

West Nile virus in Canada, 2000-2003:
The impact of an emerging infectious disease

Authors:

Anne M. Arthur

M.Sc. (candidate)

Department of Community Health & Epidemiology

Faculty of Health Sciences

Queen's University

Dick Zoutman, MD, FRCPC

Infection Control Service

Kingston General Hospital

Departments of Pathology & Molecular Medicine,
and of Community Health & Epidemiology

Faculty of Health Sciences

Queen's University

Correspondence to:

Anne M. Arthur

Department of Community Health & Epidemiology

2nd floor Abramsky Hall, Arch Street

Queen's University

Kingston, ON

K7L 3N6

phone: (613) 533-6000 ext. 78014

fax: (613) 533-6686

e-mail: 1ama@qmlink.queensu.ca

Abstract:

West Nile virus is an emerging infectious disease in Canada, first detected in birds and mosquitoes in southern Ontario in 2001. This review article summarizes current information regarding the natural history and epidemiology of West Nile virus both worldwide and in Canada. Surveillance methods and preventive measures are discussed, with an emphasis on what is currently implemented in Canada.

Two years after the first reported human cases of West Nile infection in humans, there is no clear indication of the magnitude of effect on public health in Canada. However, there are practical measures that individuals can use to minimize the risk of infection, especially those at high risk of infection or those more likely to experience more severe health outcomes. This information should be available from family physicians and public health units.

Key words: West Nile virus; epidemiology; mosquito-borne disease

What is West Nile virus?

West Nile virus has recently emerged as a major public health concern in Canada, the United States and Europe with the occurrence of four epidemics in large urban areas since 1996 involving hundreds of human cases of meningoencephalitis and encephalitis¹. These epidemics occurred in southern Romania, the Volga delta in southern Russia, the northeastern United States and in southern Ontario and the prairie provinces of Canada^{2,3}. More cases of severe human disease and deaths have been reported in these four epidemics than in all known past outbreaks of West Nile disease. These were also the first reported epidemics that occurred in large urban areas and to have the common house mosquito, *Culex pipiens*, identified as the major vector. West Nile virus is endemic in much of the world including Africa, the Middle East, western Russia, southwestern Asia, Australia and parts of Europe^{1,4}.

West Nile virus was first detected in the West Nile region of Uganda in 1937 from the blood of an adult woman suffering from febrile illness⁴. Initial research showed that West Nile virus was antigenically similar to two other viruses known to cause encephalitis: St. Louis encephalitis virus and Japanese encephalitis virus. Further research confirmed its similarity to other known flaviviruses and it was placed in an antigenic group with St.

Louis encephalitis, Japanese encephalitis, Murray Valley encephalitis and other flaviviruses⁴.

Due to this similarity to other viruses known to be transmitted to humans by mosquitoes, experimental vector studies were conducted. These showed that several species of mosquito could be experimentally infected and successfully transmit West Nile virus to susceptible animals in the lab. This finding placed West Nile virus among a group of viruses called arboviruses. The defining characteristics of an arbovirus is its ability to be transmitted to susceptible vertebrates, including humans, horses and birds, by hematophagous (blood-sucking) arthropods; including mosquitoes⁵.

What are the disease states and health outcomes associated with West Nile virus?

The majority of individuals who are infected with West Nile virus do not develop symptoms^{6,7}. Following an incubation period between 2 and 14 days, symptomatic individuals with West Nile fever experience a sudden onset acute, nonspecific flu-like illness. The symptoms experienced include: high fever (> 39°C) with chills, malaise, headache, backache, mild rash, eye pain, myalgia and arthralgia. Other non-specific symptoms presented can include nausea, vomiting, diarrhea, loss of appetite, cough swollen lymph glands and sore throat. This acute illness typically lasts for less than a week, with a prolonged period of fatigue following resolution of symptoms⁸.

The more severe form of West Nile disease is that resulting in neurological disease that can be divided into three main categories: West Nile encephalitis, West Nile meningitis and West Nile meningoencephalitis. Encephalitis refers to an inflammation of the brain, meningitis is an inflammation of the meninges around the brain and the spinal cord, and meningoencephalitis refers to inflammation of the brain and the surrounding meninges. A prodromal period of fever, headache and other non-specific symptoms precede onset of neurological disease. The symptoms of encephalitis, meningitis, or meningoencephalitis include headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis. The symptoms may last for up to several weeks and in some cases, permanent neurological effects may occur.

There is no standard treatment for individuals who are admitted to hospital with severe symptoms resulting from West Nile virus infection. However, treatment generally includes provision of intravenous fluids, respiratory support and prevention of secondary infections².

Crude death rates for patients admitted to hospital in recent epidemics of West Nile virus have been between 4 to 14%⁴. Advanced age is the most significant risk factor contributing to death from infection. Other risk factors include: presence of profound weakness, coma, immunosuppression, failure to produce IgM antibodies and co-morbid illness such as hypertension and diabetes mellitus⁴.

Epidemiological surveys following the 1999 outbreak in New York showed that approximately one in five people infected with West Nile virus developed West Nile fever, and about one in 150 developed severe neurologic disease, including encephalitis and meningitis⁷. These values are slightly higher than those seen elsewhere in the world, and are likely reflective of the viral strain now seen in Canada.

Emergence of West Nile virus in Canada

The arrival of West Nile virus in North America was first identified in the summer of 1999 in New York City. The cluster of human cases of encephalitis, along with numerous dead crows and sick birds at the Bronx zoo lead officials to suspect an outbreak of an arboviral disease. The spread of West Nile virus has been rapid. In New York in 1999 there were 62 confirmed cases and seven deaths attributed to West Nile; by 2002 the number of cases in the same area had risen to 3829 and the number of deaths was 225⁴. This rapid proliferation has also been seen in Canada. West Nile virus was first detected in birds and mosquitoes in southern Ontario in the summer of 2001. As of November 27, 2003 West Nile virus has also been documented in Quebec, Manitoba, Saskatchewan, Alberta, New Brunswick and Nova Scotia through dead bird surveillance⁹.

In 2002 the first human cases of West Nile fever were reported in Ontario, Quebec and Alberta. That year, 340 confirmed positive human cases were detected in total and 20 deaths occurred⁹. Virtually all of the cases (94%) and the deaths (90%) occurred in Ontario. Only two cases (both travel related) were detected in Alberta, with the remainder occurring in Quebec.

As of December 2, 2003 the total number of confirmed positive human cases of West Nile virus in Canada during that same year was 463 in total, with 10 deaths attributed to the disease⁹. The majority of the confirmed positive cases (58.3%) occurred in the province of Alberta. Most of the mortality due to West Nile virus infection was seen in Saskatchewan (60%) and identical rates seen in Manitoba (20%) and Ontario (20%). The most current data regarding confirmed cases and mortality due to West Nile virus infection is shown in Table 1.

The cause for the shift in distribution of West Nile virus from Ontario to Alberta is likely due to several factors. It is possible that immunity has developed in either birds, humans or both. Alternatively, the environmental conditions for proliferation of the mosquito vector may have been more favorable with respect to temperature and rainfall in Alberta compared to Ontario. Further studies need to be conducted to determine if the decline of West Nile virus in Ontario is the beginning of a new trend, or if it was merely due to unfavorable weather conditions.

Epidemiology of West Nile virus

So far, West Nile virus has been detected in 37 mosquito species, 157 bird species and 17 mammals other than humans (including horses) and alligators¹⁰. Humans and other mammals are often dead-end, or incidental, hosts for West Nile virus, and typically do not contribute to the transmission cycle by developing viremia and infecting mosquitoes. West Nile virus is maintained in a bird-mosquito-bird cycle, with birds in the Order Passeriformes serving as the primary amplifying hosts^{1;10}. In Canada, the most important passerine birds with respect to West Nile transmission are those of the Family Corvidae which includes crows, sparrows, blue jays, ravens and magpies¹⁰. West Nile virus has been isolated from the fecal and oral secretions of these birds, and bird to bird transmission has been observed in laboratory tests^{1;10}.

Mosquitoes from the genus *Culex*, especially *Culex pipiens*, are the most important vectors involved in West Nile virus transmission in Canada. In Canada, the transmission cycle begins in the spring when mosquitoes first emerge and lasts until early fall when female mosquitoes enter physiologic dormancy and rarely bite¹. Transmission involves

replication of the virus in the female mosquito, which acquires the virus by feeding on the blood of a viremic animal or human^{1;5;11-14}.

In addition to transmission by the bite of an infected mosquito, transmission by other means has also occurred. West Nile fever and associated neurological diseases have been reported to occur after receiving a blood transfusion from a donor infected with West Nile virus². As well, transplanted organs have also been identified as sources of West Nile virus infection². However, these occurrences have been very infrequent and no infection by means other than the bite of an infected mosquito has been reported in Canada. In addition there has been one case report of transmission through breast milk¹⁵ and one case report of intrauterine transmission from infected mother to baby¹⁶. However, these modes of transmission are not yet supported by epidemiological evidence.

Surveillance for West Nile virus in Canada

Public health surveillance programs can be divided into four groups: passive, active, sentinel and special¹⁷. Passive surveillance relies on receipt of reports by public health laboratories; as opposed to active surveillance, which makes explicit efforts to obtain information (such as specimens for testing or reports). Sentinel surveillance uses a sample of birds to provide an indication of the frequency of the disease occurrence. Finally, special surveillance systems typically consist of focused studies, such as surveys specifically designed to gather disease data.

Passive programs are generally considered to be the most feasible and cost-effective surveillance program to run. However, these advantages must be weighed against the lower case ascertainment rate achieved as compared with the other types of surveillance programs. The West Nile virus surveillance programs currently used in Canada are passive and sentinel surveillance programs.

The surveillance factor most closely associated with the number of human cases is dead bird densities¹⁷, or the number of birds that die from West Nile virus infection. Health Canada began testing dead birds for West Nile virus infection in 2000 as a major component of the surveillance program⁹. The number of infected birds detected has been

increasing annually, an indicator that human disease due to West Nile infection may also be expected to increase.

An additional component to surveillance programs is monitoring of the mosquito vector. The focus of mosquito surveillance differs depending on the level of current or anticipated West Nile virus activity in a given geographic region. In areas where West Nile virus has never been detected, mosquito surveillance focuses primarily on establishing presence of types of mosquito species and how many there are in the area. In areas where West Nile virus has been found, mosquitoes may also be tested for West Nile virus. This information would help identify the role different species play in spreading the virus to birds, animals and people. It would also be used to determine if, where and how to best intervene to reduce the risk of infection⁹.

The human component of West Nile virus surveillance consists of healthcare providers being watchful for symptoms of West Nile virus infection in their patients. When West Nile virus is suspected, laboratory diagnostic testing is conducted to obtain conclusive results. The diagnostic process for West Nile virus testing in blood samples consists of determining the presence or absence of antibodies to West Nile virus.

Front-line testing identifies antibodies to West Nile virus and is generally done on two separate blood samples that must be taken about three weeks apart⁹. A positive result to the first test indicates that the person has been exposed to either West Nile virus or another flavivirus, such as St. Louis encephalitis or Japanese encephalitis. At this point, information from the patient, such as travel history, can help determine the likelihood that it is West Nile. If antibody levels in the second blood sample have increased by four times or more over the first blood sample, it is indicative of a recent infection⁹. This indicates a "probable" case of West Nile virus infection. The results of front-line tests are used by physicians to modify treatments and therapies for their patients.

There are two laboratory testing methods used during front-line testing for West Nile virus detection: hemagglutination-inhibition (HI) test and enzyme-linked immunosorbent assay (ELISA)⁹. Both tests are valid and produce results within 48 hours; however, more samples can be tested at once using the ELISA test.

West Nile virus prevention

There is currently no human vaccine for West Nile virus, although vaccine research is underway. Given the low incidence of West Nile viral disease in humans in most parts of the world it is unlikely that such a vaccine would be cost-effective for public health use. A more appropriate method for controlling West Nile virus in Canada is transmission prevention.

Effective prevention of West Nile virus infection of humans is dependent on the development of comprehensive, integrated viral surveillance and targeted mosquito control programs in area where the virus is know or likely to occur. Maps should be generated highlighting breeding sites for all species of mosquito vectors that could be involved in West Nile virus transmission⁹. Pesticides act at one of two stages of the mosquito life cycle. Agents that act against larva are called larvicides, and those that work against full grown mosquitoes are termed adulticides^{9;18}. Larvicides are generally preferred over adulticides, primarily because application can be targeted to mosquito breeding sites which limits pesticide exposure to humans and other non-target organisms¹⁹. Control programs targeted at specific points in the mosquito life cycle should be applied early in the spring to disrupt springtime viral amplification in mosquitoes and birds.

Perhaps the most important component in any West Nile virus prevention program is public education campaigns designed to teach the community how to avoid or reduce the risk of being bitten by potentially infected mosquitoes. The information should cover: areas where mosquitoes are commonly found, peak mosquito biting periods, how to identify and eliminate potential mosquito breeding sites and repellent use.

The majority of commonly recommended mosquito repellants contain DEET, which is short for N, N – diethyl-m-toulamide²⁰. DEET is applied to the skin and works by repelling biting insects, including mosquitoes, from treated areas. No carcinogenic or toxic effects to humans have been associated with use of DEET²⁰. Most public education programs targeted to the prevention of West Nile disease encourage individuals to use repellants containing DEET.

Summary

West Nile virus is an emerging infectious disease in Canada. The final geographic distribution of the disease and the effects of West Nile infection on the health of Canadians have not yet been seen. The rapid spread of disease and significant morbidity and mortality associated with symptomatic West Nile virus infections makes this an important area of study with respect to public health.

Family doctors should provide their patients with appropriate information about West Nile virus prevention, in particular to individuals who may be at higher risk of becoming infected with West Nile virus and / or who may be more likely to suffer adverse health outcomes as a result of West Nile virus infection. These individuals include the elderly and people with suppressed immune function, especially those with co-morbid medical conditions.

Tables

Table 1: Results of West Nile virus human surveillance program (2003)¹⁸.

Province/Territory	Number of probable positive humans	Number of confirmed positive humans	Number of deaths
Nova Scotia	0	2 †	0
New Brunswick	0	1 †	0
Quebec	1	16	0
Ontario	0	89 §	2 ‡
Manitoba	106	35	2
Saskatchewan	736	38	6 *
Alberta	0	270	0
British Columbia	8 †	12 †	0
Yukon Territory	1 †	0	0
<i>Canada (Total)</i>	852	463	10

† Likely related to travel outside the province / territory.

‡ A patient died from a stroke on 09/03/2003. The patient had secondary West Nile virus encephalitis. A patient died from aspiration pneumonia on 09/05/2003. Both patients were listed as probable West Nile virus cases.

* West Nile virus is reported as having been a contributing factor in two deaths.

§ One case is likely related to travel outside the province.

References

1. Petersen LR, Marfin AA, Gubler DJ. West Nile Virus. *Journal of the American Medical Association* 2003;290:524-8.
2. Nosal B, Pellizzari R. West Nile Virus. *Canadian Medical Association Journal* 2003;168:1443-4.
3. Hayes CG. West Nile virus: Uganda, 1937, to New York City, 1999. *Annals of the New York Academy of Sciences*. 2001;951:25-37.
4. Solomon T, Ooi MH, Beasley DWC, Mallewa M. West Nile Encephalitis. *British Medical Journal* 2003;326:865-9.
5. Gubler DJ. The Global Emergence/Resurgence of Arboviral Diseases As Public Health Problems. *Archives of Medical Research* 2002;33:330-42.
6. Petersen LR, Marfin AA. West Nile Virus: a primer for the clinician. *Annals of Internal Medicine* 2002;137:173-9.
7. Mostashari F, Bunning ML, Kitsutani PT, *et al.* Epidemic West Nile encephalitis, New York, 1999: results of a household-based seroepidemiological study. *Lancet* 2001;358:261-4.
8. Campbell GL, Marfin AA, Lanciotti RS, Gubler DJ. West Nile Virus. *The Lancet Infectious Diseases* 2002;2:519-29.
9. Health Canada. West Nile virus surveillance information. Health Canada website . 2003. Accessed 03/04/2004:
<http://www.hc-sc.gc.ca/pphb-dgspsp/wnv-vwn/index.html>
10. Marra PP, Griffing SM, McLean RG. West Nile virus and wildlife health. *Emerging Infectious Diseases* . 2003. Accessed 03/04/2004:
<http://www.cdc.gov/ncidod/EID/vol9no7/03-0277.htm>
11. Mellor PS. Replication of Arboviruses in Insect Vectors. *Journal of Comparative Pathology* 2000;123:231-47.

12. Bres P. Impact of Arboviruses on Human and Animal Health. In Thomas P. Monath, ed. *The Arboviruses: Epidemiology and Ecology, Volume 1.*, pp 1-18. Boca Raton, FL: CRC Press, Inc., 1988.
13. White DO, Fenner FJ. Epidemiology of Viral Infections. *Medical Virology*, pp 233-55. San Diego, CA: Academic Press, 1994.
14. Gubler DJ. Human arbovirus infections worldwide. *Annals of the New York Academy of Sciences*. 2001;951:13-24.
15. Centers for Disease Control. Possible West Nile virus transmission to an infant through breastfeeding - Michigan, 2002. *Morbidity and Mortality Weekly Report* 2002;51:877-8.
16. Centers for Disease Control. Intrauterine West Nile virus infection - New York, 2002. *Morbidity and Mortality Weekly Report* 2002;51:1135-6.
17. Eidson M. "Neon Needles" in a haystack: the advantages of passive surveillance for West Nile virus. *Annals of the New York Academy of Sciences*. 2001;951:38-53.
18. Health Canada. West Nile virus website. Health Canada website . 2003. 11-26-2003. Accessed 03/04/2004:
<http://www.hc-sc.gc.ca/english/westnile/index.html>
19. Shapiro H, Micucci S. Pesticide use for West Nile virus. *Canadian Medical Association Journal* 2003;168:1427-30.
20. United States Environmental Protection Agency. EPA and Mosquito Control. United States Environmental Protection Agency. 2003. Accessed 03/04/2004:
<http://www.epa.gov/pesticides/factsheets/skeeters.htm>