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Citation	Annual Report of FY 2007, The Core University Program between Japan Society for the Promotion of Science (JSPS) and Vietnamese Academy of Science and Technology (VAST). 2008, p. 548-551
Version Type	VoR
URL	<a href="https://hdl.handle.net/11094/13176">https://hdl.handle.net/11094/13176</a>
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# PREVENTION OF AVIAN INFLUENZA EPIDEMIC: WHAT POLICY SHOULD WE CHOOSE?

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## ABSTRACT

Human-to-human transmission of the avian influenza has been extremely rarely reported, and is considered as limited, inefficient and unsustainable. However, experts warn an occurrence of "mutant avian influenza", which can easily spread among humans, because the avian influenza is already endemic, in particular in Asian poultry, and it is evolving in domestic and wild birds, pigs and humans. Outbreak of such mutant avian influenza in the human world may have devastating consequences, which are comparable with these for the 1918 "spanish influenza". In this paper we develop a mathematical model for the spread of the mutant avian influenza, and explore the effectivity of the prevention policies, namely the elimination policy and the quarantine policy.

## KEYWORDS

Epidemic model; Avian influenza; Mutation; Elimination policy; Quarantine policy

## INTRODUCTION

Influenza is an ancient disease that sometimes in the recorded history had devastating effects on the humans. The best recorded catastrophic influenza pandemic was the 1918 "Spanish influenza". It is estimated that at least one third of the world population (or 500 million people) was infected and had clinically apparent illnesses during the 1918--1919 influenza pandemic. The disease was exceptionally severe: fatality rates exceeded 2.5%, compared to  $< 0.1\%$  for other known influenza pandemics. The total death toll was estimated at 50 million and were arguably as high as 100 million. The cause of this 1918 pandemic is unknown, as it is unknown whether that was linked to avian or swine influenza. Avian influenza (H5N1) is an infection caused by avian (bird) influenza (flu) viruses. These influenza viruses occur naturally among birds. Wild birds worldwide carry the viruses in their intestines, but usually do not get sick from them. However, avian influenza is very contagious among birds and can make some domesticated birds, including chickens, ducks, and turkeys, very sick and kill them.

Usually, "avian influenza virus" refers to the influenza A virus, which is found mainly in birds. The risk of direct passing of this virus to the humans is generally very low. Nevertheless, a number of confirmed cases of human infection with several subtypes of the avian influenza have been recorded since 1997 in Hong Kong. The most of these cases have been resulted from contacts with the infected poultry, or with the surfaces contaminated with secretion/excretions of the infected birds. The human-to-human transmission of avian influenza virus has been exceptionally rarely reported, and is considered as limited, inefficient and unsustainable. However, there are warnings, by

experts, on occurrence of the so-called "mutant avian influenza", which can be easily transmitted among the humans. The spread of this mutant strain can potentially have the consequences comparable with these of the spanish influenza. The only presently available medicine to fight the virus is the antiviral drug "Tamiflu". This drug is clinically effective against the avian influenza virus and can be used for both treatment and prevention. But the drug is expensive, and the supply is limited. On the other hand, the WHO estimates that the egg-based H5N1 vaccine production yield is inferior to seasonal influenza strains, with the result that the maximum annual vaccine yield may be of the order of 500 million doses. Under such circumstances, it appears that prevention by all means of the avian influenza from spreading in the human world is the best available policy. It is important, therefore, to know the mechanism of this spreading. Furthermore, to choose the best (or at least successful) prevention policy, we have to explore the likely outcomes for several alternative policies which have been suggested. In this paper, we construct a mathematical model, which interprets passing of the avian influenza from birds to the humans, and evaluates the effectivity of prevention policies.

## MATERIALS AND METHODS

Avian influenza virus does not usually infect humans; however, several instances of human infections and outbreaks of avian influenza have been reported since 1997. The avian influenza virus can be transmitted directly from birds or from avian virus-contaminated environments to humans. We postulate, therefore, that the transmission of the avian influenza for the humans is restricted to the interaction from birds to the humans. We suggest the following mathematical model to interpret the spread of the avian influenza:

$$X' = c - bX - \omega XY,$$

$$Y' = \omega XY - (b+m) Y,$$

$$S' = \lambda - \mu S - \beta_1 SY,$$

$$B' = \beta_1 SY - (\mu + d_1)B.$$

Here, X, Y, S and B denote respectively the susceptible birds, the birds infected with the avian influenza, the susceptible humans and the humans that are infected with the wild avian influenza. The parameters c and  $\lambda$  are the rates of birth for the birds and the humans, respectively. The birds and the humans die from the natural causes at the rates b and  $\mu$ , respectively. Furthermore, m and  $d_1$  are the death rates inflicted by the disease. The parameters  $\omega$  and  $\beta_1$  are the rate at which avian influenza is contracted from an average infected bird (i.e. the infection transmission rate); then  $\omega Y$  and  $\beta_1 Y$  can be viewed as the force of infection from the infected birds for the wild avian influenza.

In 2003, during an outbreak of the avian influenza among poultry in the Netherlands, the people who handled the infected poultry and members of their families was infected with the influenza A (H7N7). Human infections with H5N1 were reported at the beginning of 2004; these cases also mostly resulted from contacts with infected poultry. The mentioned cases are believed to be the results of the direct contacts of the humans with the infected poultry or the contaminated environment. However, at least one instance of the human-to-human spread is thought to have occurred in Thailand. More than 80 cases of the disease were confirmed by tests. Fortunately, there was evidence that the person-to-person spread of the infection was limited, and that no sustained human-to-human transmission occurred in this or other outbreaks of the avian influenza. However, in fact, the avian influenza viruses are inherently unstable. These viruses lack of a genetic proof-reading mechanism, and therefore the small errors, which occur when the virus copies itself, go undetected and uncorrected. Since the specifics of mutations and evolution of the influenza viruses cannot be predicted, it is hardly possible to know if or when a virus, such as H5N1, might acquire the properties needed to spread easily and sustainably among the humans. This difficulty is

increased by the present lack of understanding which specific mutations may increase the transmissibility of the virus among the humans. Experts warn about an occurrence of the so-called "mutant avian influenza", which can be easily transmitted among the humans with potentially devastating consequence, because the avian influenza is already endemic, in particular in Asian poultry, and is evolving in domestic and wild birds, pigs and humans. In fact, some mutant virus has been already detected in Asia, although, fortunately, so far the virus does not have the power to sustain the transmission among the humans. We now simply assume, therefore, that within the infected human hosts the virus of the wild avian influenza mutates at a sufficiently small constant rate to the mutant virus, which can spread in a human population. That is, the human infected with wild avian influenza mutates to one with mutant avian influenza at sufficiently small constant rate. In reality mutations may also occur in the infected birds and other vectors, such as aquatic birds and pigs. However, the mechanism of these mutations is unclear, and at this stage we disregard such possibilities. This assumption leads to the following mathematical model with the mutation process of the avian influenza:

$$X' = c - bX - \omega XY,$$

$$Y' = \omega XY - (b+m)Y,$$

$$S' = \lambda - \mu S - (\beta_1 Y + \beta_2 H)S,$$

$$B' = \beta_1 SY - (\mu + d_1 + \varepsilon)B,$$

$$H' = \beta_2 SH + \varepsilon B - (\mu + d_2)H.$$

Here,  $H$  denotes the humans infected with the mutant avian influenza; the parameter  $\varepsilon$  is the mutation rate,  $d_2$  is the additional death rate induced by mutant avian influenza, and  $\beta_2$  is the transmission rate of the mutant avian influenza in the human population. Thus,  $\beta_2 H$  can be viewed as the force of infection by infected humans for the mutant avian influenza.

## RESULTS AND DISCUSSION

By using mathematical model, we evaluate the effect of prevention policies (elimination of infected birds, quarantine of infected humans with mutant avian influenza). For example, we consider "single mutation case" in our mathematical model. If the probability of mutation is low and the mutation rate is sufficiently small, then a long period without recurrent mutations follows after an occurrence of a single mutation. Then we can neglect the mutation process (i.e.,  $\varepsilon = 0$ ).

For the elimination policy, we can conclude as follows; if the mutant virus has a lower level of virulence than the wild virus ( $d_1 > d_2$ ), then the elimination of the infected birds increases the total number of the infected humans. However, if the mutant virus has higher virulence ( $d_1 < d_2$ ), then the policy has a favorable outcome leading to reduction of the number of cases. Further, the complete quarantine policy is very effective because the total number of the infected humans decreases, and the mutant avian influenza dies out. However, in the real life situation we can hardly expect that the execution of the complete quarantine policy would be possible. Further, we can obtain the following results about the incomplete quarantine policy; if the mutant virus has a lower virulence than the wild virus, then the incomplete quarantine policy is effective. On the other hand, if the mutant virus has a higher virulence, then the effectivity of the policy depends on the transmission rate of the wild strain  $\beta_1$ . That is, the incomplete quarantine policy is effective when the transmission rate of the wild avian influenza  $\beta_1$  is low. But the incomplete quarantine policy is ineffective when the transmission rate is relatively high.

## CONCLUSIONS

In this study we focus at the effectivity of the two types of prevention policies, namely the elimination policy and the quarantine policy. Our qualitative and theoretical results are as follows: the effectivity of the policies depends on the mutation rate, the transmission rates and the virulence evolution. The optimal choice of a policy depends on the properties of the new mutant strain, and it is crucial, therefore, for the correct choice to obtain in the shortest possible time virological understanding (such as the virulence of the mutant virus) and epidemiological surveillance (such as the transmissibility of the mutant virus) for this new strain.

## ACKNOWLEDGEMENT

This study is partial supported by Research Fellowships of the Japan Society for the Promotion of Science for Young Scientists, the Japan Society for the Promotion of Science and is currently supported by the Science Foundation Ireland Mathematics Initiative through MACSI and the National Natural Science Foundation of China (10571143), the Science Foundation of Southwest University (SWNU2004001) and the Japanese Government (Monbukagakusho:MEXT) Scholarship.

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