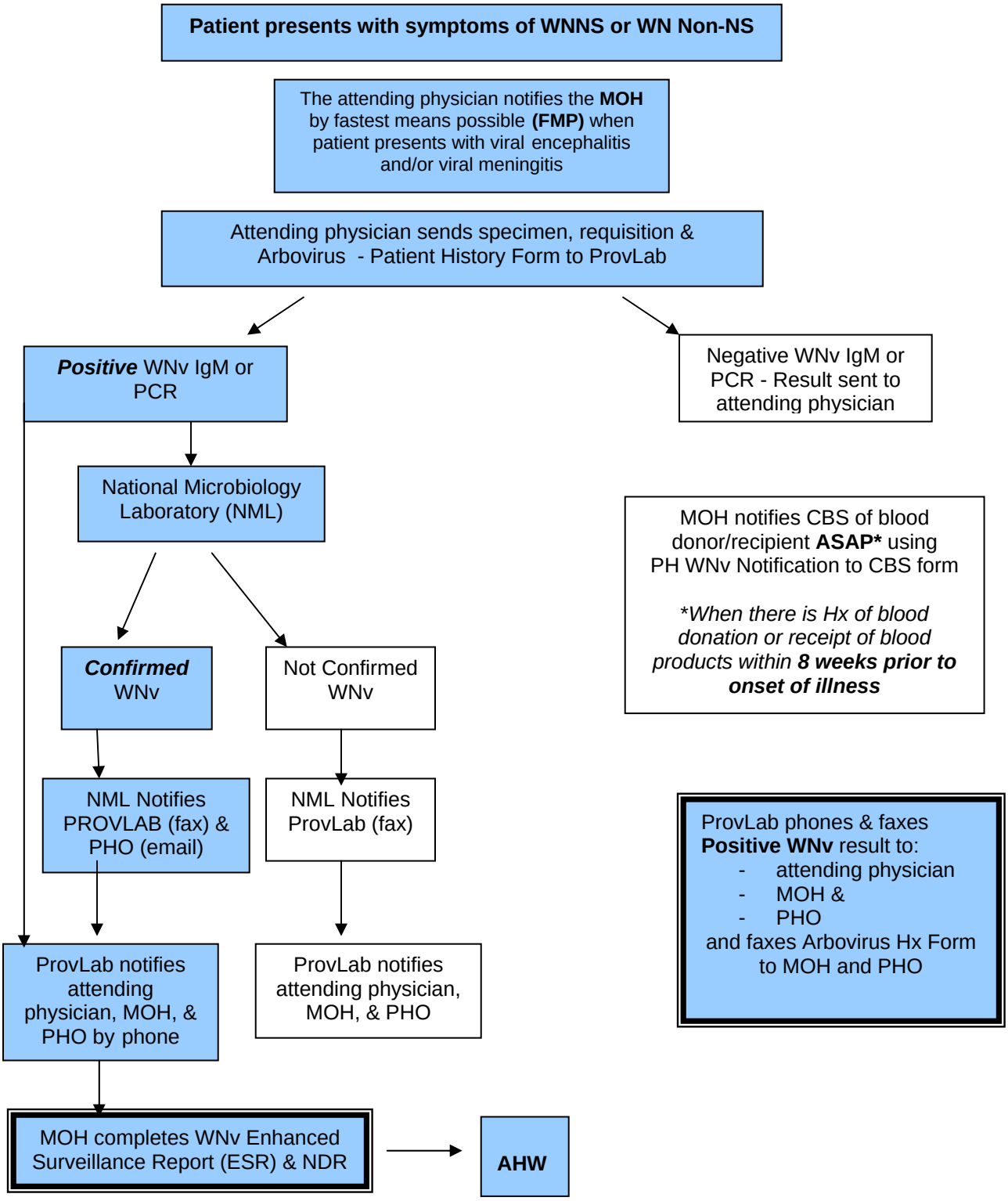
Past residence in tropical regions: □ No_____ □Yes_____
(To assess Dengue, JE cross-reactivity)

Developed by Dr. Peter Tilley/PLPD for 2005 WNv Season

APPENDIX D

Reporting Algorithm for WNNS and WN Non-NS

Reporting Algorithm for WNNS and WN Non-NS



APPENDIX E

Laboratory Confirmations for Case Definitions for WNv

Laboratory Confirmations for Case Definitions for WNv

	Confirmed	Probable	Suspect
WNNS	**FMP** ▪ WNv NAT positive, plasma, or CSF, **OR** ▪ WNv IgM positive, low avidity antibody, WNv PRNT positive, **OR** ▪ Significant rise in WNv IgG, WNv PRNT positive **OR** ▪ Fourfold or greater rise in WNv HI titre, WNv PRNT positive.	**FMP** ▪ WNv IgM positive, low avidity antibody **OR** ▪ WNv IgM positive, sinificant rise in WNv IgG, **OR** ▪ WNv IgM positive, fourfold or greater rise in WNv HI titre.	▪ Clinical illness: Viral encephalitis or viral meningitis (excluding acute flaccid paralysis) in the absence of any other cause *and* in the absence of or pending laboratory results.
WN Non-NS	As above	As above	Not applicable
WNAI	As above	Canadian Blood Services NAT +	Not applicable

Source: Adapted with permission from Dr. Peter Tilley, Medical Microbiologist, Provincial Laboratory for Public Health (Microbiology), by Alberta Health & Wellness, Disease Control & Prevention Branch, Communicable Disease Control Program. Prepared May 31, 2004, Revised April 2006.

APPENDIX F

Canadian Blood Services (CBS) Responsibilities

CANADIAN BLOOD SERVICES (CBS) RESPONSIBILITIES

Key components of the CBS WNv plan are:

- Screening of blood donors for illness and symptoms such as fever.
- Beginning July 1, 2003 all donated blood is tested for WNv by nucleic acid testing (NAT) 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 public health is informed.
- 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 are identified and followed up for possible WNv infection. Untransfused blood products from this blood donor will be discarded. CBS only requires notification if the recipient is suspected to have transfusion-transmitted WNv infection.

Asymptomatic blood donors with a positive WNv NAT** test will be notified by telephone, followed by a letter from CBS.

- Public Health will be notified based on NAT (+) individual donation results for that individual. The form *Canadian Blood Services Notification to Public Health of West Nile Virus* (Appendix H) outlines information provided to the MOH and Provincial Health Officer.
- Donors are deferred for 8 weeks following a positive donation and are then eligible to return to donate if WNv screening is negative.
- With donor consent, the results of WNv testing will be forwarded to the donor's personal physician who will be responsible for any necessary follow-up. Donors will be informed that they will likely be contacted by the MOH or his/her designate.

****Note**: 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 WN virus and 9 other viruses.

Blood/blood product recipients/donors with WNv infection:

All *probable* and *confirmed* cases that were blood/blood product recipients or have donated blood within 56 days (8 weeks) prior to illness onset should be immediately reported by the MOH to the CBS. The form *Public Health West Nile Virus Notification to Canadian Blood Services* outlines information to be forwarded to the CBS (See Appendix I – *Public Health West Nile Notification to Canadian Blood Service*).

Detection of cases related to blood/blood component transfusions.

- Regular blood recipients who receive blood on an outpatient basis should be informed of WNv symptoms and participate in a self-monitoring program.
- All blood recipients should be encouraged to report fever or any new onset of neurological signs occurring 3 days or more post transfusion to their physician.

The CBS report ***Action Plan to Protect the Blood System From West Nile Virus*** describes blood safety measures (refer to CBS website): http://www.bloodservices.ca

Organ/tissue donors with WNv infection.

Organ/tissue donors are tested for WNv by the ProvLab. During 2003, of 440 organs/tissue tested, none were found to be positive. 598 were tested in 2004 and 536 in 2005, none were found to be positive. (P. Tilley, personal communication, May 5, 2006). It is anticipated that the risk of WNv infection through organs/tissue will be very low.

Public health at the regional and provincial level will receive WNv positive lab reports as well as the ordering physician, i.e. the medical director for the HOPE program or the Comprehensive Tissue Centre, Southern Alberta Tissue Program, or Lion's Eye Bank.

The medical director of the organ/tissue procurement agency, in collaboration with the MOH, will:

- Ensure that organs/tissue from the WNv positive donor are not used for transplant. In some situations a transplant may proceed following an assessment of the risks and benefits of the procedure.
- Ensure follow-up of recipients who received organs/tissue from the donor.

Organ/tissue recipients with WNv.

All possible, probable, suspect, and confirmed cases that received organ or tissue transplants within 56 days (8 weeks) prior to illness onset should be reported by the MOH to the transplanting surgeon. The transplanting surgeon, in collaboration with the MOH, will:

- Investigate the source of WNv infection in the recipient.
- In the event of a positive donor, ensure that organs/tissue from the same donor are not used for future transplant without an assessment of the risks and benefits of the procedure.
- Ensure follow-up of other recipients who have received organs/tissue from the same donor.

Testing of donated organs and tissues for WNv.
Routine testing of donated organs and tissue for WNv will occur in Alberta. The organ/tissue procurement agencies have a tracking system in place to identify recipients and donors of organs/tissue. Other than corneas, tissue is quarantined until all serology and microbiology results are received prior to release for use. If a WNv positive donor is found, the tissue will be destroyed.

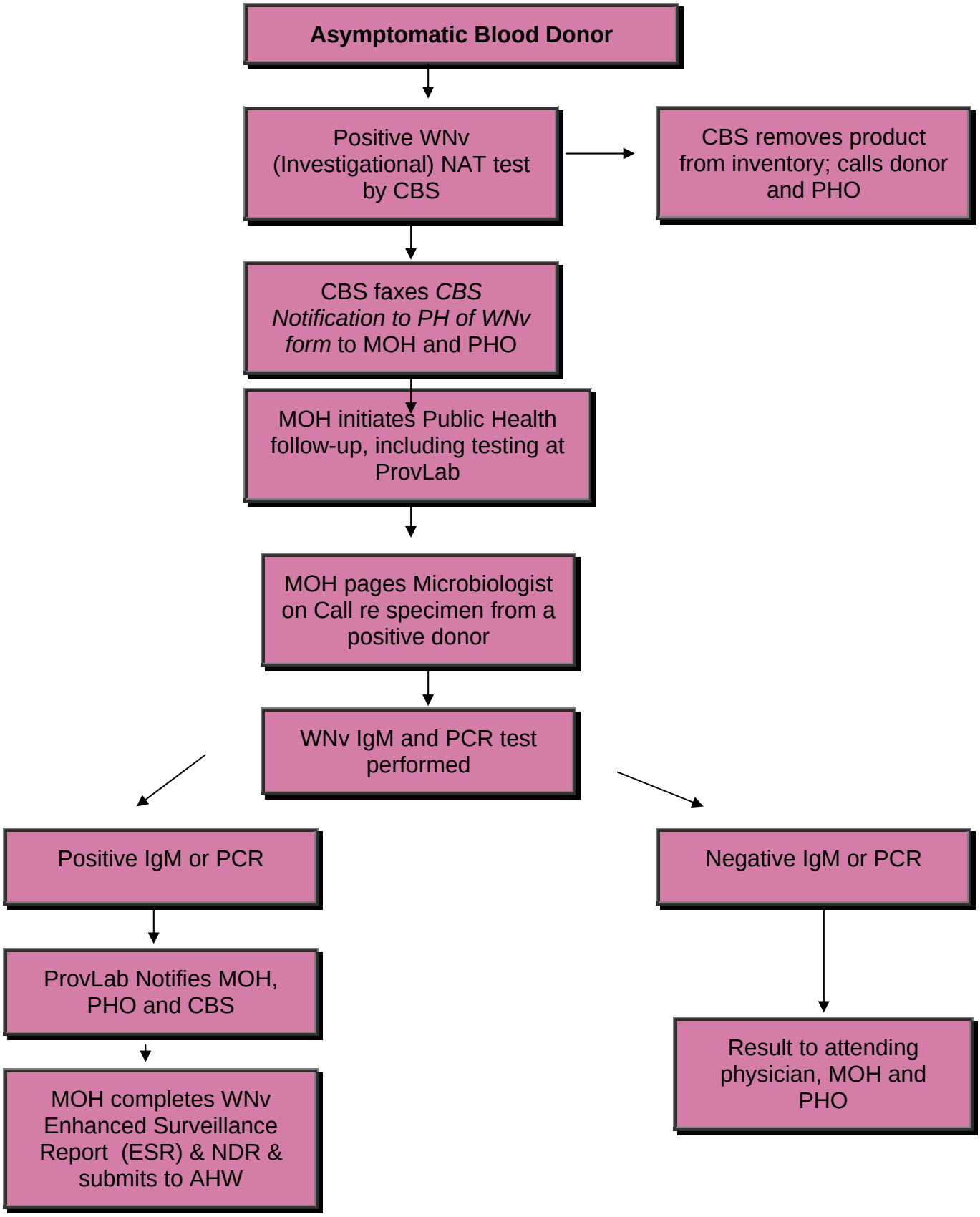
Infants born to mothers infected with WNv
Based on a February 2004 CDC publication in MMWR,[12] *Alberta WNv Public Health Guidelines* recommends that infants born to mothers with WNv during pregnancy, as well as infants with positive WN laboratory tests, undergo clinical evaluation for WNv infection. Medical infectious disease specialists should be involved in the assessment. (See algorithm *Alberta Pregnancy Algorithm for WNv* and *Pre & Post-Natal Assessment and Investigations for WNv* in Appendix G - *Reporting Algorithm for WNAI – Canadian Blood Services*).

Source: Author: Dr. Judy Hannon, Canadian Blood Services, prepared May 2005, updated April 2006

APPENDIX G

Reporting Algorithm for WNAI - Canadian Blood Services

Reporting Algorithm for WNAI – Canadian Blood Services



APPENDIX H

Canadian Blood Services Notification to Public Health of WNv

CANADIAN BLOOD SERVICES | SOCIÉTÉ CANADIENNE DU SANG

<Lookback / Traceback – Centre>

To: <name>
Medical Officer of Health - <Regional Health Authority>

Provincial Health Officer
Pager (780) 419-9339
Fax (780) 427-7683

From: <name>
Medical Director
Canadian Blood Services

Date:

Subject: Canadian Blood Services Notification to Public Health of West Nile Virus

CBS Reference No:

This is to provide notification that the following individual has tested positive for West Nile Virus from a blood specimen provided for blood donation:

Name:
Address:
Phone No.:

DOB:
Gender:

Blood Specimen Date:

Disease: West Nile Virus

Laboratory Tests:

The laboratory tests were completed by Canadian Blood Services Transmissible Disease Testing.

signature

<name>
Medical Director
Canadian Blood Services
cc: <name>, Lookback/Traceback Coordinator

APPENDIX I

Public Health West Nile Notification to Canadian Blood Service

Public Health West Nile Virus Notification to Canadian Blood Service

1. Obtain the Following Donor or Recipient Information:

Name:	DOB:
Address:	
City:	Province:
Postal Code:	
Onset date of symptoms _____ YYYY - MM - DD	
WNv Case Classification: □ Suspect WNNS □ Probable/Confirmed WN Non-NS	□ Probable/Confirmed WNNS □ Confirmed WNAI
Test Result (if available): □ Positive □ Negative ****Please attach copy of WNv serology result****	Test Date: _____ YYYY – MM - DD

2. History of blood *DONATION* in the 56 days (8 weeks) prior to onset of symptoms? □ Yes □ No
If yes, CBS Donor Number: _____ (if available)

Centre - City of Donation	Name at time of Donation

3. **History of blood/blood component *TRANSFUSION* in the 56 days (8 weeks) prior to onset of symptoms?** □ Yes □ No

Hospital	City	Transfusion Date (if known)	Name at time of Transfusion
		YYYY - MM - DD	
		YYYY - MM - DD	
		YYYY - MM - DD	

Form completed by:	Contact Phone #:
Signature:	Date:
RHA	

Forward completed information to the CBS by phone and fax:

Edmonton	**Calgary** Mon – Fri, 0800 – 2100 hrs	**Calgary** Mon – Fri, 2100 – 0800 hrs Sat & Sun after 1600 hrs
Phone: 780-431-0777 (24 hrs)	Phone: 403-410-2671	Phone: 403-589-3399
Fax: 780-433-4478	Fax: 403-410-2791	Fax: 403-410-2791

APPENDIX J

Enhanced Surveillance Report (ESR) West Nile Virus Infection

ENHANCED SURVEILLANCE REPORT
WEST NILE VIRUS INFECTION (2006)

Case Count _____
(For AHW use only)

Please fax completed reports to (780) 644-7092
Attn: WNv Human Surveillance Coordinator
Phone (780) 644-0004

Instructions:
1. This form is to be filled out in addition to the Notifiable Disease Report (NDR) form.
2. Clinical information related to West Nile virus-related Syndrome (Page 3 of the form) is to be completed ***by a physician or MOH/designate in consultation with client's physician*** only if the patient/client is classified as having WN Neurological Syndrome (WNNS).

Report Date: _____/_____/_____ (yyyy/mm/dd)

NDR #_____

Is this the first Enhanced Surveillance Report submitted for this case? O Yes O No If No, please provide Update Number _____

SECTION A. REPORTER INFORMATION

Person reporting: Last name _____ First Name_____

RHA _____ Tel: _____-_____-_____

In the event that the patient/client was unavailable for consultation in completing this report, please check

☐ and provide brief explanation:

_____

Was a physician consulted for any of the patient/client information? O Yes O No

If yes, List physician contact information: Last name _____First name _____

City/Town_____ Prov _____

Tel: _____-_____-_____

SECTION B. PATIENT/CLIENT INFORMATION:

Last name _____ First name _____Middle name _____

Date of Birth ____/____/____(yyyy/mm/dd) (if Date of Birth not available; Age_____ years/ months/ weeks)

Sex: O Male O Female O Unknown PHN _____

Regional Health Authority: _____

The First Nations and Inuit Health Branch, Health Canada, is very interested in collecting the following information for public health measures for First Nations and Inuit peoples:

Is client/patient Aboriginal? ☐ Yes ☐ No ☐ Refused to answer

If Yes, please specify: ☐ First Nations ☐ Métis ☐ Inuit ☐ Non-status Indian

If Yes, is primary residence on reserve? ☐ Yes ☐ No

SECTION C. CASE CLASSIFICATION (*please check applicable classification*)

Consult the 2005 WNv Alberta Case Definitions for explanation of categories online:
www.health.gov.ab.ca/public/WNv/pdf/case_definitions.pdf

	Suspect	Probable	Confirmed
West Nile Neurological Syndrome (WNNS)			
West Nile Non-Neurological Syndrome (WN Non-NS)			
West Nile Asymptomatic Infection (WNAI)			

SECTION D. PREGNANCY INFORMATION

In the three (3) weeks prior to date of symptom(s) onset, was patient/client pregnant?

O Yes O No O Unknown O Not applicable

If Yes, please specify the expected confinement date (ECD): Date _____/_____/_____ (yyyy/mm/dd)

Has the prenatal medical care provider has been notified? O Yes O No O Unknown

SECTION E. TRAVEL AND RESIDENCE HISTORY

Did the patient/client travel more than 100 km distance (1 hour drive on highway roads) from his/her residence in the three (3) weeks *before onset of symptoms*? O Yes O No O Unknown

If Yes please provide the following information:

City/Town	Province/Territory/State	Country
For AHW use only: Is case related to travel to WNv endemic area? O Yes O No O Unknown If YES, specify travel location:		

SECTION F. CLINICAL INFORMATION:

Hospitalized: O Yes O No O Unknown Hospital name_____

Symptom onset date ____/____/____ (yyyy/mm/dd) **(Please try to complete).**

OR O Asymptomatic → *if asymptomatic, skip to Section G*

Signs and Symptoms ***(to be completed with information from patient/client)***	**Yes**	**No**	**Don't Know /Unsure**
Fever (≥ 38° or ≥ 100°F)	O	O	O
Headache	O	O	O
Muscle pain	O	O	O
Joint pain	O	O	O
Confusion or unusual forgetfulness	O	O	O
Blurred vision or deterioration in eyesight	O	O	O
Eye sensitivity to light	O	O	O
Unusual fatigue/sleepiness	O	O	O
Weakness	O	O	O
Stiff neck	O	O	O
Rash	O	O	O
Enlarged glands	O	O	O
Other signs/symptoms (Please specify)	O	O	O

West Nile virus-related Neurological Syndrome **This section to be completed *by a physician or MOH/designate in consultation with client's physician* <u>only</u> if the patient/ client is classified as having Neurological Syndrome**	**Yes**	**No**	**Don't Know/ Unsure**
Viral meningitis	O	O	O
Viral encephalitis	O	O	O
Acute Flaccid Paralysis, please specify:	O	O	O
Poliomyelitis-like Syndrome	O	O	O
Guillain-Barré-like Syndrome (GBS)	O	O	O
Other, please specify:	O	O	O
Movement disorders (e.g. tremors, myoclonus)	O	O	O
Parkinsonism (e.g. cogwheel rigidity, bradykinesia, postural instability)	O	O	O
Rhabdomyolysis	O	O	O
Peripheral neuropathy	O	O	O
Polyradiculopathy	O	O	O
Optic neuritis	O	O	O
Ocular Motor Disorder	O	O	O
Acute demyelinating encephalomyelitis (ADEM)	O	O	O
Facial muscle weakness	O	O	O
Other, please specify:	O	O	O

Underlying health conditions (chronic and/or immunocompromising) that may influence WNv symptoms) **This section to be completed for *<u>all</u>* WNv case classifications**	**Yes**	**No**	**Don't Know/ Unsure**
Cancer: specify	O	O	O
Heart Disease, specify	O	O	O
Diabetes, specify	O	O	O
Alcoholism	O	O	O
Cerebrovascular disease, specify	O	O	O
Liver disease, specify	O	O	O
Lung disease, specify	O	O	O
Renal disease, specify	O	O	O
Immunocompromising condition(s), specify	O	O	O
Neurological disorder, specify	O	O	O
Musculoskeletal disorder, specify	O	O	O
Other chronic health condition(s), please specify:	O	O	O

SECTION G. MODES OF TRANSMISSION

POSSIBLE Modes of Transmission	**Yes**	**No**	**Don't Know/ Unsure**
Mosquito transmission	O	O	O
Non-Mosquito transmission, including:			
Receipt of blood component	O	O	O
Receipt of Organ/Tissue transplant	O	O	O
Breastfed Infant	O	O	O
Infant infected *in utero*	O	O	O
Laboratory-acquired infection	O	O	O
Occupationally acquired infection → if Yes, please specify:	O	O	O
Direct contact with sick/dead birds 3 weeks prior to symptom onset → if Yes, please specify	O	O	O
Other route of transmission, please specify:	O	O	O

Please identify the MOST LIKELY Mode of Transmission	**Tick only one mode**
Mosquito transmission	O **Note: unless other mode identified, tick as default**
Receipt of blood component	O
Receipt of Organ/Tissue transplant	O
Breastfed Infant	O
Infant infected *in utero*	O
Laboratory-acquired infection	O
Occupationally acquired infection	O
Direct contact with dead or sick birds	O
Other route of transmission, please specify	O

SECTION H. BLOOD/PLASMA/ORGAN(S)/TISSUE DONORS and RECIPIENTS

Blood, plasma or blood components	*Donated* in past 8 weeks? ☐No ☐Yes ☐ Unknown	*Received* in past 8 weeks? ☐No ☐Yes ☐ Unknown
Organs or tissues	*Donated* in past 8 weeks? ☐No ☐Yes ☐ Unknown	*Received* in past 8 weeks? ☐No ☐Yes ☐ Unknown

For any 'Yes' response in Section H: has the form '*Public Health Notification to Canadian Blood Services*' has been completed and processed? O Yes O No O Unknown

APPENDIX K

West Nile virus (WNv) Notes for Clinicians

West Nile virus (WNv) Notes for Clinicians

Author: Dr. Geoff Taylor; Infectious Diseases Specialist, May 2006

After initial introduction and spread in 2002 – 2003, especially in south eastern Alberta, there were very few documented cases of WNv infections in Alberta in 2004 – 2005, making it difficult to predict what to expect in the 2006 season. Nevertheless, clinicians will again need to consider the possibility of WNv infection in their patients this summer and fall.

When should WNv infection be considered in a differential diagnosis?

WNv infection should be considered if:

- The patient's clinical presentation is compatible; and
- Epidemiologic considerations are met.

What are the clinical features of WNv infection?

About 80% of WNv infections are sub-clinical, 20% result in a milder self-resolving non specific febrile illness (West Nile Non-Neurological Syndrome, formerly West Nile Fever) and <1% result in an acute neurologic illness (West Nile Neurologic Syndrome).

West Nile Non-Neurological Syndrome is a febrile illness with onset 2-14 days after infection and can be characterized by malaise, myalgia , arthralgia ,nausea, vomiting headache or retro-orbital pain. Maculo-papular or morbilliform rash occurs in about 50% and more often in children. Hepatomegaly is reported in about 20% and splenomegaly in 10%. Symptoms resolve over 3-6 days. Surveillance data indicates that fever is not present in approximately 33% of cases.

West Nile Neurologic Syndrome occurs in about 1/150 infected individuals, developing 1-7 days after onset of fever. In this syndrome about 2/3 develop encephalitis with or without meningitis and about 1/3 meningitis alone. Headache and eye pain occurs in West Nile Fever and is not itself indicative of neuro-invasive disease. Age (>50 years) is by far the greatest risk factor for neurologic involvement. The overall case fatality rate for neurologic disease is 4-14% (higher in elderly, immunocompromised and those with co-morbidities). Neurologic sequelae are very common amongst survivors – at one year 1/3 have not fully recovered. In paralytic cases, little long term improvement will occur.

Clinical features of West Nile Neurologic Syndrome include one or more of:

- Altered level of consciousness
- Neuromuscular weakness, including acute flaccid paralysis reminiscent of Guillain Barre syndrome or polio
- Movement disorders such as ataxia or extrapyramidal signs
- Meningitis
- Cranial nerve palsies
- Myelitis
- Seizures
- Polyradiculopathy

What laboratory or radiologic features suggest WNv infection?

- Blood hematology and chemistry values are usually normal or non specifically abnormal eg leukocytosis, leucopenia , hyponatremia.
- Neurologic involvement is characterized by typical CSF abnormalities: lymphocytic pleocytosis, elevated protein, normal glucose.
- Brain imaging studies (CT,.MRI) may either be normal or non-specifically abnormal.
- EEG may show diffuse slowing and in some cases seizure activity.
- EMG studies may be helpful in paralytic cases.

What epidemiologic features will support the possibility of WNv infection?

In the southern USA, WNv can be transmitted much of the year. Compatible symptoms in a returned traveler should prompt WNv infection consideration. In infection acquired in Canada, WNv cases occur beginning in mid-July. None have become symptomatic after late September. Based on the epidemiology in previous years, clinicians should consider WNv in non-travelers who present from late June to early October. If there is evidence of WNv from local surveillance reports of mosquitoes, birds or animals then the possibility of WNv infection should be considered much more likely.

Other more uncommon modes of transmission that have recently been described include receipt of blood and blood products, organ and tissue transplantation, occupational exposure in laboratory settings*, in utero* and possibly breast milk.

What alternatives to WNv Neurologic Syndrome should be considered?

Because of the variety of presentations of WNv infection, a number of infectious and non-infectious causes should be explored, depending on the particular clinical presentation, while waiting for laboratory tests. The major alternative viruses causing encephalitis in Alberta are herpes simplex virus (sporadic) and enteroviruses (usually late summer and fall but can be seen at other times). If in doubt, consultation with a Neurologist or Infectious Disease specialist is recommended.

When should testing for WNv infection be considered?

Specific laboratory testing of blood or CSF for WNv infection is required for definitive diagnosis. Testing of patients with non-neurologic febrile illness is of no clinical utility and so is not recommended. Blood, organ, and tissue, donors are screened to prevent transmission.

Testing patients with acute neurologic presentations is potentially helpful, even without available treatment for WNv. Unnecessary or potentially harmful diagnostic and therapeutic strategies can be avoided, and a prognosis can be given. Testing should be strongly considered when a patient presents with any of the clinical neurologic features, and has compatible CSF findings, especially if animal or mosquito surveillance supports local WNv transmission.

What is the management of WNv encephalitis?

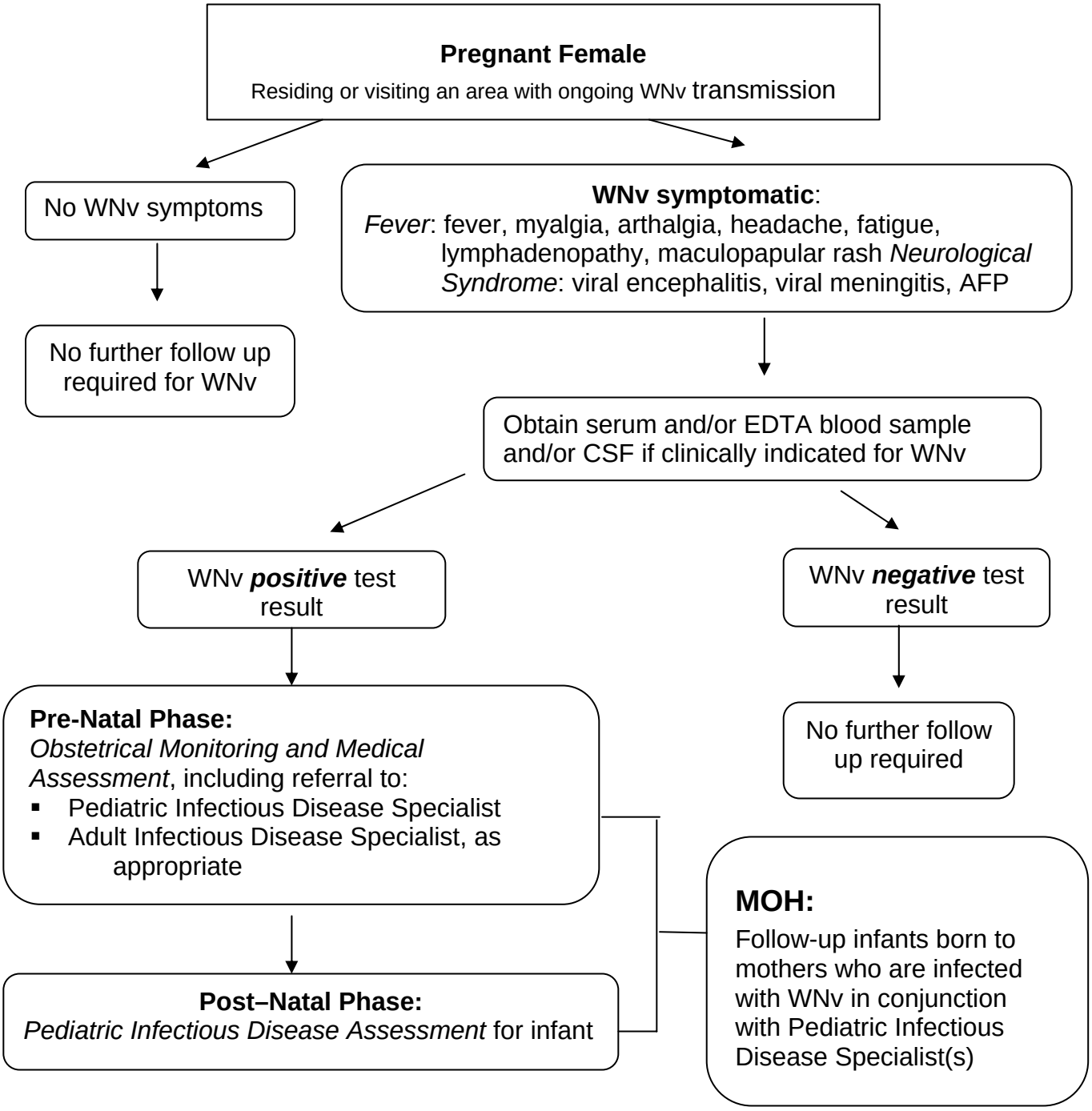
In the absence of antiviral therapy of known value management is entirely supportive/rehabilitative as would be the case for other forms of viral encephalitis.

APPENDIX L

Pregnancy Algorithm for WNv

Pre & Post-Natal Assessment and Investigations for WNv

Pregnancy Algorithm
West Nile virus (WNv) 2006



Source: Adapted from MMWR. June 2004

HEALTH AND WELLNESS

Pre - Natal Assessment and Investigations for West Nile Virus (WNv)

WNv ***positive*** test result in pregnancy →

Pre-Natal Investigations - Maternal

- Repeat maternal serology 2 weeks after initial positive IgM including:
  - EDTA blood sample for WNv PCR (if not done on first sample)
  - IgG and HI to establish acuity
  - Monitor according to adult protocol
  - Detailed ultra sound 2-4 weeks *post onset* of maternal WNv Symptoms

Referrals will be made to:

- Pediatric Infectious Disease Specialist in your region
- Adult Infectious Disease Specialist, as appropriate

Note: If miscarriage or induced abortion, test all products of conception for WNv infection (For documenting WNv Infection on pregnancy outcome)

Post - Natal Assessment and Investigations for WNv – INFANT

Infants born to mothers infected with WNv during pregnancy:

Clinical Exam	Investigations	Pathology
Thorough physical exam of newborn, including: ▪ 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 N.B. 1. Photograph dysmorphic features and skin abnormalities. 2. If an abnormality is noted, consultation with an appropriate specialist is recommended.	Serology: Within 2 days of birth and at age 8 weeks: ▪ IgM and IgG antibody to WNv Newborn hearing screen: 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	▪ Initial examination of placenta by a pathologist is recommended. If congenital WNv infection is identified or strongly suspected, retain: ▪ 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) **Caution:** Wharton's Jelly can cause a very high incidence of false positive WNv serology from cord blood.

Infants with Clinical or Laboratory Evidence of Possible Congenital WNv Infection

Clinical Exam	Investigations	Pathology
▪ Evaluation by a dysmorphologist or clinical geneticist. ▪ Further evaluation to determine alternative causes of congenital abnormalities including: • 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.	Blood/Serology: ▪ 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 CT scan: ▪ If abnormal, a pediatric neurologist should be consulted CSF: ▪ Consider, and if done, should include testing for IgM to WNv Hearing Test: Repeat at 6 months	Placenta and Umbilical Cord tissue: ▪ Histopathologic examination ▪ Testing of frozen tissue for WNv nucleic acid Neonatal blood ▪ IgM and IgG antibody to WNv. ▪ WNV PCR (investigational) **Caution:** Wharton's Jelly can cause a very high incidence of false positive WNv serology from cord blood.

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

APPENDIX M

Role of Canadian Blood Services

ROLE OF CANADIAN BLOOD SERVICES

Since July 1, 2003 all blood donations in Canada have been routinely tested for WNv using a pooled nucleic acid (investigational) screening test (NAT). This approach employs a pooled sample format where aliquots of 6 donations are combined for testing, a process referred to as mini-pool testing (MPT). If a positive MPT occurs, each of the 6 donations contributing too the pool is tested separately (single unit testing or SUT) to identify the positive donor. The donation is then quarantined and destroyed, the donor and public health are notified and follow-up is initiated. In areas of high prevalence for WNv infection, as determined by surveillance data, SUT is implemented for all donations without initial MPT. This heightens the sensitivity of the assay for very low level viremia.

Due the prevalence of WNv in Saskatchewan (positive donations > 1/ 500), CBS implemented single unit testing (SUT) on September 2, 2003 for blood collected in Saskatchewan. On September 2, 2003 2 donations were identified as positive by SUT. These donations were non-reactive on MPT due to extremely low viral titres.

In addition to the implementation of the WNv NAT, CBS implemented other contingencies in 2003 to reduce the risk to the blood supply. These included stockpiling of frozen plasma (collected over the winter/spring) for use during WNv season, adding a question to the "Record of Donation" to identify possible WNv symptoms in potential donors, increasing the inventory of red blood cells prior to the appearance of the first human case, developing an "in house " assay for back-up of the commercial test, and providing risk information to physicians and their patients to assist in informed consent and treatment decisions.

In 2004, all blood donations continued to be tested with the investigational NAT assay. SUT was introduced in areas considered at higher risk of WNv based on surveillance data. The CBS capacity to perform SUT was restricted to approximately 10 to 15% of donations although higher levels of SUT were achieved for short periods of time. Frozen plasma was again stockpiled for use during WNv season. CBS continued to provide risk information to physicians and their patients, and to work with public health officials to share information and coordinate relevant WNv risk reduction efforts and public communications. No WNv NAT positive donors were identified in Canada in 2004, and no cases of transfusion-transmitted WNv occurred.

In 2005, CBS based the decision to convert to SUT on predetermined triggers of the finding of a WNv NAT (+) blood donor or newly confirmed human community cases >1:1000 population (in rural areas) or >1:2500 (in urban regions). An algorithm was developed based on donor testing information, donor and clinic demographic information, and public health surveillance data which allowed 'real-time' assessment of risk in each health region across the country and targeting of SUT to areas of higher risk. Testing was expanded to include contiguous regions depending on test capacity. SUT was discontinued, and MPT restarted if there were no reported cases in a region over the preceding 2 weeks. Using this approach SUT was effectively and rapidly targeted to areas of highest risk for WNv infection. Frozen plasma stockpiling did not occur in 2005.

In 2005, CBS identified 15 WNv positive donors across Canada. 9/15 donors were detected by MPT and 6/15 were detected by SUT. 2 donors could not be confirmed on alternative NAT and may have represented very low level viremia or false positive test results. There were no cases of WNv transmitted through blood transfusion in Canada in 2005.

Canadian Blood Services plans to follow the same format for WNv testing and follow-up in 2006 with one exception. For 2006 once SUT is discontinued, MPT will be restarted if there are no reported cases in a region over the preceeding **7 days** rather than 2 weeks.

It is important that the public do not self-defer during WNv season. A significant concern is a shortage of needed blood products for transfusion during this period.

CBS will continue to work closely with public health agencies to ensure that surveillance information is used to support efforts to protect the blood supply, and that reporting of possible cases of WNv infection occurs in a timely manner.

Source: Author: Dr. Judy Hannon,; Canadian Blood Services, Updated May 2006