An Update on the H7N9 Strain of the Influenza A Virus

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ABSTRACT

Currently, humanity lives in the verge of a world-wide epidemic of the H7N9 influenza A virus. This strain has turned out to be very virulent for humans and there have been many reported casualties already in several places around the globe. Concordantly, not much is known for the H7N9 strain. Herein, the authors intend to establish a modest database of current knowledge and informed opinion in different key areas of the H7N9 virus. The source of the virus, its infection routes and mutations remain unclear. Results of several recent studies will be further analyzed including clinical, virological and histopathological manifestations of H7N9, diagnosis modes and viral transmissibility. Treatment, vaccination and public concerns about a pandemic threat will be discussed as well. The present work is expected to act as an updated world reference for the H7N9 influenza A strain. Moreover, modes for tackling H7N9 will be proposed, focusing on RNA polymerase for further investigation as a potential pharmacological target. Hence, invaluable conclusions may be drawn that will lead to insights in the fight against the most recent and rather lethal H7N9 strain.

Keywords: Bioinformatics, Infection Routes, Influenza A Virus, Mutations, Novel Avian-Origin Influenza A (H7N9) Strain

H7N7 OUTBREAK

In February 2013, a novel avian-origin influenza A (H7N9) virus emerged in Eastern China. H7N9 infection is a grave medical concern, as it was reported to have infected humans for the first time. The World Health Organization (WHO) notified of illness onset between February 19 and March 15, 2013 when three human cases of influenza A (H7N9) were confirmed in Shanghai and in Anhui province. Five to ten days later, these patients developed severe pneumonia and progressive respiratory distress with a lethal outcome (Gao et al., 2013). What it is known about H7N9 so far is that as of 15 August 2013, 135 documented human cases have been confirmed, 44 cases have ended in death and approximately 87 patients have recovered, according to WHO.

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H7N9 is a serotype of the species Influenza virus A that causes influenza in avians and is an enveloped virus. Influenza, commonly referred to as "the flu", is an acute respiratory disease of avians and mammals. It is caused by emerging influenza enveloped RNA viruses of the Orthomyxoviridae family (orthos, Greek for "straight"; myxa, Greek for "mucus"). H7N9 infection is considered a new crossspecies zoonosis as it crossed from avian to human causing atypical influenza. According to further classification of influenza A virus that is based on two glycoproteins of its surface, H7N9 strain has the seventh type of hemagglutinin (H7) and the ninth type of neuraminidase (N9).

In the 20th century influenza A strains have caused three major flu epidemics among humans; the Spanish Flu in 1918, the Asian flu in 1957 and the Hong Kong Flu in 1968. These claimed the lives of approximately 50 million, 2 million and 1 million people, respectively. In 1997 and 2003, the H5N1 subtype emerged in Asia and caused a major outbreak in wild waterfowl in China in 2005 with lethal outcomes. The H7N9 virus was transmitted from animals to humans with a demonstrated >20% mortality rate (Gao et al., 2013; Tang & Chen, 2013; Yang et al., 2013). According to WHO, the H7N9 strain is the most lethal strain of influenza and is more transmissible to humans and more difficult to track down, as compared to H5N1 (Parry, 2013). However, there are a lot of unknown aspects of the H7N9 virus as well as diseases that might result from it, including the source of the virus, the infection routes and its mutations.

Cases are characterized by high fever and cough. Many of them have developed very serious illness, including severe pneumonia, acute respiratory distress syndrome (ARDS), hypoxemia, septic shock and multi-organ failure leading to death (Zhang et al., 2013; Lu et al., 2013). Most patients are male (68.5%) and elderly. In particular, 42.3% were 65 years of age or older (Li et al., 2013) indicating that the elderly may be at high risk for severe disease (Guan et al., 2013). A total of 61.3% of the patients had at least one underlying medical condition. In the meantime, an unusual case of a child infected in Beijing is being observed. This child displayed no symptoms while testing positive for H7N9, as he had been in contact with Beijing’s first confirmed case of H7N9 (Dai & Jiang, 2013).

Confirmed cases are mainly identified on China’s eastern coast around Shanghai (contiguous provinces; Anhui, Fujian, Henan, Hunan, Jiangsu, Jiangxi, Shandong, and Zhejiang), but have also been reported from Beijing and Shanghai (Koopmans & de Jong, 2013). Moreover, a case has been exported to Taiwan from mainland China (Chang et al., 2013). Although some patients have a history of contact with infected live poultry, contaminated environments or visiting live-animal markets before the onset of illness, the source of infection remains unclear (Bao et al., 2013; Chen et al., 2013). Moreover, there is no or limited evidence of sustained human-to-human transmission so far. The vast majority of confirmed cases seem to be epidemiologically unrelated, except a report of two family clusters of H7N9 cases (Rudge & Coker, 2013).

The important factor will be to determine the exact way of transmission. With this in mind, a research regarding infectivity and transmissibility of human H7N9 Influenza in Ferrets and Pigs has been conducted (Zhu et al., 2013). It was shown that the virus can transmit via air-borne exposure among mammals. Specifically, H7N9 replicated in the upper and lower respiratory tracts of the ferrets and was shed for 6 to 7 days, with ferrets showing relatively mild clinical signs. It was also transmitted via direct contact. Pigs could be infected and shed the virus for 6 days but were unable to transmit it to other animals. In this regard, under appropriate conditions, human-to-human transmission of the H7N9 virus may be possible and only careful serological surveys in China can reveal if such transmissions are underway (Nicoll & Danielsson, 2013).
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