Avian Influenza A(H7N9) 6 February 2014 Surveillance Update

Summary

The WHO has reported 298 human infections including 63 deaths with onset since February 2013. There are still no signs of ongoing, efficient, or sustained human transmission of this virus.

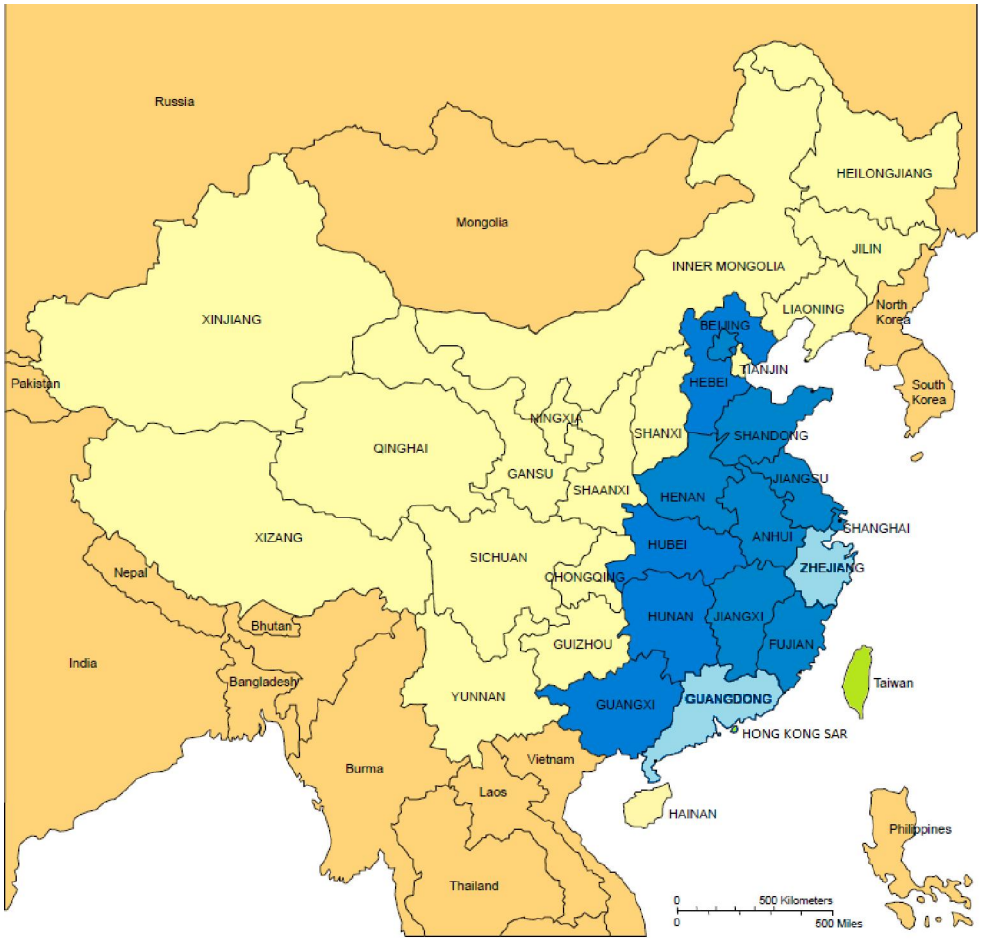
Key Points

- The H7N9 outbreak in southern China continues unabated, mainly affecting elderly people in contact with domestic poultry.
- No adaptation to efficient person-to-person transmission has been observed so far.
- Since 1 October 2013 there have been 165 sporadic cases reported in a 'second wave' of human H7N9 infections. All laboratory confirmed human infections have occurred in China (including Hong Kong), with imported cases reported in Taiwan.
- The Chinese government continues to take the following surveillance and control measures:
  - strengthen surveillance and situation analysis;
  - reinforce case management and treatment;
  - conduct risk communication with the public and release information;
  - strengthen international collaboration and communication; and
  - conduct scientific studies.
- Further sporadic human cases of A(H7N9) infection are expected in affected and possibly neighbouring areas, especially given expected increases in the trade and transport of poultry associated with the Lunar New Year celebrations.
- The epidemiology and virology of the second wave is similar to the first with sporadic cases and the majority reporting exposure to infected poultry and live market settings.
- Unlike the first wave which was mainly in the central eastern provinces, southern provinces are driving most of the H7N9 activity in the second wave of infections.
- Activity in the second wave is also far more concentrated with 125 (total second wave =165) reported from only two provinces: 73 from Zhejiang and 52 from Guangdong (Figure 1).
- Authorities across several provinces in eastern China announced market closures and bans on live poultry trading commencing in late January.

Cases

- The 2nd wave of cases, which began in October [2013] but rapidly increased in January, has reached 165 cases, compared with the first wave total of 136 (Figure 2).
- Accumulation of almost 300 cases in less than a year appears to be unprecedented for human cases of avian flu. For comparison, data from the WHO shows that the most active calendar year for the H5N1 strain, in 2006, saw 115 cases.
- As of 28 Jan 2014, the case fatality rate of all confirmed cases is 22 percent, but many cases are still hospitalized. Of all cases, 67 percent were male. The median age of reported cases is 58 years and that of fatal cases is 66 years (Figure 3).
- The disease caused by the virus is characterized by rapidly progressing severe pneumonia. Common symptoms are not disease specific and those of typical acute respiratory infection, such as fever, cough, and shortness of breath. Complications include the acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure requiring intensive care and mechanical ventilation. A small number of patients with mild clinical illness have been detected through on-going influenza-like illness (ILI) surveillance systems and contact tracing in otherwise healthy children and young adults.

Figure 1 Distribution of cumulative number of human cases of avian influenza A(H7N9), by province, China, to 4 February 2014 (n=299)



*299 total cases/64 deaths

Province/ City	Number of Cases
Anhui	4
Beijing	4
Fujian	18
Guangdong	53
Guangxi	1
Hebei	1
Henan	4
Hunan	6
Jiangsu	39
Jiangxi	6
Shandong	2
Shanghai	42
Zhejiang	119

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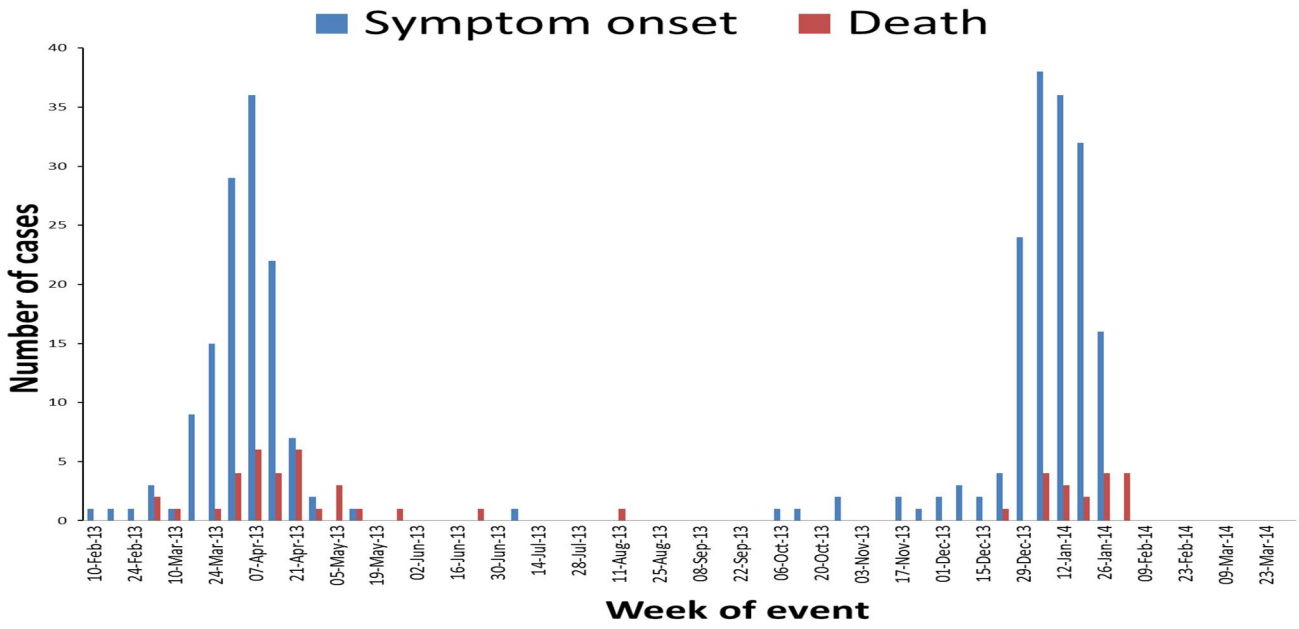
Note: Chinese provinces with reported cases are shaded in blue. Provinces with disease high disease activity are shown in pale blue. Regions with cases acquired in mainland China subsequently exported are shown in green. This figure includes cases and deaths confirmed by local authorities; some of these cases have not yet been acknowledged by WHO.

Figure 2 Epi-curve of avian influenza A(H7N9) cases and deaths by *Date of Symptom Onset* or *Death*, as of 6 February 2014



Note: Six confirmed cases are missing from the figure due incomplete data.

Figure 3 Distribution of confirmed avian influenza A(H7N9) cases by age and gender, to 27 January 2014, China (n=246*)[1]

** Five cases were excluded because age or gender was unknown.*

Human Diagnosis and Treatment

- A review of the capacity of European labs to detect the H7N9 virus found that 27 of 29 countries said that their generic influenza A detection assays will correctly detect the new virus. The survey also found that 22 countries have containment facilities that are appropriate for isolating and propagating the H7N9 virus[1].
- Thus far the H7N9 viruses detected in China are nearly identical at a genetic level.
- Sequence analyses have shown that the genes of the H7N9 viruses from China are of avian origin, but with signs of adaptation to mammalian species. The adaptation includes increased ability to bind to mammalian cell receptors, and to grow at temperatures close to the normal body temperature of mammals, which is lower than that of birds.
- Antigenically, the H7N9 viruses are different from seasonal influenza viruses infecting humans, but closely related to A/Anhui/1/2013 (H7N9), the recommended virus for H7N9 vaccine development.
- Early information from China suggests that when oseltamivir was given early in the course of illness, it has been found to be effective against H7N9 virus infection in reducing severe illness and deaths. Oseltamivir resistance has been reported in several patients with severe illness shortly after the initiation of the antiviral treatment and concluded in unfavourable outcomes.
- In general, seasonal influenza strains become less transmissible once they develop resistance to neuraminidase inhibitors. In contrast, a recent preliminary study showed that the common resistance mutation in the neuraminidase gene did not impair infectivity, viral multiplication or shedding of H7N9 viruses in animal models [2].

[1] Figure taken from ECDC Updated Risk Assessment (27 January 2014)

Animal infections and environment detection

- The Food and Agriculture Organization of the United Nations (FAO) and the African Union's Inter-African Bureau for Animal Resources (AU-IBAR) have been encouraged to increase their preparedness for H7N9 avian influenza.
- Preparedness activities include identification of critical points of entry where surveillance should be targeted and management measures enhanced. Such measures could include cleaning and disinfection of live bird markets and introducing market rest days with no poultry, among others. The highest risk of spread is associated with legal or illegal trade of live birds through humans, and the avian species most implicated so far are chickens, quail, and pigeons.
- While the recent report of avian influenza A(H7N9) virus being detected in live poultry imported from the mainland to Hong Kong SAR shows the potential for the virus to spread through live poultry, at this time, there is no indication that international spread of avian influenza A(H7N9) has occurred through humans or animals.(WHO H7N9 DoN 5 Feb 2014)
- A recent study has demonstrated that finches, sparrows, and parakeets can be productively infected with H7N9. Further, following infection, they can shed enough virus from their beaks into drinking water to infect other birds. These findings suggest that these birds could act as intermediate hosts with the ability to facilitate transmission and dissemination of A(H7N9) virus to other birds and humans [3].

References

1. Broberg E, P.D., Struelens M, Palm D, Meijer A, Ellis J, Zambon M, McCauley J, Daniels R., *Laboratory preparedness in EU/EEA countries for detection of novel avian influenza A(H7N9) virus, May 2013.* Euro Surveill, 2014. **9**(4): p. pii=20682.
2. Hai, R., et al., *Influenza A(H7N9) virus gains neuraminidase inhibitor resistance without loss of in vivo virulence or transmissibility.* Nat Commun, 2013. **4**.
3. Jeremy C. Jones, S.S., Zeynep A. Koçer, Karthik Shanmuganatham, Patrick Seiler, Yuelong Shu, Huachen Zhu, Yi Guan, Malik Peiris, Richard J. Webby, and Robert G. Webster, *Possible Role of Songbirds and Parakeets in Transmission of Influenza A(H7N9) Virus to Humans.* Emerg Infect Dis, 2014. **20**(3).

History

31 January 2014

Cases

- The epidemic curve by week of illness onset (Figure 2) indicates there was a peak in week beginning 7 April 2013, followed by a sharp decrease of cases in May. From June through October, only sporadic single cases were reported. Since November however, the number of cases of confirmed influenza A(H7N9) have increased (Figure 2).
- Human infection is characterised by rapid progression to severe pneumonia with small numbers of clinically mild cases occurring mainly in children. In contrast, previous infections with subtype H7 avian influenza viruses have generally been mild and associated with conjunctivitis.
- The overall age of the cases ranges from three to 91 years, with a median age of 56 years. The age group between 10 and 19 years of age is least affected (Figure 4).
- More men are infected than women (Figure 4).
- Human-to-human transmission remains inefficient. From follow-up of almost 3 000 contacts, only four were reported to develop symptoms. These four cases were part of several small family clusters identified in February and March 2013.
- Exposure information is available for 82 confirmed cases, suggesting that 63 (77%) of the cases have been exposed to live animals. There is, however, no information available on the number of exposed Chinese citizens by age group.
- While ongoing H7N9 influenza activity in China is mainly a zoonotic event, its parallel rise with seasonal flu poses a virus reassortment threat. The WHO reports that seasonal flu activity is high and still increasing in China, with all three strains circulating. Though the H7N9 virus doesn't appear to have the capacity for efficient human-to-human spread, new reassortants with seasonal flu strains could arm it with the ability to transmit more easily

H7N9 vaccine developments

- Six clinical trials have been initiated in Australia, Canada and the United States to assess safety and immunogenicity. Studies are currently conducted in healthy adults and include adjuvanted and unadjuvanted candidate vaccines. Trials will elucidate whether one or two doses will be needed.
- Preliminary scientific data point toward the need for two doses, which would be expected given the virus-naïve population.
- Initial results have been reported for two trials: a virus-like particle vaccine from Novavax and a cell-culture adjuvanted vaccine from Novartis.
- Two phase 1 studies are currently enrolling participants, one supported by the US National Institute of Allergy and Infectious Diseases (NIAID) and one by GlaxoSmithKline.

Human Diagnosis and Treatment

- Based on sequence analysis, it is expected that the generic RT-PCR assays for influenza A virus, which is based on highly conserved viral gene sequences, e.g. in the M-gene, will detect H7N9.
- Infection can also be retrospectively diagnosed by heamagglutination-inhibition (HI) tests.
- The current treatment practices do not differ from treatment of other severe influenza disease. WHO recommends immediate empirical treatment of symptomatic individuals exposed to A(H7N9) with neuraminidase inhibitors. Chemoprophylaxis of asymptomatic exposed individuals is not recommended.

Animal infections and environment detection

- The most plausible underlying scenario for human infections is of a zoonotic avian influenza that is circulating in poultry in parts of south-eastern China. The severe nature of the disease and the genetic features of the virus present a threat to humans because of the human pandemic potential. The persistence of this virus in poultry represents a significant long-term threat either as a zoonosis or perhaps a pandemic virus.
- Active surveillance is ongoing in China, where public health authorities sample chickens, waterfowl, captive-bred pigeons, quails and wild birds. Additionally, environmental samples are collected at wholesale live bird markets, live bird trading areas (stalls) at farmers' markets, large-scale poultry farms, village/backyard poultry holdings, poultry slaughterhouses, wild migrating bird habitats, and other locations. The Chinese Ministry of Agriculture has notified the World Organization for Animal Health (OIE) about the detection of some genetically similar influenza A(H7N9) isolates from birds.

- The virus has been detected in ducks, pigeons and chickens, but it has not been detected in pigs. Also, samples from the environment, particularly from live poultry markets, have tested positive for influenza A(H7N9) in 2013 and 2014. Goose meat has also tested positive for influenza A(H7N9). A positive sewage sample was identified at the same wet market; the market was subsequently closed and disinfected.
- A significant difference between influenza A(H5N1) and A(H7N9) avian influenza viruses is the reduced pathogenicity of the H7N9 virus in poultry. H5N1 is highly pathogenic in poultry and can be detected by flock die-offs. H7N9 does not severely affect poultry, and it is likely that influenza A(H7N9) can circulate silently in poultry and other bird populations. The human cases may be the first indication of infections in birds.
- The major source of infection for humans seems to be poultry handled in the poultry market, while wild birds are the reservoir for H7 and N9 genes of influenza viruses. Live bird markets seem to amplify the infection: wild birds mixing with poultry can lead to environmental contamination. The Ministry of Agriculture reported that ‘stamping-out’ control measures were implemented in poultry markets; also, some markets were temporarily closed. These closures were associated with a decrease in the number of human cases in those localities. Following the occurrence of new cases, at least one provincial government closed live poultry markets in 2014.