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Using egg production data to quantify within-flock transmission of low pathogenic avian influenza virus in commercial layer chickens

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ABSTRACT

Even though low pathogenic avian influenza viruses (LPAIv) affect the poultry industry of several countries in the world, information about their transmission characteristics in poultry is sparse. Outbreak reports of LPAIv in layer chickens have described drops in egg production that appear to be correlated with the virus transmission dynamics. The objective of this study was to use egg production data from LPAIv infected layer flocks to quantify the within-flock transmission parameters of the virus. Egg production data from two commercial layer chicken flocks which were infected with an H7N3 LPAIv were used for this study. In addition, an isolate of the H7N3 LPAIv causing these outbreaks was used in a transmission experiment. The field and experimental estimates showed that this is a virus with high transmission characteristics. Furthermore, with the field method, the day of introduction of the virus into the flock was estimated. The method here presented uses compartmental models that assume homogeneous mixing. This method is, therefore, best suited to study transmission in commercial flocks with a litter (floor-reared) housing system. It would also perform better, when used to study transmission retrospectively, after the outbreak has finished and there is egg production data from recovered chickens. This method cannot be used when a flock was affected with a LPAIv with low transmission characteristics ($R_0 < 2$), since the drop in egg production would be low and likely to be confounded with the expected decrease in production due to aging of the flock. Because only two flocks were used for this analysis, this study is a preliminary basis for a proof of principle that transmission parameters of LPAIv infections in layer chicken flocks could be quantified using the egg production data from affected flocks.

1. Introduction

Low pathogenic avian influenza (LPAI) is a mild disease of various avian species, which is caused by Influenza A viruses belonging to one of 16 Hemagglutinin (H) and 9 Neuraminidase (N) subtypes (Fouchier et al., 2005; Alexander, 2007). LPAI virus (LPAIv) infections in poultry with H5 or H7 virus subtypes are of major importance due to their ability to mutate to a highly pathogenic avian influenza virus (HPAIv) (Alexander, 2007). In addition, H9 and H6 LPAIv subtypes in particular, have been affecting the poultry industry of different countries in Asia (Cheung et al., 2007; Xu et al., 2007; Hadipour, 2011; Park et al., 2011).

LPAIv surveillance programmes have been implemented in many countries (Gonzales et al., 2010). Although

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these programmes may be useful to determine whether the prevalence of infected birds is below a pre-set level, their usefulness in early detection is still unknown. To establish the latter (Graat et al., 2001; Fischer et al., 2005), quantitative knowledge of transmission of LPAIv is necessary.

The transmission characteristics of a pathogen can be determined in transmission experiments (van der Goot et al., 2003; Velthuis et al., 2007) or in field outbreaks (Stegeman et al., 1999; Bos et al., 2009). Transmission experiments allow for quantifying transmission parameters in a controlled environment, but, in case of LPAIv, there appears to be considerable variation in the transmission characteristics of different virus strains even within the same H subtype (van der Goot et al., 2003; Gonzales et al., 2011, 2012). To quantify the existing variability experimentally would be very costly. An alternative would be the quantification of transmission from field data. The latter would have the following benefits: (i) the quantified transmission parameters would be a direct indicator of the transmission characteristics of the virus in the field, (ii) transmission could be studied faster than with transmission experiments, and (iii) the use of indicators already available would be cheaper and more desirable from the perspective of animal welfare.

LPAIv infections in poultry are often subclinical or present unspecific clinical signs. However, drops in egg production have been often reported during outbreaks involving chicken layers flocks (Henzler et al., 2003; Zanella, 2003; de Wit et al., 2004); with sudden drops in production ranging from 10% (de Wit et al., 2004) to 40% (Zanella, 2003) in a couple of weeks followed by a slight increase (from the biggest drop level) some weeks later. Such drops in egg production have been also observed in experimentally infected layer chickens (Trampel et al., 2006; Gonzales et al., 2012). Consequently, it would be worthwhile to examine whether the drop in egg production can be used to estimate transmission parameters. This would be a cheap alternative to transmission experiments.

In 2003, a cross-sectional serological survey was performed in The Netherlands (de Wit et al., 2004) and a high prevalence of seropositive animals to H7N3 LPAIv was detected in a cluster of three farms: one turkey (10 seropositives out of 10 samples) and two free-range layer chicken farms (30 seropositives out of 30 samples). The H7N3 virus was later isolated from the turkey farm (de Wit et al., 2004; Velkers et al., 2006). The objective of this study was to estimate the transmission characteristics of this H7N3 LPAIv in a transmission experiment and from the egg production data of the two infected layer flocks.

2. Methods

2.1. Experimental estimation of within-flock transmission parameters

The chicken-to-chicken transmission characteristics of the H7N3 LPAIv (cleavage side: PEIPKGR*GLF (Velkers et al., 2006)) causing the outbreaks here analysed were first quantified in a transmission experiment. The experimental procedure and data analysis was similar to that described elsewhere (van der Goot et al., 2003; Gonzales et al., 2011). Briefly, two experimental trials were carried out. Each trial consisted of 10 specified pathogen free (spf) White Leghorn chickens (6 weeks old). Five chickens were inoculated and the remaining five were kept as contacts. Chickens were inoculated both intranasally and intratracheally with 0.1 ml/route of inoculum containing 10^6 EID_{50} (50% egg infectious dose)/ml. Virus transmission was monitored by regularly collecting cloaca and trachea swab samples, which were examined for the presence of virus (virus isolation in embryonated chicken eggs). Samples were taken daily from day post inoculation (d.p.i.) 1 to d.p.i. 10 and later at d.p.i 14, 17 and 21. The data from this experiment were used to estimate the transmission rate parameter β (day^{-1}), which is the expected number of contact infections caused by an infectious individual per day, the infectious period T, which is the average time (days) that an infected individual remains infectious, and the recovery rate γ (day^{-1}), which is the expected number of animals recovering from infection per day. β was estimated using a generalised lineal model (GLM) method, assuming a latent period $\leq$1 day. The mean length of T was estimated using a parametric survival model with a Weibull distribution (the distribution that best fitted the data) and γ was estimated as the inverse of T ($\gamma = 1/T$). The basic reproduction ratio R_0 was estimated as the product of β and T. Because the correlation between β and T was unknown, confidence intervals for R_0 were derived by Monte Carlo (MC) simulations assigning to β and T Lognormal and Weibull distributions, respectively (Table 2). All the analysis were performed using the statistical package "R" (R Development Core Team, 2005). The library Survival was used for the survival analysis.

The transmission experiment was approved by an ethical committee and complied with the Dutch law on Animal experiments. The experiment was carried out in the High Containment Unit at the Central Veterinary Institute part of Wageningen University and Research centre, in Lelystad, The Netherlands.

2.2. Estimation of within-flock transmission parameters from egg production data

Egg production data from the two infected free-range layer chicken flocks, here referred to as Farm-3 and Farm-4 as reported by de Wit et al. (2004), were used for the analysis. Egg production data consisted of weekly averages of daily egg production. For both flocks, we selected data from week 38 (calendar week) of 2002 – when production in both flocks appeared to be maximal and stable – to the last week (week 10 of 2003) that production was reported by de Wit et al. (2004). This period resulted in a total of 25 data points (Fig. 1). To analyse these data, we simulated the infection dynamics in these flocks constructing deterministic susceptible-infectious-recovered (SIR) and susceptible-exposed-infectious-recovered (SEIR) models, in which we assumed a homogeneous contact structure (Keeling and Rohani, 2008). The transmission term was formulated as $\beta S(t)I(t)/N(t)$, with $S(t)$, $I(t)$ and $N(t)$ denoting the number of susceptible S and infectious I chickens in the total population of size N at time t (days). This formulation implies that the transmission pressure is independent