INSPQ
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Integrated West Nile Virus Surveillance

Québec

Integrated West Nile Virus Surveillance

ANALYSIS PLAN

Direction des risques biologiques et de la santé au travail

Laboratoire de santé publique du Québec

Direction de la santé environnementale et de la toxicologie

September 2014

Institut national de santé publique Québec

AUTHORS

Anne-Marie Lowe, M. Sc.,
Direction des risques biologiques et de la santé au travail, Institut national de santé publique du Québec

Najwa Ouhoumanne, Ph. D.,
Direction des risques biologiques et de la santé au travail, Institut national de santé publique du Québec

Christian Back, M. Sc.,
Medical Entomology Consultant

Germain Lebel, M. Sc.,
Direction de la santé environnementale et de la toxicologie, Institut national de santé publique du Québec

François Milord, M.D.,
Direction des risques biologiques et de la santé au travail, Institut national de santé publique du Québec

Christian Therrien, Ph. D.,
Laboratoire de santé publique du Québec, Institut national de santé publique du Québec

Stéphane Lair, D.M.V.,
Centre québécois sur la santé des animaux sauvages, Faculty of Veterinary Medicine, Université de Montréal

Isabelle Picard, D.M.V.,
Direction de la santé et du bien-être animal, Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec

IN COLLABORATION WITH

Groupe d'experts scientifiques sur le virus du Nil occidental (VNO)

LAYOUT

Murielle St-Onge,
Direction des risques biologiques et de la santé au travail, Institut national de santé publique du Québec

TRANSLATION

The translation of this publication was made possible with funding from the Public Health Agency of Canada.

LEGAL DEPOSIT – 2nd QUARTER 2015
BIBLIOTHÈQUE ET ARCHIVES NATIONALES DU QUÉBEC
LIBRARY AND ARCHIVES CANADA
ISBN: 978-2-550-71688-4 (FRENCH PDF)
ISBN: 978-2-550-73104-7 (PDF)

Table of Contents

1 Introduction

A new government intervention plan was adopted in early 2013 to protect public health against West Nile virus (WNV) infection, since WNV infection epidemiological activity had resumed in Québec in 2011 and 2012[1]. This new plan establishes the strategy to be pursued for the years 2013 to 2015. The primary objective of the strategy adopted by public health authorities is to prevent the complications and human mortality related to WNV infection.

Interventions are planned to combat the WNV vector, namely mosquitoes. The intervention plan also includes communication activities aimed at the general public and health care and social services network professionals. An integrated surveillance program was set up in 2013 to continue monitoring the situation. This program allows us to characterize WNV activity in Québec in humans and animals.

This analysis plan was prepared by the INSPQ's Groupe d'experts scientifiques sur le VNO [WNV scientific expert panel]. It is a working document that is continuously changing, according to the availability of information and needs. A preliminary version was accepted by the panel at their meeting on September 24, 2013. The analysis plan was then elaborated in connection with the WNV surveillance report for 2013.

2 Integrated WNV surveillance

WNV surveillance data allow us to determine the preventive interventions to be used for personal, community and environmental protection. The data also allow us to document the epidemiology of this disease in Québec and to shape the preventive interventions to be implemented in the coming years.

Objectives of integrated WNV surveillance

Human surveillance

Necessary to document disease burden, and to identify seasonal trends as well as the geographic distribution of the disease.

Entomological surveillance (mosquitoes) and animal surveillance

Necessary to document viral transmission in the regions (predetermined in the case of entomological surveillance), in order to estimate the risk of infection in humans.

2.1 Human surveillance

West Nile virus is most commonly transmitted to humans by a mosquito bite from a mosquito that became infected after feeding on the blood of a WNV-carrier bird. Human-to-human transmission following a transfusion of contaminated blood[2] or an organ transplant[3] is also possible, but remains rare. Cases of perinatal transmission have also been reported[4].

WNV infection often goes undetected since it is estimated that nearly 80% of human cases are asymptomatic[5]. Most symptomatic cases present a clinical picture that is similar to a flu-like syndrome, including fever, headache, myalgia and gastrointestinal problems[6, 7]. Less than 1% of cases may develop neuroinvasive disease (encephalitis, meningitis, meningoencephalitis and acute flaccid paralysis), which particularly affects people aged 50 and over and those who are immunodepressed[8, 9]. This severe manifestation of the disease may cause lasting sequelae, such as depression, chronic fatigue and cognitive deficiencies. Death occurs in nearly 5 to 10% of neurological cases[10, 11].

Chronic kidney failure has also been reported in people infected by WNV, even in mild or asymptomatic cases. The data of a cohort study of 139 patients with WNV infection who were monitored over a period of 1 to 9 years indicated chronic kidney failure in 50 subjects (40%), 42% of which were mild or asymptomatic cases[12]. Information from animal models and on WNV excretion in urine is also available, but the results are not conclusive regarding whether WNV affects kidney function. An expert review published in 2013, the purpose of which was to summarize the literature on this topic, indicated that further studies were necessary to demonstrate whether kidney function could be affected after severe WNV infection. This review particularly stresses the importance of increasing knowledge regarding the long-term complications that can occur in people infected by WNV.

2.1.1 OBJECTIVES OF HUMAN SURVEILLANCE

The purpose of human surveillance is to characterize the disease and to identify the main risk factors for human transmission. The specific purposes are:

- To document the number of human cases, by region of residence, probable region where the disease was acquired, age, and sex;
- To characterize the clinical presentation and the course of these cases (e.g., clinical type, duration of hospitalization, short-term sequelae);
- To identify the risk factors associated with severe forms of WNV infection (e.g., medical history);
- To estimate the associated mortality and morbidity;
- To quantify the requests for tests submitted to the Laboratoire de santé publique du Québec [Québec public health laboratory] (LSPQ) for identification of WNV infection.

Human surveillance indicators

The human surveillance indicator sheet is presented in Appendix 1:

- Number of human cases of WNV infection:
  - by CDC week (according to symptom onset date for symptomatic cases and to episode date[1] for asymptomatic cases);
  - by area of residence or by probable region where the disease was acquired when this is known;
  - by sex and age group;
  - by clinical presentation (WNV non-neurological syndrome, WNV neurological syndrome, and WNV asymptomatic infection (Héma-Québec [Québec's blood collection agency] blood donors, others)).
- Mortality and morbidity[2]:
  - hospitalization and intensive care (duration);
  - death (associated with WNV);
  - sequelae (three months post-diagnosis);
  - risk factors (e.g., medical history).
- Crude incidence rate:
  - by clinical category;
  - by age group;
  - by sex.
- Number of requests for laboratory tests to identify WNV infection:
  - according to the population of the regions.

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1 Date the case was reported to the Direction régionale de santé publique [regional public health department].

2 Data from the MED-ÉCHO database and the death registry of the Institut de la statistique du Québec [Québec bureau of statistics] is used to complement the tests related to disease burden. As well, an assessment project regarding this matter is in progress in order to assess the disease burden at 3, 6 and 12 months post-diagnosis.

2.1.2 METHODOLOGY

Case reporting

WNV infection has been a notifiable disease [maladie à déclaration obligatoire - MADO] in Québec since 2003. Physicians and microbiology laboratories must report all WNV-positive cases to the Direction de santé publique [public health department] (DSP) and must submit serum specimens from the patients for confirmation of WNV infection to the Laboratoire de santé publique du Québec (LSPQ).

The DSP concerned carries out an epidemiological investigation for all of the reported cases in order to document the infection, determine the likely place of acquisition and collect specific clinical and social-demographic information concerning the patient.

In addition, as part of their prevention and control strategies to reduce the risks related to transfusion, Héma-Québec has been carrying out, since 2003, a systematic WNV screening of blood donors during the West Nile virus season, i.e., from June 1 to November 30 each year. Blood donors who test positive for WNV are for the most part asymptomatic (otherwise, they wouldn't have been allowed to give blood). The test used (a gene amplification test RT-PCR) detects WNV RNA in a person in the acute phase of primary infection. All positive donors are reported to the DSP concerned that is responsible for the epidemiological investigation. Héma-Québec also performed a screening test between December 1 and May 31, 2013 on donors who had travelled outside the country during the 56 days before they gave blood. As in 2012, and for each region, the donated blood was first tested by groups of six. If there was a positive group, each of the blood donations in the group was then re-tested individually and all of the blood donations from the same region were tested individually for a period of one week. If at the end of the week no blood donations were positive, testing the blood donations by groups of six was resumed.

Case definition

To standardize the diagnosis of WNV infection, a case definition was established by the Ministère de la Santé et des Services sociaux (MSSS) [Québec's ministry of health and social services]. This definition includes three categories according to the clinical manifestations and the laboratory results: WNV neurological syndrome, WNV non-neurological syndrome, and WNV asymptomatic infection, all three subdivided into confirmed cases and probable cases (Appendix 1).

Specimen testing at the LSPQ

The LSPQ uses a test that detects WNV IgM antibodies in the serum using an enzyme immunoassay (EIA). WNV IgM antibodies may persist in patients for more than one year and a positive result can reflect prior exposure to the virus. The positive IgM specimens are then tested for the presence of IgG.

The specimens found to be positive for IgM and IgG are sent to the National Microbiology Laboratory in Winnipeg to detect the presence of WNV-neutralizing antibodies by PRNT (plaque reduction neutralization test). In 2013, the confirmatory criterion for the diagnosis of WNV infection for the first case in any region was the presence of neutralizing antibodies. Note that the case definition of WNV infection was reviewed by the Groupe d'experts scientifiques sur le VNO [WNV scientific expert panel] at the request of the MSSS and this criterion will be modified.

2.2 Entomological surveillance

The purpose of entomological surveillance is to document the presence of the vector and of the virus in a given geographic sector, in order to estimate the risk of transmission to humans. It also allows the communication activities aimed at the general public and at health care professionals to be adjusted in order to reduce the risk. This surveillance can also contribute to the assessment of the WNV transmission risk, allowing sectors where preventive interventions are necessary to be identified.

The presence of a group of positive mosquitoes indicates a localized area of a potential active WNV transmission, with a risk of transmission to humans, depending on the species present. In Québec, the primary vectors of WNV are mosquitoes of the genus *Culex*, i.e., the species *Culex pipiens and Culex restuans*. Therefore, in 2013, viral detection mainly targeted these two species.

2.2.1 OBJECTIVES OF ENTOMOLOGICAL SURVEILLANCE

- To estimate the abundance of the species of mosquitoes by region and by trapping week.
- To document the presence of the virus in the populations of mosquitoes for which surveillance is conducted by region and by trapping week.

Entomological surveillance indicators

A main indicator (the *Culex pipiens/restuans* vector index) and three associated indicators come from the analysis of entomological surveillance data, namely the number of pools of WNV-positive mosquitoes, the abundance, and the infection rate of *Culex pipiens/restuans*. The indicators are defined and the calculation methods are presented in Appendix 3.

- Number of pools of positive mosquitoes:
  - by CDC trapping week
  - by region
  - by species.
- Abundance of the species *Culex pipiens/restuans*:
  - by CDC trapping week.
- *Culex pipiens/restuans* infection rate:
  - by CDC trapping week.
- *Culex pipiens/restuans* vector index:
  - by CDC trapping week.

2.2.2 METHODOLOGY

Mosquito traps and collection methods

Between July and October 2013, active mosquito surveillance was conducted in 63 fixed traps spread over areas where the application of larvicide was planned and in the surrounding areas, as well as in some places where cases of WNV infection had been documented between 2002 and 2012[13]. Each mosquito trap consisted in a CDC Miniature Light Trap containing a UV lamp and dry ice (CO_2), which attracts female mosquitoes that are looking for a blood meal. All of the specimens

collected were classified and counted by species or group of species. According to the list of species of mosquitoes that were a priority for viral detection and taking into account a quota of admissible pools per sample, a selection of pools was made composed of at most 50 specimens of a same species coming from the same sample, to be used for viral detection. Each sample came from one standardized trapping night in a mosquito trap and a specific date. In the case of large samples (e.g., 1,000 mosquitoes), subsampling was performed by dividing the sample into two, three, four or more samples. Then only one portion was identified and the subsampling ratio was recorded in order to calculate the numbers in the whole sample. The pools selected were subjected to WNV detection by real-time reverse transcription polymerase chain reaction assay (RT-PCR) conducted by the LSPQ.

2.2.3 WEATHER MONITORING

Weather conditions, in particular a high temperature, influence the development of mosquitoes and WNV amplification in mosquitoes and consequently, the risk of transmission to humans[14-16]. In a study carried out in California, the authors established beyond a threshold of 14°C, WNV can amplify in mosquitoes[17]. The extrinsic incubation period for WNV in *Culex tarsalis* mosquitoes (the main vector in the region studied), i.e., the median time between a meal of infected blood and the female's capacity to transmit the virus, was estimated at 109 degree-days above 14°C in the last 14 days[17]. Weather monitoring was used in Québec on an exploratory basis since the methodology used has not been validated specifically for Québec (different species of mosquitoes and climate).

Weather monitoring indicators

- Daily sum of degree-days above the theoretical threshold for viral amplification in mosquitoes (14°C) for the 14 preceding days at the McTavish weather station in Montréal.

2.3 Animal surveillance

2.3.1 BIRD SURVEILLANCE

Birds are the main reservoir for WNV. They also play the role of virus amplifier. Most birds survive the infection and develop permanent immunity. Some bird species, such as corvids (including crows, ravens, magpies and jays), are more sensitive to WNV infection and have a high mortality rate. Certain bird species can transmit the virus to mosquitoes during several days of high and sustained viremia.

Passive surveillance of wild birds is conducted by the Centre québécois sur la santé des animaux sauvages (CQSAS) [Québec wild animal health centre] as part of bird flu surveillance.[3]

Surveillance of wild birds is not a good geographic indicator of WNV activity, since most of these birds travel long distances once infected. However, it allows us to identify the various species of birds affected by WNV and to detect the presence of species newly affected by WNV.

[3] Bird carcasses, including corvids (American crow, blue jay, common raven) are reported by individuals to a central telephone line managed by MAPAQ [Québec's ministry of agriculture, fisheries and food] (1-877-644-4545). When a predetermined number of carcasses are found together (this criterion varies based on surveillance needs; it is currently five carcasses), for example, at the same site on the same day, a wildlife officer travels to the site and picks up the carcasses which are then sent to the CQSAS for a necropsy. If WNV infection is suspected (based on the results of the necropsy), tissue specimens are submitted for nucleic acid detection of WNV by RT-PCR technique (reverse transcription polymerase chain reaction assay) at the Complexe de pathologie et d'épidémiosurveillance du Québec [Québec pathology and epidemiological surveillance complex]. Lastly, the data is compiled by the CQSAS[13].

Objectives of bird surveillance

The purpose of bird surveillance is to gather information on WNV activity in the different regions of Québec.

Bird surveillance indicators

- Number of WNV-positive birds:
  - by species
  - by region
  - by week the bird was discovered.

2.3.2 SURVEILLANCE OF OTHER ANIMALS

Passive surveillance is carried out of domestic and wild animals. The Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec [ministry of agriculture, fisheries and food] (MAPAQ)[4] carries out passive surveillance of domestic animals (primarily horses). Since May 2003, WNV has been an immediately notifiable disease for domestic animals under a federal law. Veterinarians must report all suspicious or confirmed cases of WNV infection to MAPAQ. They are also encouraged to submit samples for WNV infection diagnosis to MAPAQ laboratories. A serological test or a PCR are used to diagnosis WNV infection.

Horses are susceptible to developing encephalitis related to WNV infection. A small number of other mammals are affected by WNV, in particular llamas, alpacas, dogs and cats.

The CQSAS also carries out passive surveillance of wild animals. Squirrels have tested positive for WNV in certain regions.

Objectives of animal surveillance

The purpose of animal surveillance is to identify the regions where there is active WNV transmission in mammals.

Animal surveillance indicators

- Number of WNV-positive animals:
  - by species
  - by region
  - by week corresponding to clinical symptom onset date, date the dead animal is discovered, or date of diagnosis.

[4] MAPAQ receives reports as part of its *Programme de surveillance de l'encéphalite équine de l'Est (EEE) et du VNO* [eastern equine encephalitis and West Nile virus surveillance program], while the Canadian Food Inspection Agency (CFIA) receives reports concerning WNV in connection with immediately notifiable diseases pursuant to the *Health of Animals Regulations*.

3 *Système intégré de données de vigie sanitaire* (SIDVS-VNO) [integrated health monitoring data system for WNV]

At the request of the Ministère de la Santé et des Services sociaux (MSSS), the Institut national de santé publique du Québec (INSPQ) developed, in 2003, an information system which allowed for real time presentation of human, entomological, and animal WNV surveillance data. The *système intégré de données de vigie sanitaire VNO* (SIDVS-VNO) also allows us to generate a cartographic representation of all of the data.

Human cases of WNV infection are reported directly to the SIDVS-VNO web site by the DSPs and the LSPQ. Asymptomatic cases identified by Héma-Québec are reported to the DSP of the patient's area of residence. The results of the epidemiological investigations carried out by the DSPs for reported cases are also entered into the SIDVS-VNO. Thus, the SIDVS-VNO provides information on, among other things, clinical presentation (neurological, non-neurological or asymptomatic), serological status (confirmed or probable), symptom onset date, date the episode started (date reported), complications (hospitalization, duration of hospital stay, stay in intensive care, death), the patient's condition on discharge from the hospital and certain sociodemographic characteristics of the patient, including age, sex and area of residence.

For animal surveillance, cases confirmed WNV-positive by MAPAQ and CQSAS are entered into the SIDVS-VNO by the system administrator (with the MSSS).

4 Deliverables

4.1 Integrated WNV surveillance bulletins

2013

- Produced weekly during the 2013 season.
- Schedule: Friday afternoons, from the end of July to the end of September (or according to how the season was progressing).
- Human, entomological and animal surveillance and weather monitoring in Québec for the preceding week; summary of the situation in the rest of Canada and the United States.
- Five to six pages.
- Posted on the INSPQ's website at: http://www.inspq.qc.ca/dossiers/zoonoses/vno.asp#bulletin_vno.

2014

- Two bulletins during the 2014 season.
- Schedule: No. 1 at the end of July and No. 2 at the end of September.
- Human, entomological and animal surveillance and weather monitoring in Québec; summary of the situation in the rest of Canada and the United States.
- Five to six pages.
  Posted on the INSPQ's website at: http://www.inspq.qc.ca/dossiers/zoonoses.

4.2 Annual report on integrated WNV infection surveillance in Québec

- Annual.
- Schedule: June 2014 (for the 2013 season) and March-April 2015 (for the 2014 season).
- Human, entomological and animal surveillance and weather monitoring in Québec for the season; summary of the situation in the rest of Canada and the United States.

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Appendix 1

Excerpt from the document "Surveillance des maladies à déclaration obligatoire au Québec – Maladies d'origine infectieuse définitions nosologiques" [notifiable disease surveillance in Québec – infectious diseases – case definitions]

Source: Ministère de la Santé de des Services sociaux

Excerpt from the document "Surveillance des maladies à déclaration obligatoire au Québec – Maladies d'origine infectieuse définitions nosologiques" [notifiable disease surveillance in Québec – infectious diseases – case definitions]

WEST NILE VIRUS (WNV) INFECTION

WNV Neurological Syndrome

Confirmed case

Presence of the three following conditions:

1) Fever

AND

2) One of the following clinical manifestations:

- 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, Guillain-Barré-like syndrome)

OR

- movement disorders (e.g. tremors or myoclonus)

OR

- Parkinsonism or Parkinson's-like conditions (e.g., cogwheel rigidity, bradykinesia, postural instability)

OR

- other neurological syndromes

AND

3) At least one of the following seven laboratory results:

- isolation of the WNV from, or demonstration of WNV-specific genomic sequences in an appropriate clinical specimen

OR

- demonstration of a significant increase in WNV-neutralizing antibody titers between acute and convalescent sera, or CSF using a plaque-reduction serum neutralization (PRN[5]) or other kind of neutralization assay

OR

- detection of WNV antigens in tissue

OR

[5] A confirmatory PRN result or other kind of neutralization assay is not necessary if the case has a history of exposure in Québec and at least one case acquired in Québec has already been confirmed during the same season.

- detection of WNV IgM antibodies in a single serum sample or CSF sample using an EIA, confirmed by a PRN[6]

OR

- detection of a significant increase in the flavivirus antibody titer between acute and convalescent sera by a haemagglutination inhibition (HI) test, and detection of WNV specific antibodies using a PRN[6] (acute or convalescent serum sample)

OR

- demonstration of a seroconversion using a WNV IgG EIA and detection of WNV-neutralizing antibodies using a PRN[6] (convalescent serum sample)

OR

- demonstration of WNV-specific genomic sequences using an appropriate gene amplification technique by screening on donor blood by Héma-Québec.

Probable case

Presence of the three following conditions:

1) Fever

AND

2) One of the following clinical manifestations:

- 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)

OR

- movement disorders (e.g., tremors or myoclonus)

OR

- Parkinsonism or Parkinson's-like conditions (e.g., cogwheel rigidity, bradykinesia, postural instability)

OR

- other neurological syndromes

AND

3) At least one of the following five laboratory results:

- detection of WNV IgM antibodies in a single serum sample or CSF sample using an EIA, without confirmation by a PRN-type test

OR

- detection of a significant increase in the flavivirus antibody titer between acute and convalescent sera by an HI test without a confirmatory test (e.g., PRN)

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[6] A confirmatory PRN result or other kind of neutralization assay is not necessary if the case has a history of exposure in Québec and at least one case acquired in Québec has already been confirmed during the same season.

OR

- demonstration of a seroconversion using a WNV IgG EIA without a PRN-type confirmatory test

OR

- detection of WNV IgG antibodies in a single serum sample using an HI test or an EIA, confirmed by a PRN[7]

OR

- demonstration of Japanese encephalitis serocomplex-specific genomic sequences by an appropriate gene amplification technique by screening on donor blood by blood operators in Canada.

WNV Non-Neurological Syndrome

Confirmed case

Presence of the two following conditions:

1) At least two of the following clinical manifestations:
   - fever
   - myalgia
   - arthralgia
   - headache
   - fatigue
   - lymphadenopathy
   - maculopapular rash

   AND

2) At least one of the following seven laboratory results:
   - isolation of the WNV from, or demonstration of WNV-specific genomic sequences in an appropriate clinical specimen

   OR

   - demonstration of a significant increase in WNV-neutralizing antibody titers between acute and convalescent sera, or CSF using a plaque-reduction serum neutralization (PRN[7]) or other kind of neutralization assay

   OR

   - detection of WNV antigens in tissue

   OR

   - detection of WNV IgM antibodies in a single serum sample or CSF sample using an EIA, confirmed by a PRN[8]

   OR

[7] A confirmatory PRN result or other kind of neutralization assay is not necessary if the case has a history of exposure in Québec and at least one case acquired in Québec has already been confirmed during the same season.

[8] A confirmatory PRN result or other kind of neutralization assay is not necessary if the case has a history of exposure in Québec and at least one case acquired in Québec has already been confirmed during the same season.

- detection of a significant increase in the flavivirus antibody titer between acute and convalescent sera by a haemagglutination inhibition (HI) test, and detection of WNV specific antibodies using a PRN[8] (acute or convalescent serum sample)

OR

- demonstration of a seroconversion using a WNV IgG EIA and detection of WNV-neutralizing antibodies using a PRN[8] (convalescent serum sample)

OR

- demonstration of WNV-specific genomic sequences using an appropriate gene amplification technique by screening on donor blood by Héma-Québec.

Probable case

Presence of the two following conditions:

1) At least two of the following clinical manifestations:

- fever
- myalgia
- arthralgia
- headache
- fatigue
- lymphadenopathy
- maculopapular rash

AND

2) At least one of the following five laboratory results:

- detection of WNV IgM antibodies in a single serum sample or CSF sample using an EIA, without a PRN-type confirmatory test

OR

- detection of a significant increase in the flavivirus antibody titer between acute and convalescent sera by an HI test without a confirmatory test (e.g., PRN)

OR

- demonstration of a seroconversion using a WNV IgG EIA without a PRN-type confirmatory test

OR

- detection of WNV IgG antibodies in a single serum sample using an HI test or an EIA, confirmed by a PRN[9]

OR

- demonstration of Japanese encephalitis serocomplex-specific genomic sequences by an appropriate gene amplification technique by screening on donor blood by blood operators in Canada.

[9] A confirmatory PRN result or other kind of neutralization assay is not necessary if the case has a history of exposure in Québec and at least one case acquired in Québec has already been confirmed during the same season.

WNV Asymptomatic Infection

Confirmed case

In the absence of clinical manifestations, the presence of at least one of the following seven laboratory results:

- Isolation of the WNV from, or demonstration of WNV-specific genomic sequences in an appropriate clinical specimen

OR

- Demonstration of a significant increase in WNV-neutralizing antibody titers between acute and convalescent sera, or CSF using a plaque-reduction serum neutralization (PRN[9]) or other kind of neutralization assay

OR

- Detection of WNV antigens in tissue

OR

- Detection of WNV IgM antibodies in a single serum sample or CSF sample using an EIA, confirmed by a PRN[9]

OR

- Detection of a significant increase in the flavivirus antibody titer between acute and convalescent sera by a haemagglutination inhibition (HI) test, and detection of WNV specific antibodies using a PRN[9] (acute or convalescent serum sample)

OR

- Demonstration of a seroconversion using a WNV IgG EIA and detection of WNV-neutralizing antibodies using a PRN[9] (convalescent serum sample)

OR

- Demonstration of WNV-specific genomic sequences using an appropriate gene amplification technique by screening on donor blood by Héma-Québec.

Probable case

In the absence of clinical manifestations, the presence of at least one of the following five laboratory results:

- Detection of WNV IgM antibodies in a single serum sample or CSF sample using an EIA, without a PRN-type confirmatory test

OR

- Detection of a significant increase in the flavivirus antibody titer between acute and convalescent sera by an HI test without a confirmatory test (e.g., PRN)

OR

- Demonstration of a seroconversion using a WNV IgG EIA without a PRN-type confirmatory test

OR

- Detection of WNV IgG antibodies in a single serum sample using an HI test or an EIA, confirmed by a PRN[10]

OR

- Demonstration of Japanese encephalitis serocomplex-specific genomic sequences by an appropriate gene amplification technique by screening on donor blood by Blood Operators in Canada.

[10] A confirmatory PRN result or other kind of neutralization assay is not necessary if the case has a history of exposure in Québec and at least one case acquired in Québec has already been confirmed during the same season.

Appendix 2

Human WNV infection surveillance indicator sheet

WEST NILE VIRUS INFECTION INCIDENCE RATE (*SYSTÈME DE SURVEILLANCE INTÉGRÉE DE DONNÉES DE VIGIE SANITAIRE DU VIRUS DU NIL OCCIDENTAL* – SIDVS-VNO) [INTEGRATED HEALTH MONITORING DATA SYSTEM FOR WNV]

JOINT SURVEILLANCE PLAN LINE NO.: 443

Definition

Ratio of the number of cases of West Nile virus infection, over a given period, to the population for the same period.

The *Système de surveillance intégrée de données de vigie sanitaire du virus du Nil occidental* (SIDVS-VNO) was implemented in 2002 at the Institut national de santé publique du Québec (INSPQ) following the appearance of the virus in Québec and after a government intervention plan was set up (Government of Québec, 2002). The system integrates human surveillance data (2003 to present), animal surveillance data (2003 to 2005 and 2013) and entomological surveillance data (2003 to 2006 and 2013).

The West Nile virus (WNV) belongs to the Flaviviridae family. It was first isolated in the West Nile district of northern Uganda in 1937. It appeared in North America for the first time in 1999 in the New York City area and then rapidly spread throughout the northern region of the continent. In 2002, the first cases of bird and human infection were reported in Québec.

WNV infection is transmitted to humans by a bite from an infected mosquito, in particular mosquitoes from the genus *Culex*. Birds are WNV reservoirs and act as WNV amplifiers (Koné et al., 2006). Passerine birds (corvids, house sparrows, etc.) develop high viremia and have been particularly affected by high mortality in the past. Humans and horses are accidental hosts.

Calculation method

$$\frac{\text{Number of new cases of West Nile virus infection, for a given period}}{\text{Population for the same period}} \times 100{,}000$$

Data sources

Numerator

- Système de surveillance intégré de données de vigie sanitaire VNO, Institut national de santé publique du Québec.

Denominator

- Estimates and demographic projections, Institut de la statistique du Québec.

Variables being crossed and categories

Period

- Year (calendar)[11] (starting 1990)
- Month
- Period (fiscal or CDC)
- CDC week of acquisition or related to the episode
- Day (for monitoring).

Territory

- Area of residence:
  - all of Québec
  - 18 health regions
  - local service networks [*réseaux locaux de services*] (RLS) and the name of the health and social services centre [*centre de santé et de services sociaux*] (CSSS) corresponding to each local service network
  - territories of the local community service centres [*centre local de service communautaire*] (CLSCs)
  - service points of the local community service centres (unmerged CLSC)
- Region where the virus was probably acquired.

Age

- < 1 year, 1-4 years, 5-9 years, 10-14 years, 85-90 years, 90 years and over
- Five-year age group (up to 90 years and over)
- Each age (for monitoring)
- All ages.

Sex

- Total
- Male, female.

Associated measurement(s)

- Number of new cases of West Nile virus infection[12]
- Number of female mosquitoes (abundance) for certain species
- Number of WNV-positive animals

[11] The mean annual rates are calculated for periods of 1 year, 2 years, 3 years, 4 years and 5 years.

[12] If the number is higher than the alert threshold, a warning is posted.

Associated indicator(s)

- Lethality
- Number of deaths by serological status (Héma-Québec – reported, Héma-Québec – confirmed, serologically suspicious, probable, confirmed)
- Number of cases by serological status (Héma-Québec – reported, Héma-Québec – confirmed, serologically suspicious, probable, confirmed, invalidated)
- Number of cases by clinical category (asymptomatic, WNV infection (non-neurological), WNV infection (neurological), other, unknown, invalidated)

Limitations in interpretation

Case data is regularly entered into a central database, the SIDVS-VNO database, separately by each of the 18 Directions régionales de santé publique (the DSPs) and by the LSPQ. The LSPQ is generally the first to enter the data in the system, except for cases from Héma-Québec that are reported to the DSP of the donor's residence. However, the DSPs and the LSPQ may enter data simultaneously. The system administrator checks the cases to eliminate duplicates.

WNV surveillance is primarily based on a passive system and its sensitivity can be low. Approximately 80% of people infected present no symptoms and the remaining 20% have moderate symptoms (West Nile fever). Only one person in 150 will develop neuroinvasive disease (Koné et al., 2006). Passive surveillance therefore tends to underestimate the prevalence of WNV infection.

Bibliographic references

Government of Québec. Plan d'intervention gouvernementale 2013-2015 pour la protection de la population contre le virus du Nil occidental.

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Indicator sheet written by

- Annie Doucet, Direction des risques biologiques et de la santé au travail, INSPQ
- Anne Fortin, Direction des risques biologiques et de la santé au travail, INSPQ
- Louise Lambert, Direction de la santé publique, ASSS de la Montérégie
- François Milord, Direction des risques biologiques et de la santé au travail, INSPQ

People consulted

- Suzanne Gingras, Infocentre, INSPQ
- Mathieu Langlois, Infocentre, INSPQ
- Germain Lebel, Direction de la santé environnementale et de la toxicologie, INSPQ
- Anne-Marie Lowe, Direction des risques biologiques et de la santé au travail, INSPQ

Indicator sheet last updated

- October 30, 2013

Appendix 3

Entomological surveillance indicator sheet

WNV-INFECTED MOSQUITO VECTOR INDEX

Definition

Estimated number of female mosquitoes of a species infected by West Nile virus by trapping effort.

Context

The West Nile virus (WNV) belongs to the Flaviviridae family. It was first isolated in the West Nile district of Uganda in 1937. It appeared in North America in for the first time in 1999 in the New York City area and then rapidly spread throughout northern region of the continent. In 2002, the first cases of bird and human infection were reported in Québec.

WNV infection is transmitted to humans by the bite of an infected mosquito, in particular mosquitoes from the genus *Culex*. Birds are WNV reservoirs and act as WNV amplifiers (Koné et al., 2006). Passerine birds (corvids, house sparrows, etc.) develop high viremia and have been particularly affected by high mortality in the past. Humans and horses are accidental hosts.

In response to the appearance of WNV in Québec in the summer of 2002, the Government of Québec adopted a government intervention plan to protect public health against WNV in 2003. This intervention plan was updated and was continued in 2004 and 2005. The plan provided for, in particular, the implementation of an integrated health monitoring data system for the WNV (SIDVS-VNO). The Institut national de santé publique du Québec was mandated to ensure the implementation of the SIDVS-VNO. Since the number of human cases of WNV infection had decreased, the activities provided in the intervention plan were stopped, in particular entomological surveillance in 2007.

Following an upsurge in human cases of WNV infection in 2011 and 2012, the 2013-2015 government intervention plan to protect public health against WNV was adopted in 2013. This plan provides for, in particular, the resumption of entomological surveillance, the application of larvicide and the updating of the SIDVS-VNO.

Entomological surveillance

Entomological surveillance of WNV is an active method of surveillance. Entomological surveillance is done by setting up CDC Miniature Light Trap mosquito traps comprised of a trap containing a UV lamp and dry ice (CO_2) that attracts female mosquitoes looking for a blood meal. In 2013, 63 mosquito traps were in operation in six regions in Québec. Trapping is done using a standardized protocol: the traps are set up in the afternoon and the mosquitoes are trapped during the night, then the sample is collected the following morning. The specimens are identified by species or group of species (depending on the condition of the specimens) using a binocular microscope and counted. Pools of a maximum of 50 specimens of a same species are selected from the same sample to be used for viral detection, according to a list of priority species of mosquitoes for viral detection and taking into account a quota of admissible pools per sample. In the case of very large samples (e.g., 1,000 mosquitoes) subsampling may be done, by dividing the sample into two, three, four, or more equal parts. A single part is then identified and the subsampling ratio is recorded in order to calculate the count for the whole sample. The pools selected are submitted to WNV detection by RT-PCR (real time reverse transcription polymerase chain reaction) performed at the Laboratoire de santé publique du Québec (LSPQ).

Culex pipiens/restuans mosquitoes are given priority for viral detection, as they are the primary vector for birds (enzootic cycle) and for humans. The quota was arbitrarily set at three pools selected per sample (2013) to minimize testing costs.

Calculation method

To calculate the vector index, the abundance and infection rate of adult female mosquitoes must first be calculated.

Abundance

The number of female mosquitoes of the various species in a sample expresses the abundance of the number of female mosquitoes (A). When the entire sample of mosquitoes is identified, the abundance is equal to the crude count. When the sample of mosquitoes is too large, subsampling is performed; the abundance (A) is then estimated by the calculation:

A = [crude count] x [subsampling ratio]

Infection rate

The WNV infection rate is calculated **for a species or a group of species** (e.g., *Culex pipiens/restuans*). The WNV infection rate can be estimated in two ways: the minimum infection rate or MIR (taux d'infection minimum or TIM in French) and the maximum likelihood estimation infection rate or MLE-IR (taux d'infection estimé par Maximum Likelihood or TI-EML or maximum de vraisemblance in French). The calculation of the MIR is based on the assumption that there is a single infected mosquito in a positive pool. As the infection rates are generally low, around 0.1%, this assumption is true most of the time, except when the infection rate is high or when pools are large. We must specify that the MIR is calculated using the number of mosquitoes actually tested by the laboratory rather than the abundance.

The infection rate may also be calculated for a pool made up of different samples (e.g., from several traps, or for one month, or for an entire summer season). In this case, the average number of mosquitoes tested must be used. Since the number of mosquitoes tested per trap per week does not respect a normal distribution, it is common practice to use the geometric mean rather than the arithmetic mean of the number of mosquitoes tested. Therefore, this aspect must be considered in the calculation of the vector index.

The MIR formula is:

MIR = [number of positive pools] / [average number of mosquitoes tested] X 1,000.

The maximum likelihood estimation infection rate (MLE-IR) is the most likely P-value (proportion) (according to a binomial distribution) of infected mosquitoes to obtain n positive pools among N pools tested of a variable size. The MLE-IR is calculated using an Excel add-in developed by the CDC that performs maximum likelihood iteration and produces the estimated P-value and its confidence interval (http://www.cdc.gov/ncidod/dvbid/westnile/software.htm). Note that an English version of Excel is required to use this add-in.

Vector index

The vector index (VI) is obtained by multiplying the mean number of female mosquitoes trapped by the infection rate of the same females, for one species and for one sample (one trapping night, one site) or for several samples. For the infection rate, either the minimum infection rate (MIR) or the infection rate calculated using the maximum likelihood method (MLE-IR) may be used. The formula is:

VI = A x (MIR/1,000)

or using the maximum likelihood method (MLE-IR):

VI = A x (MLE-IR/1,000)
VI-ll = A x (MLE-IR-ll/1,000)
VI-ul = A x (MLE-IR-ul/1,000)

where:

A = number of females trapped (mean abundance)
MLE-IR-ll = lower limit of the 95% confidence interval of the MLE-IR
MLE-IR-ul = upper limit of the 95% confidence interval of the MLE-IR
VI-ll = lower limit of the 95% confidence interval of the VI
VI-ul = upper limit of the 95% confidence interval of the VI

Detailed examples of calculating the infection rate and the vector index are provided in the "*Guide for Epidemiologic Analysis of West Nile Virus Mosquito Trap Data in Dallas County"*.

Data sources

- Système intégré de données de vigie sanitaire VNO, Institut national de santé publique du Québec

Variables being crossed and categories

Territory

- Administrative division
- Municipalities
- Regions
- Trap

Period

- Year
- Month
- Epidemiological week (CDC week)

Associated indicators

- Abundance of female mosquitoes
- Infection rate of female mosquitoes

Limitations in interpretation

Amount of time before specimens become available for WNV detection

The mosquitoes are always collected the day after the mosquito traps were set up, because the trapping effort is standardized and is done at night. It takes 24 hours for the mosquitoes to arrive at the laboratory and the tests are done within the following 24 hours. Therefore, it takes a minimum of two to four days after the mosquitoes are collected to obtain the identification data for the mosquitoes and the pools ready for viral detection.

Amount of time for obtaining WNV detection results

The pools selected for WNV detection must be sent from the identification laboratory to the LSPQ. The data on mosquito infection rates is therefore available from seven to nine days after the date the mosquitoes were collected.

Representativeness of the mosquito traps

Mosquito traps are placed in locations representative of a geographical area that is relatively homogenous in terms of environment (landscape, infrastructure, natural environments, larval habitats of mosquitoes), demographics (density of the human population) or operations (treated or untreated area). Multiple criteria must be considered in choosing where to place the trap at a sampling station, in particular the trapping performance (absence of competition from light, shelter from the wind, etc.), safety (from theft, vandalism, dry ice danger, etc.) and access (permission from the landowners). Caution must be exercised when extrapolating data (ad hoc) from a trap in the neighbouring sector.

Accuracy of infection rate estimates

The MIR is based on the assumption that a pool of positive mosquitoes contains only one infected mosquito. This can be invalid when the infection rates are high, for example in *Culex pipiens/restuans* mosquitoes during the WNV epidemics.

The infection rate can also be estimated using the maximum likelihood method that calculates the infection rate without resorting to the assumption used in the MIR calculations. The accuracy of the MLE-IR and its confidence intervals is based on detection sensitivity criteria. In the presence of a positive sample, the optimal conditions would consist of having several positive pools of different sizes (e.g., 5, 15, 30, 50 mosquitoes) and at least one negative pool. The MLE-IR is mainly useful in outbreaks of WNV, in active periods, when there is more than one infected mosquito per species, per trap and per night.

Relevance of the indicator

Since the development of the concept of vector index as an indicator for monitoring WNV in the early 2000s, its usefulness has been demonstrated in numerous programs in Canada and the USA.

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Indicator sheet last updated

- March 2014

Appendix 4

Animal surveillance indicator sheet

NUMBER OF WEST NILE VIRUS-POSITIVE ANIMALS (SYSTÈME DE SURVEILLANCE INTÉGRÉE DE DONNÉES DE VIGIE SANITAIRE DU VIRUS DU NIL OCCIDENTAL – SIDVS-VNO)

JOINT SURVEILLANCE PLAN LINE NO.: 443

Definition

Number of new cases of West Nile virus infection in animals over a given period.

The système de surveillance intégrée de données de vigie sanitaire du virus du Nil occidental (SIDVS-VNO) was implemented in 2002 at the Institut national de santé publique du Québec (INSPQ) following the apparition of the virus in Québec and after a government intervention plan was set up (Government of Québec, 2002). The system integrates data on human surveillance (2003 to present), animal surveillance (2003 to 2005 and 2013) and entomological surveillance (2003 to 2006 and 2013).

The West Nile virus (WNV) belongs to the Flaviviridae family. It was first isolated in the West Nile district of northern Uganda in 1937. It appeared in North America for the first time in 1999 in the New York City area and then rapidly spread throughout the northern region of the continent. In 2002, the first cases of bird and human infection were reported in Québec.WNV infection is transmitted to humans by the bite of an infected mosquito, in particular those of the genus *Culex*. Birds are the reservoirs for WNV and play the role of amplifiers of the virus (Koné et al., 2006). Passerine birds (corvids, house sparrows, etc.) develop high viremia and have been particularly affected by high mortality in the past. Humans and horses are accidental hosts.

Domestic animals, primarily horses, are the subject of heightened passive surveillance. This surveillance allows information to be gathered on the activity of the virus in various regions of Québec compared to areas at risk. The presence of an infected animal in a region, when the animal has not travelled, confirms active WNV transmission in that area. Veterinarians are asked to report all suspicious or confirmed cases of WNV infection to MAPAQ. They are now encouraged to submit samples for WNV diagnosis thanks to free tests. Horses benefit particularly from this surveillance program. WNV infection has been an immediately notifiable disease in animals since May 2003, under a federal law. Positive cases reported to MAPAQ are entered into the système intégré de données de vigie sanitaire (SIDVS-VNO).

Wild birds are also the subject of passive surveillance. The presence of a WNV-positive bird is not necessarily an indicator of active transmission in the region where the bird was found, because it may have travelled. However, the occurrence of cases in birds generally precedes the reporting of human cases by a few weeks.

Calculation method

Number of new cases of West Nile virus infection in animals, for a given period.

Data sources

Ministère de l'Agriculture, des Pêcheries et de l'Alimentation (MAPAQ), Centre québécois sur la santé des animaux sauvages (CQSAS), Système de surveillance intégré de données de vigie sanitaire VNO, Institut national de santé publique du Québec.

Variables being crossed and categories

Period

- Year (calendar)[13] (as of 1990)
- Month
- Period (fiscal or CDC)
- CDC week of discovery or of onset of clinical signs
- Day (for monitoring)

Territory

- Place of residence or of discovery:
  - all of Québec
  - 18 health regions
  - local service networks (RLS) and the name of the health and social services centre (CSSS) corresponding to each local service network
  - territories of the local community service centres (CLSCs)
  - service points of local community service centres (unmerged CLSCs)
- Region where the virus was probably acquired

Animal species

- Equine
- Bovine
- Avian
- Camelidae
- Others

Associated measurement(s)

- West Nile virus infection incidence rates.[14]

Limitations in interpretation

The case data is entered into a central database, the SIDVS-VNO database, on a regular basis by the Ministère de la Santé et des Services sociaux, after they have received the data from MAPAQ and from CQSAS. There may be a delay in transmission of the data to the MSSS.

The surveillance of WNV in horses depends on the cases being reported by veterinarians. Furthermore, some horses are vaccinated against WNV. The bird surveillance data comes from the avian flu surveillance program in wild birds. The surveillance program depends on citizens reporting dead birds and targets species that are particularly sensitive to influenza. These species are not exactly the same as the species sensitive to WNV. The purpose of the analyses of the birds collected

[13] The mean annual rates are calculated for periods of 1 year, 2 years, 3 years, 4 years and 5 years.

[14] If the number is higher than the alert threshold, a warning is displayed.

as part of this program is to identify the cause of death in the birds, rather than WNV surveillance. Thus, there can be delays between the time the bird is discovered at a given place and the time the results are obtained.

Bibliographic references

Government of Québec. Plan d'intervention gouvernementale 2013-2015 pour la protection de la population contre le virus du Nil occidental.

KONÉ, Philippe, Louise LAMBERT, François MILORD. *Épidémiologie du virus du Nil occidental en zone rurale au Québec*, [online], INSPQ, 2006, 183 pp. [http://www.inspq.qc.ca/publications/notice.asp?E=p&NumPublication=549] (consulted on September 26, 2011).

Indicator sheet written by:

- Anne-Marie Lowe, Direction des risques biologiques et de la santé au travail, INSPQ.
- Stéphane Lair, Université de Montréal.
- Isabelle Picard, MAPAQ.

People consulted

- Anne Fortin, Direction des risques biologiques et de la santé au travail, INSPQ.

Indicator sheet last updated

- October 30, 2013.
- December 5, 2013.

Publication N°: 1988

Centre d'expertise
et de référence

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Institut national
de santé publique
Québec