

Estimating the Moment of H7N7 HPAI Virus Introduction into a Poultry Flock, Based on Mortality Data

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Abstract

Despite continuing research efforts, little is known about the transmission dynamics of the highly pathogenic avian influenza (HPAI) virus, which complicates control of an epidemic. Combining the results of transmission experiments with modelling makes it possible to gain more insight in the transmission dynamics under field conditions. The goal of this research was to back-calculate the moment of introduction of HPAI into a flock, based on flock mortality data. The back-calculation method was based on a stochastic SEIR (susceptible (S) – latently infected (E) – infectious (I) – removed (= dead; R)) epidemic model. The latent and infectious period were assumed to be gamma distributed and parameter values for the model were based on experimental H7N7 within-flock transmission data. The model was used to simulate numerous animal-level outbreaks. For each iteration the number of days it took to reach a certain number of dead animals was listed, giving estimates for the moment of virus introduction into a flock based on stochastic likelihood. The model indicates that it may take considerable time before a noticeable increase in mortality is observed after a single introduction into a flock. For example, it takes fifteen days if the threshold value is fifty dead animals on two consecutive days in a flock with 10,000 animals.

Introduction

In 2003, a highly pathogenic avian influenza (HPAI) virus of subtype H7N7 caused an epidemic in The Netherlands. Within a couple of months 255 flocks were diagnosed as infected, and around 30 million animals were killed and destroyed (Elbers *et al.*, 2004; Stegeman *et al.*, 2004). During the outbreak it became clear that HPAI can cause considerable economical and societal damage. In addition, it became clear that there was a lack of knowledge concerning the transmission dynamics of HPAI. This lack of knowledge complicated control as contact tracing was rather difficult, since it was not precisely known during which period the infected farm was infectious. Therefore, drastic measures such as mass culling, buffer zones and complete movement restrictions were also needed.

Since the epidemic transmission experiments have been conducted, giving an indication of bird-to-bird transmission parameter values for the H7N7 HPAI virus (Van der Goot *et al.*, 2005). These data give baseline estimates for epidemiologically relevant parameters (Van der Goot *et al.*, 2003). Here, the data is used to construct a stochastic SEIR (susceptible (S) – latently infected (E) – infectious (I) – removed (= dead; R)) epidemic model. With this simulation model the gap between transmission experiments and the field conditions of farms containing thousands of animals can be bridged. The model can also be used to back-calculate the moment of introduction of the virus into a flock. Then it will not only be known that a flock is infected, it will also be known when the flock is infectious for other flocks. This will be a first step to understanding flock-to-flock transmission, a necessity for a better and more economical optimized control of a next epidemic.

Materials and methods

The model is a stochastic SEIR epidemic model at animal level. To account for the fairly limited latent and infectious periods (Van der Goot *et al.*, 2005) these periods are assumed to be gamma

distributed. To model this distribution we used the ‘method of stages’ (Cox and Miller, 1967). The model randomly chooses which ‘events’ (e.g. an animal alters from S to E, or from I to R) happen after a given time-step (in this model 0.05 days, and denoted by dt). These events follow the dynamics of the model, which are represented by the following set of differential equations:

$$\begin{aligned} \frac{dS}{dt} &= -b \frac{I(t)}{N} S(t) \\ \frac{dE_1}{dt} &= b \frac{I(t)}{N} S(t) - n_E g E_1(t); & \frac{dE_i}{dt} &= n_E g (E_{i-1}(t) - E_i(t)) \text{ (for } 2 \leq i \leq n_E) \\ \frac{dI_1}{dt} &= n_E g E_{n_E}(t) - n_I m I_1(t); & \frac{dI_j}{dt} &= n_I m (I_{j-1}(t) - I_j(t)) \text{ (for } 2 \leq j \leq n_I) \\ & & \frac{dR}{dt} &= n_I m I_{n_I}(t) \end{aligned}$$

Throughout we have set $n_E = n_I = 20$. This model uses a density-dependent transmission term ($b \frac{S(t)I(t)}{N}$) in which N denotes the total number of animals present in the population at the start.

The total time spent in E and in I is given by $1/\bullet$ and $1/\mu$ respectively, with $\bullet = 0.5$ / day (i.e. the mean latent period is two days) and with $\mu = 0.159$ / day (i.e. the mean infectious period is 6.3 (95% CI: 3.9 – 8.7) days) in agreement with the transmission experiments of Van der Goot *et al.* (2005). See Figure 1 for the probability density plots for the gamma distributions of the latent and the infectious period.

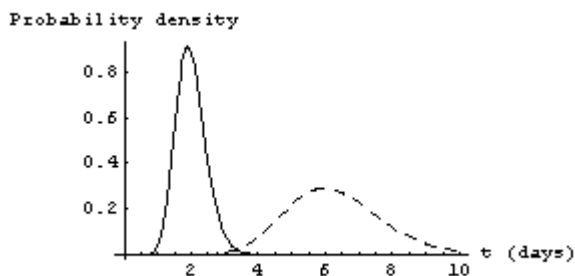


Figure 1 Probability density plot for gamma distribution of the latent (solid line) and infectious (dashed line) period, in agreement with Van der Goot *et al.* (2005)

Simulations are started with one latently infected animal in a population of susceptibles, totalling 10,000 animals. The output of interest is the number of removed animals, in this model representing dead animals. The number of days it takes to reach a certain threshold value of dead animals per day (detection rule for determining AI) is listed for every of 1,000 iterations. With these outcomes estimates are given for the time since infection, based on stochastic likelihood. Subsequently, we can determine the moment of virus introduction into the flock.

Results

Figure 2 shows examples of the model output for the number of S, E, I and R animals per day since infection. If the monitoring threshold in the Netherlands is applied on a farm with 10,000 animals (for layers: mortality $>0.5\%$ on two consecutive days; in this case 50 animals) (LNV, 2006), according to this model, we find that the virus was introduced 15 (minimum – maximum: 14-17) days before notification. If, for example, a threshold is used of 15 dead animals on two consecutive days, the virus was introduced 14 (13-16) days before notification.

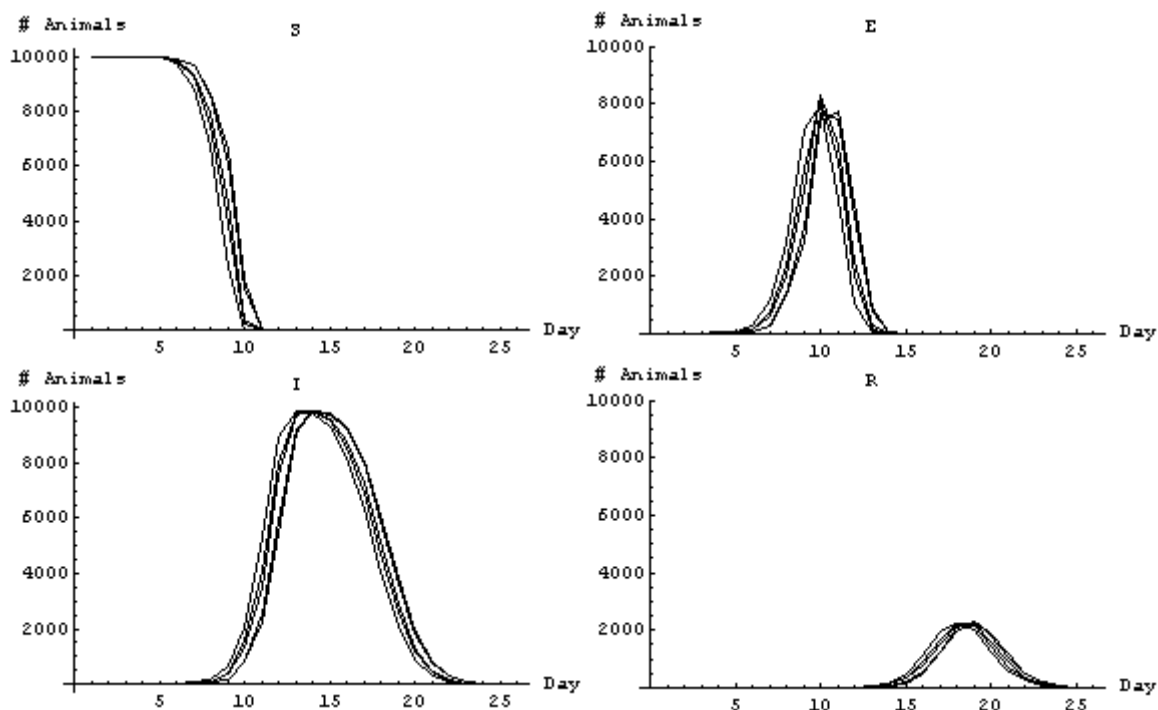


Figure 2 Examples of the model output; 5 iterations are shown. Shown are the number of susceptible animals per day (top left-hand), the number of latently infected animals per day (top right-hand), the number of infectious animals per day (bottom left-hand) and the number of dead animals per day (bottom right-hand) since the introduction of H7N7 into the flock and the infection of one animal

Discussion

For this model parameter values were taken from only two transmission experiments with five infectious and five susceptible animals. It is also unclear whether these values truly represent field data. Dosis effects under field conditions are unknown, as well as contact rates between the animals.

Another assumption made in this model, is that all R animals are dead. However, in the transmission experiment three out of ten susceptible animals survived a contact infection (Van der Goot *et al.*, 2005), meaning that some R animals in the experiments did not die. In field data there may be more infected animals than the counted dead ones; thus the model may overestimate the number of dead animals. This model may therefore lead to an underestimation of the time since introduction, unless there are multiple introductions in the field data. Multiple introductions would lead to a more quickly increase of the number of dead animals in contrast to the model, therefore the model would overestimate the time since introduction. Further effort will focus on sensitivity analysis, as well as on estimating the transmission parameter values from field mortality data.

Conclusion

The model indicates that after a single introduction into a flock it may take considerable time before a noticeable increase in mortality is observed, more so if not all infected animals die.

References

Full references are available from the author.

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