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Qualitative dynamics of lowly- and highly-pathogenic avian influenza strains

F.B. Agusto [a], A.B. Gumel [b,*]

[a] Department of Mathematics, Austin Peay State University, Clarksville, TN 37040, USA
[b] Department of Mathematics, University of Manitoba, Winnipeg, Manitoba, Canada R3T 2N2

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ABSTRACT

A new deterministic model for the transmission dynamics of the lowly- and highly-pathogenic avian influenza (LPAI and HPAI) strains is designed and rigorously analyzed. The model exhibits the phenomenon of backward bifurcation, where a stable disease-free equilibrium co-exists with a stable endemic equilibrium whenever the associated reproduction number is less than unity. It is shown that the re-infection of birds infected with the LPAI strain causes the backward bifurcation phenomenon. In the absence of such re-infection, the disease-free equilibrium of the model is globally-asymptotically stable when the associated reproduction number is less than unity. Using non-linear Lyapunov functions of Goh–Volterra type, the LPAI-only and HPAI-only boundary equilibria of the model are shown to be globally-asymptotically stable when they exist. A special case of the model is shown to have a continuum of co-existence equilibria whenever the associated reproduction numbers of the two strains are equal and exceed unity. Furthermore, numerical simulations of the model suggest that co-existence or competitive exclusion of the two strains can occur when the respective reproduction numbers of the two strains exceed unity.

1. Introduction

Avian influenza is a contagious disease of animals caused by influenza viruses belonging to the family *Orthomyxoviridae* [2]. The *Orthomyxoviridae* family consists of five genera: *Influenzavirus* A, *Influenzavirus* B, *Influenzavirus* C (also known as Influenza Types A, B and C), *Isavirus* and *Thogotovirus*. Only viruses of the *Influenzavirus* A genus are known to infect birds (thus, termed avian influenza (AI) viruses). The Type A influenza viruses are divided into subtypes based on the antigenic relationships in the surface glycoproteins, haemagglutinin (HA) and neuraminidase (NA). At present, 16 HA subtypes (H1–H16) and nine NA subtypes (N1–N9) have been identified [19]. Each virus has one HA and one NA antigen, apparently in any combination. All influenza A subtypes in the majority of possible combinations have been isolated from avian species [3]. Influenza A viruses that infect poultry can be categorized into two main disease forms, distinguished by low and high extremes of virulence. The lowly virulent viruses causes the lowly-pathogenic avian influenza (LPAI), which causes only mild symptoms and may easily go undetected [2,3]. The very virulent viruses cause the highly-pathogenic avian influenza (HPAI), which is far more dramatic (it spreads very rapidly and has mortality rate of about 90–100% [3,39]). Only viruses of H5 and H7 subtypes have been shown to cause HPAI in susceptible species, but not all H5 and H7 viruses are virulent [2].

Wild birds (such as gulls, shorebirds, ducks, geese and swans) are known to be natural reservoirs of LPAI, and have been found to be either asymptomatic to, or suffer mild infection from, the LPAI strain [8,47,51]. Migratory birds (especially waterfowl) are largely the main reservoir of all 16 subtypes of influenza A viruses, including the H5 and H7 subtypes (usually in the lowly-pathogenic form) [3,47,51]. It remains unclear what role migratory birds play in the transmission dynamics of highly-pathogenic H5N1 viruses [46]. Some authors claim that migratory birds play no role in the transmission of H5N1 to domestic poultry [17,18,38,46]. In a recent study, Takekawa et al. [38] showed temporal mismatch between the timing of wild duck movements and outbreaks of HPAI H5N1. In particular, migratory wild ducks (excluding the resident Chinese spotbill and mallard ducks) moved to breeding areas in Northern China, Eastern Mongolia, and Eastern Russia *via* the East Asian Flyway along the coast (and none migrated toward Qinghai Lake on the West, thus failing to show any migratory connection to the Central Asian Flyway). Their analysis further indicated that HPAI H5N1 outbreaks reported in the flyway were related to latitude and poultry density, but not to the core migration corridor or to wetland habitats. Some other authors assert that migratory birds are responsible for the transmission of the virus (in places such as the People's Republic of China, Mongolia, Russia, Europe, Africa and Australia) [9,21,26,30,31,33,34,41,42,48]. It is also known, *via* phylogenetic analysis or genetic sequences, that wild birds contribute to further spread of the virus [12,30,37,45].

Data shows that LPAI viruses are widely distributed in wild bird species around the world [15]. Furthermore, it has been shown that

* Corresponding author.
E-mail address: gumelab@cc.umanitoba.ca (A.B. Gumel).

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wild migratory birds can be infected and may spread disease to local poultry flocks (as evident from the HPAI H5N1 isolates in egrets, herons, and peregrine falcons from Hong Kong in 2003 and 2004 and the Qinghai Lake outbreak [46]). There is a general belief that the 2010 HPAI H5N1 virus was originally introduced from wild birds to poultry as an LPAI virus, and later mutated in the domestic poultry birds from low to high pathogenicity [2,4,25,47] (and then spilled back into the wild bird population). Thus, there is an evolving interplay among avian influenza viruses that circulate back-and-forth between domestic and wild birds, and the potential for mutations in the avian system is increased.

A number of avian influenza modelling studies, focusing on the transmission dynamics within the human and avian populations, have been presented in the literature (see, for instance, [1,22,27,32]). Agusto and Gumel [1] gave a theoretical assessment of the population-level impact of an imperfect avian influenza vaccine for domestic poultry birds, using a multi-strain deterministic model. Iwami et al. [27] presented a deterministic model for the transmission dynamics of avian influenza in the avian population only (although their model allows the possibility of transmission of an avian influenza mutant within humans). Gumel [22] extended the Iwami et al. study by incorporating the dynamics of wild and domestic birds and the isolation of birds with symptoms of both the avian and mutant strains. Lucchetti et al. [32] included the wild bird population as a periodic source, feeding infection to the coupled domestic bird-human system, and allowed for mutation between the lowly- and highly-pathogenic strains. The current study extends the aforementioned studies, particularly those in [1] and the (avian component of the) studies in [22,32], by designing a new, comprehensive, model for the transmission dynamics of the lowly- and highly-pathogenic avian influenza strains within the domestic and wild birds populations. The new model incorporates the back-and-forth virus interplay between domestic and wild birds, as well as the ensuing viral mutation within the poultry population.

2. Model formulation

The total domestic birds population at time t, denoted by $N_d(t)$, is split into the compartments of susceptible ($S_d(t)$), exposed ($E_{id}(t)$), symptomatic ($I_{id}(t)$) and recovered ($R_d(t)$) birds, where $i = l, h$ represent domestic birds with LPAI and HPAI, respectively. Thus,

$$N_d(t) = S_d(t) + E_{id}(t) + I_{id}(t) + R_d(t).$$

Similarly, the total population of wild birds is divided into susceptible ($S_w(t)$), exposed ($E_{iw}(t)$), symptomatic ($I_{iw}(t)$) and recovered ($R_w(t)$) wild birds (where $i = l, h$ represent wild birds with LPAI and HPAI, respectively), so that

$$N_w(t) = S_w(t) + E_{iw}(t) + I_{iw}(t) + R_w(t).$$

In this study, "exposed birds" are infected birds with no disease symptoms but are capable of transmitting the infection to susceptible birds.

The population of susceptible domestic birds is generated by birth (recruitment) of domestic birds at a constant rate π_d. It is decreased by infection, following effective contact with infected domestic birds with LPAI and HPAI, at rates

$$\lambda_{ld} = \beta_{ld}(E_{ld} + \eta_1 I_{ld}) \text{ and } \lambda_{hd} = \beta_{hd}(E_{hd} + \eta_2 I_{hd}), \quad (1)$$

respectively. It should be stated that mass action incidence function is used in (1) for mathematical convenience (see also [22,27,32]). Furthermore, it is assumed that susceptible domestic birds acquire infection from infected wild birds, with LPAI and HPAI, at the rates

$$\lambda_{lw} = \beta_{lw}(E_{lw} + \eta_3 I_{lw}) \quad \text{and} \quad \lambda_{hw} = \beta_{hw}(E_{hw} + \eta_4 I_{hw}), \quad (2)$$

respectively. In (1) and (2), the parameters $\beta_{ld}, \beta_{hd}, \beta_{lw}$ and β_{hw} represent the associated contact rates, and η_i $(i = 1, \ldots 4) > 1$ are the modification parameters accounting for the assumption that infected birds in the symptomatic classes ($I_{id}; I_{iw}$) are more infectious than infected birds in the corresponding exposed classes ($E_{id}; E_{iw}$). Domestic birds in all epidemiological classes suffer natural death (at a rate μ_d).

Exposed domestic birds with LPAI are generated when susceptible domestic birds acquire LPAI infection from infected (both exposed and symptomatic) domestic and wild birds with the LPAI strain (at the rates λ_{ld} and λ_{lw}), respectively. The exposed LPAI population is reduced by mutation into the HPAI strain (at a rate ξ; a fraction, m, of these mutants is assumed to be in the E_{hd} class, while the remaining fraction, $(1 - m)$, is assumed to be in the I_{hd} class). This population is decreased by development of disease symptoms (at a rate σ_{ld}; a fraction, κ_1, of these symptomatic birds are assumed to be in the I_{ld} class, while the remaining fraction, $(1 - \kappa_1)$, is assumed to be in the I_{hd} class). Furthermore, the population of exposed birds in the E_{ld} class is decreased by re-infection following effective contacts with infected domestic birds with HPAI (at a reduced rate $\theta_1\lambda_{hd}$; with $0 \leqslant \theta_1 < 1$ accounting for the lower probability of re-infection occurring in comparison to primary infection) and infected wild birds with HPAI (at a rate $\theta_1\tau_1\lambda_{hw}$; where $0 \leqslant \tau_1 < 1$ accounts for the reduced likelihood of the wild birds re-infecting domestic birds). It is assumed that only birds with clinical symptoms of the HPAI strain can re-infect birds infected with the LPAI strain (see also [32]). It is further assumed that re-infected domestic birds with LPAI move to the symptomatic domestic HPAI class.

The population of symptomatic domestic birds with LPAI is generated at the rate $\kappa_1\sigma_{ld}$. This population is reduced by recovery (at a rate α_d), natural death (at the rate μ_d) and re-infection (at a rate $\theta_2(\lambda_{hd} + \tau_2\lambda_{hw})$; with θ_2 and τ_2 defined in similar way as θ_1 and τ_1 above). The population of recovered domestic birds with LPAI is generated at the rate α_d. This population is reduced by natural death (at the rate μ_d). It is assumed that recovered birds receive sufficiently enough immunity so that they are no longer susceptible to re-infection (that is, there is no transition from the recovered to the susceptible class).

The population of exposed domestic birds with HPAI is generated by the infection of susceptible domestic birds (following effective contacts with infected (both exposed and symptomatic) birds with the LPAI and HPAI strains (at the rate λ_{hd} and λ_{hw}, respectively). It is further increased by the mutation of exposed birds with LPAI (at the rate $m\xi$). This population is decreased by the development of disease symptoms (at a rate σ_{hd}) and by natural death (at the rate μ_d). The population of symptomatic domestic birds with HPAI is generated by the progression of exposed birds with LPAI (at the rate $(1 - \kappa_1)\sigma_{ld}$), mutation of exposed birds with LPAI (at the rate $(1 - m)\xi$) and the progression of exposed birds with HPAI (at the rate σ_{hd}). This population is further increased by the re-infection of domestic birds with LPAI. It is decreased by natural death (at the rate μ_d) and disease-induced death (at the rate δ_d). It is assumed that both exposed and symptomatic domestic birds with HPAI do not acquire re-infection (see also [32]). Furthermore, it is assumed that domestic birds with symptoms of HPAI do not recover, since the HPAI-associated mortality rate is about 90–100% (see also [3,39]).

The equations for the dynamics of the wild birds are similarly formulated (and the detailed description of their derivation is not repeated here), except to state that wild birds suffer natural death at a rate μ_w, disease-induced death occurs at a rate δ_w and no mutation is assumed for the exposed wild birds with the LPAI (unlike in the case of exposed domestic birds with LPAI [32]). It is also assumed that recovered wild birds do not become susceptible to re-infection again (and that wild birds with clinical symptoms of