Geographic distribution of West Nile virus reported in humans and corvids in southern Ontario, 2006

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This study analyzes the spatial risk distribution of West Nile virus (WNV) in humans and birds across southern Ontario for 2006. The relationship between bird and human risk is also investigated. Surveillance data was obtained for the number of human WNV cases and the fraction of dead birds testing positive in each public health unit. The presence of disease clustering in humans and birds was investigated using a spatial scan test. Choropleth risk maps of regional empirical Bayesian smoothed estimates were created to investigate the spatial distribution of WNV in humans and birds. Isopleth risk maps were created through kriging of smoothed estimates, and were used to identify high-risk areas as well as investigate the relationship between human and bird risk. One disease cluster was found in both humans and birds. The human disease cluster was not significant when the bird data was used as a covariate in the analysis. The choropleth and isopleth maps identified the southern portion of southern Ontario to be the highest risk area for both humans and birds. This study indicates that bird outbreaks are a potential indicator for an increase in human risk. As well, WNV risk is greatest in the southern portion of southern Ontario and is geographically spreading in comparison to previous years.

West Nile virus (WNV) was first isolated in 1937 from a patient in the West Nile district of Uganda.¹ In 1999, the virus was introduced into the United States and led to an outbreak in New York City, which resulted in seven human case fatalities.² In 2001 and 2002, the first Canadian bird and human cases were detected in Ontario, respectively.³

The United States Centre for Disease Control and Prevention (CDC) has estimated that 80% of humans infected with WNV will be asymptomatic and more than 19% will develop West Nile fever, which includes general flu like symptoms.⁴ The remaining one in 150 human cases will lead to severe West Nile disease which involves the nervous system and may include meningitis, encephalitis, paralysis, or death.⁴

The life cycle of WNV involves birds and mosquitoes. Birds act as the reservoir since once they are infected they amplify the virus allowing for further transmission.⁵ Mosquitoes act as a vector and feed on infected birds. During later blood meals, mosquitoes can transmit the virus either to other birds or a dead-end host.⁶ For WNV, dead-end hosts most often include humans and horses.⁷ Mosquitoes are also able to transmit the virus vertically; and infected females have been shown to hibernate over winter and still be infectious the following season. Though it is unknown how often these transmission processes occur in nature.^{8,9} The *Culex* species are thought to be the primary mosquito type involved in WNV transmission.¹⁰ WNV has been identified in 255 bird species, however the primary species of importance for transmission remains unknown.^{11,12}

In 2000, the Public Health Agency of Canada established a surveillance program to respond to the discovery of WNV in the United States.¹³ This surveillance program included monitoring the virus in humans, birds, mosquitoes and horses. In 2006, dead birds of the *Corvidae* family were tested to monitor the virus in birds.¹⁴ Corvids are used as an indicator of the virus distribution in birds since they have a high mortality rate from WNV infection.¹⁵ Many studies have demonstrated that bird outbreaks of WNV typically precede an increase in human cases.^{16,17,18} For southern Ontario specifically, Beroll *et al.*¹⁹ discovered a significant association between the spatial pattern of WNV risk in humans and birds.

The aim of this study was to investigate the spatial distribution of WNV in humans and birds for southern Ontario in 2006. A secondary aim of the study was to provide further insight into the potential of WNV dead bird surveillance as basis for an early warning system for public health.

METHODS

For southern Ontario in 2006, the number of birds tested for WNV as well as their disease status was obtained from the Canadian Cooperative Wildlife Health Centre (CCWHC).²⁰ The number of detected human cases in each public health unit was collected from the Ontario Ministry of Health and Long Term Care (OMHLTC).²¹ Population estimates for

public health units in 2005 as well as the corresponding boundary map was acquired from Statistics Canada.^{22,23}

Dead bird surveillance in Ontario has relied on voluntary reporting by the public.¹⁴ Reported dead birds are collected and sent to the CCWHC where oral swabs were taken and tested for WNV antigen.²⁴ Human testing on the other hand relies on detecting antibodies of WNV performed at the OMHLTC Central Public Health Laboratory.²⁴ Because WNV is a reportable disease in Canada, human cases must be reported to local and provincial health authorities.²⁵

Raw estimates of human incidence and bird mortality fractions (also known as bird proportional mortality fractions) were geo-located in the centroids of each public health unit. The estimates were used to identify clusters of disease in humans and birds separately using a spatial scan statistic.²⁶ Human cases were rare and assumed to follow a Poisson distribution, and the more common bird cases a Binomial distribution. The attained level of significance (p-value) was estimated by the Monte Carlo method using 999 replications.²⁷ A spatial scan test of human incidence when bird mortality fraction was treated as a covariate was also done to assess if in 2006, bird mortality helped to explain human cases as has been previously found.¹⁹

Empirical Bayes estimation is used to adjust the raw estimates of human incidence and bird mortality fractions for their sample size.²⁸ Choropleth maps of these adjusted incidence and mortality fractions were created to visualize the regional estimates.

Isopleth risk maps were created using ordinary kriging of the empirical Bayes estimates.²⁹ Here, kriging was based on an exponential semivariogram fitted by maximum likelihood estimation.

The analyses involved the software: R³⁰, SaTScan²⁷ and ArcMap.³¹

RESULTS

The raw bird mortality fractions ranged for the 29 health units in southern Ontario from 6.25% to 87.5%. Raw human incidence ranged from 0 to 1.51 cases per 100,000 people. After the data were smoothed using empirical Bayes estimation, bird mortality ranged from 18% to 39% and human incidence ranged from 0.16 to 0.80 cases per 100,000 people. In total there were 31 human cases reported in southern Ontario for 2006. Choropleth maps displaying empirical Bayesian smoothed risk estimates for humans and birds can be seen in **Figure 1a)** and **1b)** respectively. The disease in both humans and birds is concentrated in the southern area of southern Ontario.

One disease cluster was found in both the human and bird raw data. The p-values for the clusters were 0.01 and 0.003 respectively. The location of the clusters can be seen in **Figure 1a)** and **1b)**. There were 17 public health units included in the bird cluster and 10 in the human cluster. All 10 public health units that were part of the human cluster were also part of the bird cluster. When the bird data was

used as a covariate for the scan test to detect clusters of human disease, none were detected.

For the human and bird data, maximum likelihood fit semivariogram models were of the exponential form without a nugget effect. Four public health units were treated as outliers and removed from the dataset when the maximum likelihood model was fit to the semivariogram for humans. These four units were all detected to be a part of the disease cluster in humans; however they displayed an unexpected low risk.

The human and bird isopleth risk maps resulting from kriging of the smoothed risk estimates can be seen in **Figure 1c)** and **1d)** respectively. The Health Units with the highest smoothed human incidences were found to be: Brant County, Lambton, and Windsor-Essex County. It should be noted that the Windsor-Essex County health unit had the highest smoothed incidence at 0.80 cases per 100,000 people. Lambton and Brant County had the next highest smoothed incidence at 0.54 cases per 100,000 people. The health units with the highest bird mortality fractions were: Middlesex-London, Brant County, and the City of Toronto. The bird mortality fraction estimates in these three areas are all greater than 35%.

DISCUSSION

The spatial scan statistic detected a human and bird disease cluster in the southern area of southern Ontario (see **Figure 1a)** and **1b)** respectively). The cluster locations are consistent with findings from previous years, however the human cluster size is larger than had been detected in the past.¹⁹ The circular spatial scan statistic was used here for explorative purposes. This method is useful in determining the general location of disease clusters. It does not however detect all regions involved in clusters that are non-circular. For the exact location and extent of irregularly shaped clusters, other detection methods such as the spatial scan statistic by Tango and Takahashi³² may be more appropriate. This is likely why the Windsor-Essex Health Unit was not included in the bird disease cluster.

An outbreak of WNV in birds has been shown to precede an excess of human cases by two to five weeks.¹⁸ When the scan statistic was used to detect human clusters of disease with bird mortality fractions treated as a covariate, no clusters were found. This is consistent with findings from previous years and indicates that an outbreak location of WNV in birds has the potential to serve as a early warning system, i.e. it is possible to predict a high-risk area for humans.¹⁹ When an outbreak in birds is detected, local health authorities have about two weeks lead time to put preventative methods into place and limit the number of resulting human cases.

While the bird data is valuable for predicting an increase in human incidence, it does have limitations. In Ontario, bird surveillance has relied on the general public to report the locations of dead corvids.¹⁴ The effect of this bird sampling

Figure 1 WNV risk estimates for the 29 public health units of southern Ontario in 2006. (a) Choropleth map of empirical Bayesian smoothed human incidence of WNV per 100,000 population overlaid with disease cluster location as detected by the scan test; (b) Choropleth map of empirical Bayesian smoothed bird mortality fractions overlaid with disease cluster location as detected by the scan test; (c) Isopleth map of smoothed human incidence estimates (per 100,000 population); (d) Isopleth map of smoothed bird mortality fraction estimates.

process being dependent on the public is not entirely understood. It is reasonable to assume that within a health unit, urban areas have been sampled more intensely than rural areas as a result of having a greater population density. This would lead to a mortality fraction that is more representative of urban areas if there is any difference. In addition, public health units have not been required to begin and end bird testing at the same time. Health units that have done the majority of their testing in the beginning of the season when WNV risk is lower would therefore have had a lower mortality fraction comparatively. In addition, localized disturbances in the multifactorial cause of death of corvids

for reasons other than WNV infection may distort the mortality fraction in affected health units.

The overall Bayesian smoothed estimates of risk for humans and birds from 2002 to 2006 can be seen in **Figure 2** and is based on a study by Beroll *et al.*¹⁹ as well as the findings from this study. Both human and bird WNV risk decreased from 2002 to 2004, and then increased in 2005. For 2006 however, the human incidence decreased drastically from 2.14 cases per 100,000 people to 0.32, while the bird mortality fraction increased from 25.2% of birds testing positive to 27.8%. Weather has been found to impact WNV transmission.³³ The nearly seven-fold decrease in

Figure 2 Trend in WNV risk for humans and birds in southern Ontario from 2002 to 2006.

human incidence may be a result of dry weather across southern Ontario in the late summer of 2006, which would have decreased the number of mosquitoes infecting humans. Another factor that may account for this decrease in human risk is an increase in public awareness of the virus and how to prevent infection.

Geographically, areas considered high risk in 2006 have expanded when compared to areas that were considered high risk in the past. In previous years, clusters of the disease in humans contained at most four health units and were focused in the Niagara, Toronto, or Windsor areas.¹⁹ In 2006 the human cluster of disease increased to include 10 public health units indicating a spread of the disease. In addition, high-risk areas were found outside of the Niagara, Toronto, and Windsor areas where increased risk had previously not been observed. The geographical spread is also demonstrated by the bird isopleth map, which displays high risk in the Middlesex-London health unit and the Brant County health unit, which have consistently been low risk areas in the past.¹⁹ While areas of comparatively high risk have expanded from 2005 to 2006 for both humans and birds, the overall risk for humans has decreased from 2005 while bird risk has increased.

The isopleth maps and spatial scan statistics indicate that both human and bird WNV risk is concentrated in the southern area of southern Ontario but is present all across southern Ontario. In addition, human risk continues to be spatially associated with bird risk and their cluster locations overlapped in 2006. Due to this spatial relationship, empirical Bayes smoothed bird mortality fraction continues to be an early warning indicator or increased human risk. This means that if bird outbreak locations are detected, prevention methods that are immediately put in place may control an outbreak in the human population.

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