Research Review of Human Infections with Avian Influenza A(H7N9) Virus in China

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Abstract. The emergence of H7N9 virus attracted worldwide concerns about the possibility of a new influenza pandemic in March 2013, and the human cases were mainly distributed in the southeast coastal areas in China, and the winter-spring season was the peak period for human infection with H7N9 virus. The studies on Human infections with avian influenza A(H7N9) virus at present are mainly divided into three categories: gene research, animal model research, outbreak simulation and risk prediction model research. The former two kinds of studies can provide lots of useful information on the mechanisms of H7N9 virus and the principles of infection, and the third kind of research can provide scientific basis and information decision-making tool for the prevention and monitoring of Human infections with avian influenza A(H7N9) virus. The impacts of environmental factors on H7N9 outbreak should be taken into account in the future study, and the closure of live poultry market as well as the suspension of live poultry trading should be vigorously pursued to control the spread of H7N9 epidemic in the high incidence areas in China.

Introduction

Following the H5N1, H9N2, H7N7, H7N2, H7N3 avian flu virus infected humans, in March 2013, the emergence of H7N9 virus attracted worldwide concerns about the possibility of a new influenza pandemic [5, 8, 15]. The world's first infection of H7N9 human case was started in mainland China, and H7N9 virus could cause a large number of infections in poultries and wild bird populations, as well as a very large threat to human health [31].

Human infections with avian influenza A(H7N9) virus of China kept recurring in recent years, and the human cases were mainly distributed in the southeast coastal areas in China, such as Jiangsu, Zhejiang, Fujian, Guangdong and Shanghai), at the same time increasing in the number of cases also gradually appeared in other areas such as Hunan, Anhui, Jiangxi, Henan, Guangxi, Shandong, Beijing, Hebei and Xinjiang, and the outbreak showed obvious trend of spatial diffusion. Overall, the winter-spring season was the peak period for human infection with H7N9 virus. Although there have been some families with cases of human infections of the H7N9 avian influenza in history, so far, the H7N9 virus has no evidence of sustained and effective human-to-human transmission [9, 21, 23, 28].

Research status analyses

Human infections with avian influenza A(H7N9) virus in China were affected by many factors such as natural environment, ecological environment, social environment and the epidemiological characteristics, the space-time propagation and infection mechanism of which were very complex. So far, scholars at home and abroad have mainly done research on Human infections with avian influenza A(H7N9) virus in the following three aspects:

Gene Research of H7N9 Virus. Genetic analyses showed that H7N9 avian influenza virus was a new multiple reassortment virus of H7N3, H7N9 and H9N2 [6, 12, 18]. H7N9 virus was reassorted

by HA gene of H7, NA gene of N9 and six internal gene fragments of H9N2 virus [20]. Although each fragment is highly homologous with the previously popular bird flu virus in east Asia, such genetic makeup has never been found in birds, humans or other animals [16, 19]. Tommy et al. found that [26] the HA gene of the H7N9 avian influenza virus may originate from the H7 subtype of avian influenza virus in the Chinese Yangtze river delta. Chengli et al. found that [7] the combination of H7N9 avian influenza virus with human receptor was much easier than with poultry receptors, and the virus could almost asymptomatic infected poultry, but it would cause severe respiratory disease in humans and lead to high mortality rate in humans. The above research results all showed that the complexity and the uncertainty of H7N9 avian flu virus, the particularity and severity of human infection with the virus, and the unknown virus transmission way, those all brought great difficulties in the disease controlling of Human infections with avian influenza A(H7N9) virus for relevant departments.

Animal Model Research of H7N9 Virus. Kreijtz et al. [17] estimated the pathogenesis of the H7N9 avian influenza virus based on a ferret model, and an effective animal model was constructed to show that the H7N9 bird flu virus causes pneumonia and determined the high pathogenicity of H7N9 virus in mammals. Gabbard et al. found that [11] H7N9 virus was able to replicate and spread effectively in guinea pig models, showing the adaptation to some mammals. In addition, some studies have confirmed that H7N9 virus can be transmitted through the mucosa and fecal - oral approach among mice in the same cage [24, 29, 32]. The above results of animal model researches indicated that although H7N9 virus had not fully adapted to humans, the high pathogenicity and adaptability of H7N9 virus to mammals could be determined, and the virus might already have the ability of spreading between mammals, all those increased the risk of human infections of H7N9 virus.

Outbreak Simulation and Risk Prediction Model Research of H7N9 Human Infections. Yu et al. [30] built a statistical model to explain the outbreak pattern for each city, using the Markov chain Monte Carlo method to fitting model, and found that closing live poultry markets could significantly reduce the incidence of Human infections with avian influenza A(H7N9) virus. Nishiura et al. [21] proposed a cluster distribution mathematical model to estimate the number of human-to-human transmission of the H7N9 virus, and found that there was not likely to appear large-scale human-to-human transmission nationwide in the short term. Pan et al. [22] analyzed the outbreak pattern of H7N9 epidemic empirically, and found that the space-time networks among the connected cities were distributed along the time sequence of the outbreak, which revealed that some areas in eastern China had higher non-uniform distribution risk of Human infections with avian influenza A(H7N9) virus. Chen et al. [4] believed that enhanced monitoring of humans and animals could ensure early detection and diagnosis of suspected cases, while the closure of live poultry markets also could reduce the risk of disease. Ai et al. [3] used conditional logistic regression factor analysis in cases and control, and found that H7N9 virus infection was significantly related with the live poultry exposure, the chronic medical conditions and related environmental exposure. Wang et al. [27] proposed a thermodynamic model based on entropy, and the dynamic process of urban infectious diseases was predicted and then found the possibility of human transmission still exist. Nishiura et al. [21] proposed a clustering mathematical model based on the proportion of cases with exposure history of live poultry, and the increase of transmission of H7N9 avian influenza virus was estimated by fitting the model. Shi et al. [25] established an epidemic diffusion analysis model based on epidemic propagation theory, and deduced the space-time trend of the epidemic. Han et al. [13] analyzed the relationship between Human infections with avian influenza A(H7N9) virus in Huzhou city and the exposure of live poultry, and found that there was an obvious epidemiological link between them. In addition, the closure of live poultry markets and the suspension of live poultry trading were effective measures to control the spread of the H7N9 virus in the high-incidence areas, which could significantly reduce the incidence of outbreaks [2], and the live poultry markets infected by H7N9 virus were the most likely source of the epidemic [4, 6, 10].

Summary

The studies on Human infections with avian influenza A(H7N9) virus at present are mainly divided into three categories: gene research, animal model research, outbreak simulation and risk prediction model research. Among them, genetic research and animal model research can provide a lot of useful information on the mechanisms of H7N9 virus and the principles of infection, and the research of outbreak simulation and risk prediction model can provide scientific basis and information decision-making tool for the prevention and monitoring of Human infections with avian influenza A(H7N9) virus in the future. It has been extremely difficult for CDC (Centers for Disease Control) to monitor H7N9 outbreak because of the complexity of the genetic make-up and the uncertainty source of H7N9 virus, at the same time the highly pathogenic of H7N9 virus to mammals has also greatly increased the risk of human infection with H7N9 virus. However, the results of the epidemic simulation and risk prediction model researches can provide scientific reference for the defense monitoring and effective control of H7N9 epidemic. According to the analyses of this study, the current risk prediction models of Human infections with avian influenza A(H7N9) virus mainly include mathematical model, dynamic model of epidemic disease, regression model, and so on, and these models can well reflect the transmission development process of H7N9 epidemic from macro to micro. But the spreading risk of Human infections with avian influenza A(H7N9) virus is determined by the interaction of multiple factors, and the outbreak has significant correlation with some environmental factors such as migratory birds, rivers, lakes, transportation, temperature, precipitation and humidity, and so on [1, 14], so future study should take into account the impact of environmental factors on H7N9 outbreak.

To sum up, it is necessary and urgent to assess the infection risk in various provinces and cities of China as Human infections with avian influenza A(H7N9) virus has spread rapidly and the number of cases has increased, and the construction of effective risk prediction model of Human infections with avian influenza A(H7N9) virus has important scientific research significance and practical application value for the monitoring and control of the epidemic. At the same time, the closure of live poultry market and the suspension of live poultry trading should be vigorously pursued to control the spread of the epidemic in the high incidence areas of H7N9 human infections.

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