

# H7N9 Influenza: The Emerging Infectious Disease

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## Abstract

Influenza virus infection is a common respiratory pathogen. Emerging of new atypical influenza is usually a big public health threat. H7N9 bird flu is the newest atypical influenza virus infection that has just been reported since early 2013. The emerging of this new disease occurred in China and becomes the present focus for possible worldwide pandemic. In this specific article, the author will discuss and describe on epidemiology, symptomatology, pathology, diagnosis, treatment, and prevention of this new bird flu. The literature researching by PubMed and Google is used for data gathering in this collective review.

**Keywords:** Bird, Emerging, H7N9, Influenza

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## Introduction

Influenza virus infection is a common respiratory pathogen. In fact, there are several groups of influenza viruses, which are proved to be the causes of respiratory tract infections in human beings as well as in other animals. In human beings, the influenza virus infection can be seen worldwide with a wide range of epidemic areas. Each year, million illnesses are reported. As a virus, the possible mutation can be expected, and any sense mutation can result in new problematic virus. The new atypical influenza virus can be the cause of new disease that can cause the worldwide pandemic.<sup>[1,2]</sup>

There are many historical outbreaks due to emerging of new atypical influenza viruses. Within the past decade, there are several new epidemics due to new atypical respiratory viruses such as H5N1 bird flu<sup>[3]</sup> and H1N1 swine flu.<sup>[4]</sup> Emerging of new atypical influenza is usually a big public health threat. H7N9 bird flu is the newest atypical influenza virus infection that has just been reported since early 2013. Indeed, there is a previous big

outbreak of bird flu due to H5N1 influenza virus.<sup>[3]</sup> At that time, the H5N1 influenza became the great concern in global public health.

Due to the nature of a new emerging infection, there are limited data on the natural history of H7N9 influenza infection. Hence, diagnosis and treatment are difficult. The first case was an 87-years-old male from Shanghai, China, with 19 February 2013 onset, and the confirmation on this new emerging infection by Chinese CDC was on 29 March 2013. In this specific article, the author discusses on the new H7N9 influenza infection, which has just been described since early 2013.<sup>[5,6]</sup>

## The First Report on New H7N9 Bird Flu in China

Bird flu is not a new thing. Bird flu usually means the influenza infection in avian. However, the case that human beings get the avian type influenza virus infection is usually problematic, and the atypical influenza virus infection can be the result. In early 2013, there are emerging cases of atypical infections in China presenting with the signs and symptoms of acute respiratory tract infection.<sup>[5,6]</sup> The clinical presentation of this new infection is classified into the respiratory disease. However, some atypical clinical manifestations can be seen. At first, the exact pathogenic cause of this new disease was unknown. Nevertheless, due to the modern technology, the pathogenic agent was finally determined as a kind of influenza virus, H7N9.<sup>[7]</sup>

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Indeed, H7N9 influenza is a kind of virus that is primarily seen in avian.<sup>[8,9]</sup> Existence as a human pathogen is considered an actual new emerging infection.<sup>[10]</sup> The new outbreak occurred in China and the clinical scientists finally succeeded in genetic analysis of the novel H7N9 influenza virus.<sup>[7]</sup> The new virus is considered to be the result from the genetic mutated classical avian H7N9 influenza virus and has high potential to cause mammal infection.<sup>[7]</sup> The sequence of this new pathogen has never been reported elsewhere; hence, the new problematic virus is accepted as a new H7N9 influenza virus. It is proved that there are at least four origins contributing to the sequence of the new H7N9 influenza virus.<sup>[11]</sup>

Briefly, the HA gene is derived from duck origin, and the NA gene from migratory birds infected with avian influenza viruses.<sup>[11]</sup>

The first report of swine flu is from Shanghai, China. The first indexed case was in February 2013. China became the present epidemic focus of this new emerging disease. Several infected cases have been continuously reported. Also, there were some death cases. However, after the primary emerging in the primary site in mainland of China, the disease finally spread to the new setting in Taiwan Island bringing more concern on the possibility of worldwide pandemic.<sup>[6,12]</sup>

### **Epidemiology of New H7N9 Influenza Infection**

The new H7N9 influenza infection can be seen in any age groups.<sup>[6]</sup> Both males and females can be infected.<sup>[6]</sup> However, in the outbreak in China, most patients are adult.<sup>[13]</sup> Li *et al.* analyzed the clinical epidemiology of 82 Chinese infected patients and found that “the median age was 63 years (range, 2 to 89), 73% were male, and 84% were urban residents.<sup>[14]</sup>” The significant higher incidence in the elderly than other groups is the question that needs further studies to explain.<sup>[15]</sup>

Of most cases, the main clinical features are “fever and rapidly progressive pneumonia that did not respond to antibiotics.<sup>[16]</sup>” Nevertheless, not all cases are severe, and not all cases require hospitalization.<sup>[14]</sup>

At present, the main question is on the relationship between the infection and poultry contact. Similar to the previous H5N1 bird flu, the avian contact can be identified in almost all patients.<sup>[14,16]</sup> According to the report by Li *et al.*,<sup>[14]</sup> only 77% have the history of avian contact. Therefore, the next question is which contribute to the infection in case with no history of avian contact. Adding to the cross species transmission, the great concern is on human-to-human transmission.

Of interest, the genetic mutation contributing to human adaptation of virus is reported, and the human-to-human transmission is the topic to be followed up and further studied.<sup>[17]</sup> Nevertheless, according to the mathematical predictive model study, the chance for human-to-human transmission is still low at present.<sup>[18]</sup>

### **Clinical Presentation of New H7N9 Influenza Infection**

The signs and symptoms of swine flu are similar to those seen in other respiratory tract infections. The main clinical features of influenza, high fever, coughing, and myalgia can be seen.<sup>[5,6]</sup> In severe cases, the lung involvement is common.<sup>[5,6]</sup> Pneumonia is a common complication leading to tachypnea, hypoxemia, and respiratory difficulty.<sup>[5,6]</sup> In the worst case, respiratory distress and failure leading to death can be observed. Respiratory distress is the most common cause of death among the H7N9 bird flu cases, no regarding to existence of underlying personal illnesses.

In addition to the respiratory manifestation, the atypical clinical manifestations can be seen. Multiple organ involvement can be seen in severe cases. Heart failure, alteration of consciousness, alteration of thrombohemostasis, and renal impairment can be seen.<sup>[5,6]</sup> For the eye manifestation, conjunctivitis, which is common in H5N1 bird flu, is also common in H7N9 bird flu.<sup>[5,6]</sup> Also, diarrhea is also reported as an atypical gastrointestinal manifestation in H7N9 bird flu.<sup>[5,6]</sup>

### **Pathology of New H7N9 Influenza Infection**

The new H7N9 influenza virus mainly infects the respiratory tissue. However, there is no report on histopathological study of infected cases. Until present, no official autopsy reported is published. Nevertheless, there are some reports on clinical pathology assessment of the infected cases. The abnormalities of laboratory findings are reported. Leukopenia and lymphopenia, thrombocytopenia, impaired renal function and an increase in myocardial enzymes and aspartate aminotransferase are the main observations.<sup>[16,19]</sup> Increased serum cytokine or chemokine concentrations and disseminated intravascular coagulation are also observed along with disease progression.<sup>[16]</sup>

### **Diagnosis of New H7N9 Influenza Infection**

Based on clinical feature, the influenza might be preliminary diagnosed. However, it is not possible to differentiate the type of influenza, and diagnosis of specific new H7N9 bird flu needs laboratory support.<sup>[20,21]</sup> At present, the definitive diagnosis required molecular

diagnosis technique. A reverse-transcription PCR assay is required.<sup>[22]</sup> There is still no rapid test that can give the confirmation of H7N9 bird flu. The preparedness for good diagnostic tool for the new H7N9 bird flu is required.<sup>[23]</sup>

In clinical practice, it is recommended that any cases with high body temperature (more than 38.3 degree Celsius) and have the history of avian exposure or travel to the outbreak area should be primarily screened by influenza rapid test. If the result from screening is positive, starting the antiviral drug treatment is suggested, and further confirmation test for H7N9 bird flu should be done at the same time. It is observed that sputum is a better specimen than throat swab or viral detection.<sup>[16]</sup>

For diagnosis of complication of disease, chest radiography is useful for diagnosis of pneumonia. Normally, the chest radiography usually shows diffuse opacities and consolidation in complicated cases.<sup>[24]</sup> Those cases with severe progression of lung abnormalities usually end up with death.

### Treatment of New H7N9 Influenza Infection

The specific treatment is suggested for all cases with new H7N9 influenza infection. Indeed, not all new H7N9 infected cases are severe, and some cases are mild and can be treated as out - patient cases.<sup>[14]</sup> Due to the availability of antiviral drug, the use of antiviral drug is recommended for all cases. Antiviral drug is useful for not only getting rid of the infection but also controlling of disease spreading. The standard treatment for swine flu is similar to the classical influenza. The drug of choice is oseltamivir.<sup>[19]</sup> According to the interim guideline published by CDC,<sup>[25]</sup> standard dosage of oseltamivir as used for general influenza infection case should be applied. Nevertheless, until present, there is still no report on the efficacy and effectiveness of oseltamivir in treatment of new H7N9 influenza. For supportive treatment of cases with pneumonia, oxygen therapy and non-invasive mechanical ventilation should be considered.<sup>[19]</sup>

### Prevention of New H7N9 Influenza Infection

It is accepted that prevention is required for control of the expansion of the present H7N9 bird flu. The routine practice for prevention of respiratory tract infection must be applied. Avoidance for contact with ill avian is highly recommended.<sup>[26]</sup> For specific control by vaccine, there is still no vaccine for H7N9 influenza at present, but it is still under the process for production of the epidemic vaccine.<sup>[27]</sup> Focusing on chemoprophylaxis, post-exposure oseltamivir is recommended for some specific groups of patients such as diabetic patients<sup>[28]</sup> [Table 1].

**Table 1: Recommended dosage of oseltamivir for new H7N9 bird flu**

Purposes	Descriptions
Treatment	75 mg twice daily for 5 days, within 2 days of onset of symptoms
Prophylaxis	75 mg once daily for at least 10 days, within 2 days of exposure

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