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Spatial clustering of swine influenza in Ontario on the basis of herd-level disease status with different misclassification errors

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Abstract

This approach maximizes sensitivity of serology-based monitoring systems by considering spatial clustering of herds classified as false positive by herd testing, allowing outbreaks to be detected in an early phase. The primary objective of this study was to determine whether swine herds infected with influenza viruses cluster in space, and if so, where they cluster. The secondary objective was to investigate the combining of a multivariate spatial scan statistic with herd test results to maximize the sensitivity of the surveillance system for swine influenza. We tested for spatial clustering of swine influenza using the Cuzick–Edwards test as a global test. The location of the most likely spatial clusters of cases for each subtype and strain in a sample of 65 sow and 72 finisher herds in 2001 (Ontario, Canada), and 76 sow herds in 2003 (Ontario, Canada) was determined by a spatial scan statistic in a purely spatial Bernoulli model based on single and multiple datasets.

A case herd was defined by true herd-disease status for sow or finisher herds tested for H1N1, and by apparent herd-disease status for sow herds tested for two H3N2 strains (A/Swine/Colorado/1/77 (Sw/Col/77) and A/Swine/Texas/4199-2/98 (Sw/Tex/98)). In sow herds, there was no statistically significant clustering of H1N1 influenza after adjustment for pig-farm density. Similarly, spatial clustering was not found in finisher herds. In contrast, clustering of H3N2 Sw/Col/77 (prevalence ratio = 12.5) and H3N2 Sw/Tex/98 (prevalence ratio = 15) was identified in an area close to a region with documented isolation of avian influenza isolates from pigs.

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For the H1N1 subtype tested by ELISA, we used an approach that minimized overall misclassification at the herd level. This could be more applicable for detecting clusters of positive farms when herd prevalence is moderate to high than when herd prevalence is low. For the H3N2 strains we used an approach that maximized herd-level sensitivity by minimizing the herd cut-off. This is useful in situations where prevalence of the pathogen is low. The results of applying a multivariate spatial scan statistic approach, led us to generate the hypothesis that an unknown variant of influenza of avian origin was circulating in swine herds close to an area where avian strains had previously been isolated from swine. Maximizing herd sensitivity and linking it with the spatial information can be of use for monitoring of pathogens that exhibit the potential for rapid antigenic change, which, consequently, might then lead to diminished cross-reactivity of routinely used assays and lower test sensitivity for the newly emerged variants. Veterinary authorities might incorporate this approach into animal disease surveillance programs that either substantiate freedom from disease, or are aimed at detecting early incursion of a pathogen, such as influenza virus, or both.

Keywords: Influenza; Swine; Scan statistic; Sentinel surveillance; Herd test; Spatial

1. Introduction

Swine influenza (SI) causes high morbidity when introduced into naive herds (Easterday and Van Reeth, 1999), and is a component of the porcine respiratory disease complex (Thacker, 2001). Swine influenza is of public health concern because of zoonotic potential and hypothesized role in the possible future influenza pandemic (Easterday and Van Reeth, 1999; Webby et al., 2004). The influenza virus is a single-stranded negative-sense RNA virus in the family *Orthomyxoviridae* (Wright and Webster, 2001). Influenza virus type A was detected in pigs on a worldwide basis with pig seroprevalence approaching 50% (Easterday and Van Reeth, 1999) and herd prevalence of up to 96% (Maes et al., 2000). Influenza virus type B was detected only serologically in seven pigs (Brown et al., 1995), and exposure to type C was detected in 9.9% of pigs in the same study in Great Britain (Brown et al., 1995). Although most hemagglutinin (HA) subtypes of type A influenza virus can infect pigs under experimental conditions (Kida et al., 1994), the majority of field influenza infections in swine have been attributable to H1N1, H3N2 and H1N2 subtypes globally (Webby et al., 2004). Swine influenza viruses of a specific subtype might be restricted to swine populations of a particular geographic location, making the ecology of influenza virus regionally specific.

Since 1930, when swine influenza virus (SIV) was first isolated, until 1997, most influenza infections in pigs in North America were caused by classical swine H1N1 virus (Hinshaw et al., 1978; Chambers et al., 1991; Olsen, 2002) although H3N2 was isolated occasionally (Bikour et al., 1995). Currently, all three subtypes are circulating in at least some swine-producing areas of the USA (Choi et al., 2002). In addition, antigenic drift in the HA of the triple-reassortant H3N2 strain was reported (Webby et al., 2004).

In 2001, H1N1 was the endemic subtype in Ontario sow and finisher pig populations (Poljak et al., in press). We reported $> 98\%$ confidence in the absence of the H3N2 Sw/Col/77 and Sw/Tex/98 strains from the Ontario sow population in 2003, with up to seven apparently positive herds (Poljak et al., in press). Seasonal outbreaks of respiratory disease with an endemic SIV have been reported in some regions of North America (Easterday and Van Reeth, 1999), although the spread between herds was minimal in other regions in Europe (de Jong et al., 2001). For endemic SIV strains, there is a positive association between higher density of pigs in an area and pig-level seroprevalence (Maes et al., 1999, 2000). The pig density in Ontario varies across geographical