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A modeling study of human infections with avian influenza A H7N9 virus in mainland China

Zhifei Liu[a], Chi-Tai Fang[b,c,*]

[a] School of Public Health, Lanzhou University, Lanzhou, mainland China
[b] Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, 17 Xu-Zhou Road, Taipei 100, Taiwan
[c] Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

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SUMMARY

Objectives: Since February 2013, more than 400 laboratory-confirmed human cases of avian influenza A H7N9 infection have been reported in mainland China. Little is known of the dynamics of this novel virus in poultry and human populations, which is essential for developing effective long-term control strategies for this zoonosis. The aim of this study was to evaluate the impact of screening and culling of infected poultry on the evolution of the H7N9 epidemic.

Methods: A mathematical model for transmission dynamics of avian influenza A H7N9 virus in human and poultry populations was constructed. Parameters in the model were estimated using publicly available nationwide surveillance data on animal and human infections.

Results: By fitting a two-host model, it was shown that screening for H7N9 in poultry and culling could effectively decrease the number of new human H7N9 cases. Furthermore, the elimination of circulating H7N9 virus is possible if an intensive, but technically feasible, poultry screening and culling policy is adopted.

Conclusions: Screening and culling infected poultry is a critical measure for preventing human H7N9 infections in the long term. This model may provide important insights for decision-making on a national intervention strategy for the long-term control of the H7N9 virus epidemic.

1. Introduction

The first case of human infection with a novel influenza A H7N9 virus occurred in mainland China in February 2013.[1,2] By May 19, 2014, there had been 433 laboratory-confirmed human cases. Fever, cough, sputum, and shortness of breath are the most common clinical presentations.[3] More than 80% of cases have involved patients who had been exposed to live poultry.[4,5] Infection with this H7N9 virus frequently leads to severe, life-threatening disease in humans. In contrast, this new type of virus has very low pathogenicity in poultry.[6,7]

To prevent poultry-to-human transmission of this novel reassortant virus, the health authorities closed live poultry markets. The number of new-onset human cases with H7N9 virus infection decreased rapidly.[8] However, little is known of the dynamics of this novel virus in poultry and human populations, which is essential for developing effective long-term control strategies for this zoonosis.

The aims of this study were to develop a dynamic model for the transmission of H7N9 virus in both poultry and human populations in order to estimate the reproductive numbers (R_0) of this virus and to evaluate the impact of the screening and culling of infected poultry on the evolution of the H7N9 epidemic.

2. Methods

2.1. Study design

A mathematical model to describe the transmission of avian influenza A H7N9 virus among two hosts – humans and poultry – was constructed. Parameters in the model were estimated using publicly available nationwide surveillance data of animal and human infections.

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[*] Corresponding author. Tel.: +886 2 3366 8035; fax: +886 2 2351 1955.
E-mail address: fangct@ntu.edu.tw (C.-T. Fang).

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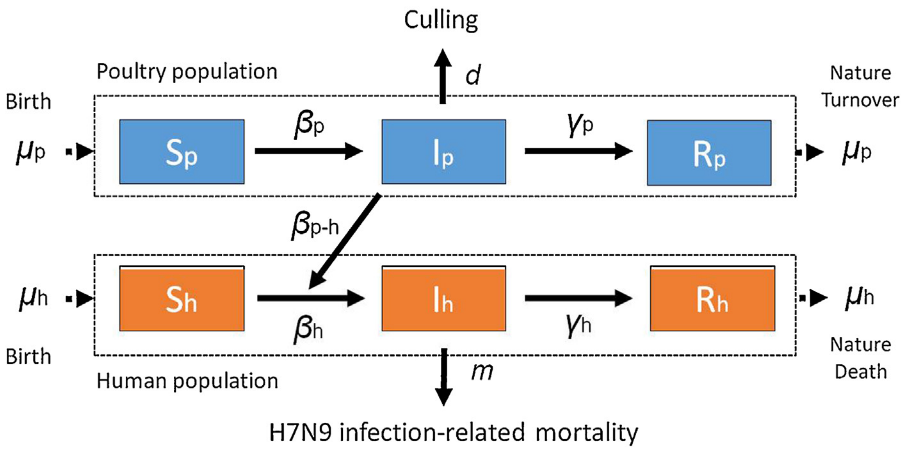

Figure 1. The two-host model of H7N9 virus transmission in humans and poultry. See text for the definitions of symbols and the dynamic differential equations.

2.2. *The two-host model*

It was assumed that the novel influenza A H7N9 virus can spread rapidly among poultry and can be transmitted easily from poultry to humans, but has only a limited capacity for human-to-human transmission. A SIR modeling approach was used; for each of the two hosts, there are three mutually exclusive states: susceptible (S), infectious (I), and recovered (R) (Figure 1).

2.3. *The poultry host*

The poultry hosts have three states: susceptible poultry (S_P), infected poultry (I_P), and recovered poultry (R_P). It was assumed that the birth rate of poultry (μ_p) is equal to their natural turnover rate in poultry-raising farms. Susceptible poultry are infected through poultry-to-poultry transmission at a rate of β_p. Infected poultry have three alternative outcomes: natural turnover, recovery, or culling (after detection of H7N9 virus in the farm). Parameters γ_p and d represent the rates of recovery and culling, respectively (Figure 1).

2.4. *The human host*

The human hosts also have three states: susceptible people (S_h), infected people (I_h), and recovered people (R_h). It was assumed that the birth rate (μ_h) of the human population is equal to the natural death rate, which is estimated by the inverse of life expectancy at birth. Susceptible people become infected through poultry-to-human transmission at a rate of β_{p-h}. Susceptible people can also become infected through human-to-human transmission at a rate of β_h. Infected people had three alternative outcomes: H7N9 infection-related death, recovery, or natural death. Parameters m and γ_h represent the rates of infection-related mortality and recovery, respectively (Figure 1).

2.5. *The interventions*

The effect of screening and culling infected poultry at different levels of intensity was modeled by adjusting the numerical value of the culling rate d. The differential equations that describe the effect of interventions are summarized below; S_P, I_P, R_P, S_h, I_h, and R_h represent proportions of the state among the total host populations, respectively.

$$
\begin{cases}
\dfrac{dS_p}{dt} = \mu_p - \beta_p S_p I_p - \mu_p S_p, \\
\dfrac{dI_p}{dt} = \beta_p S_p I_p - d I_p - \gamma_p I_p - \mu_p I_p, \\
\dfrac{dR_p}{dt} = \gamma_p I_p - \mu_p R_p, \\
\dfrac{dS_h}{dt} = \mu_h - \beta_h S_h I_h - \beta_{p\text{-}h} S_h I_p - \mu_h S_h, \\
\dfrac{dI_h}{dt} = \beta_h S_h I_h + \beta_{p-h} S_h I_p - m I_h - \gamma_h I_h - \mu_h I_h, \\
\dfrac{dR_h}{dt} = \gamma_h I_h - \mu_h R_h,
\end{cases}
$$

2.6. *Source of data*

The information on cases of human infections with influenza A H7N9 virus (Table 1) were obtained from the websites of the Chinese Center for Disease Control and Prevention (CDC) (http://www.chinacdc.cn/) and the National Health and Family Planning Commission (http://www.nhfpc.gov.cn/zhuzhan/). The data included residence, age, sex, and the date of illness onset (or the laboratory confirmation date). The date of illness onset of human cases was estimated from the laboratory confirmation date if the information on the date of onset was missing, based on the average interval of 1 week from illness onset to laboratory confirmation.[7]

Table 1
Numbers of human influenza A H7N9 infection cases in Shanghai, Zhejiang, and Jiangsu

Time (week)	Jiangsu	Zhejiang	Shanghai	Total No. of cases	Natural logarithm[a]
Feb 18 – Feb 24	0	0	1	1	
Feb 25 – Mar 3	0	0	1	1	
Mar 4 – Mar 10	0	0	0	0	
Mar 11 – Mar 17	0	0	0	0	
Mar 18 – Mar 24	6	0	0	6	1.791759[b]
Mar 25 – Mar 31	4	3	2	9	2.197225[b]
Apr 1 – Apr 7	3	8	9	20	2.995732[b]
Apr 8 – Apr 14	7	22	3	32	3.465736[b]
Apr 15 – Apr 21	0	12	0	12	
Apr 22 – Apr 28	0	1	0	1	

[a] Natural logarithm transformation of the total numbers of cases.

[b] Exponential phase (March 18 to April 14, 2013). The slope of the natural logarithm transformation (for the total numbers of cases) over time is the rate of exponential growth of the H7N9 epidemic in humans.