WHO RISK ASSESSMENT
Human infections with avian influenza A(H7N9) virus
7 June 2013

Summary

Cases of H7N9 so far

A total of 132 laboratory-confirmed cases of human infection with avian influenza A(H7N9) virus have been reported to WHO; 131 cases by China National Health and Family Planning Commission and one case by the Taipei Centers for Disease Control (Taipei CDC). Although cases have been reported in both men and women, and across a wide age range, most cases have occurred in middle-aged or older men. Thirty-seven people have died, and most of the other cases were considered severe. Cases in China have been reported from Anhui, Fujian, Henan, Hunan, Jiangsu, Jiangxi, Shandong and Zhejiang, and the municipalities of Beijing and Shanghai. In addition, the case reported by Taipei CDC had a history of recent travel from Jiangsu, China.

Comparison with other avian influenza viruses

This is the first time that human infection with the avian influenza A(H7N9) subtype has been detected. The few A(H7) human infections that have occurred have generally resulted in mild illness and conjunctivitis, with the exception of one death.

In outbreaks of H5N1, severely infected poultry were a warning signal for human infection. Previous sporadic cases of human infection with other influenza A(H7) viruses have also been associated with outbreaks of infection in poultry. However, since this H7N9 virus has not been reported to cause severe disease in poultry, and therefore the birds do not visibly seem to be infected, H7N9 infected birds will not likely provide a useful warning signal, and it may be difficult to determine when a person has been in contact with H7N9-infected poultry.

Source of human infection

Human infection appears to be related to exposure to live poultry or contaminated environments. However, much remains unknown about this virus, including the animal reservoir(s) in which it is circulating, the main exposures and routes of transmission, and the scope of the spread of this virus among people and animals. Investigations are ongoing.

So far, however, human infection appears to be related to exposure to live poultry or contaminated environments for the following reasons.

- The virus in humans is genetically similar to that found in birds and the environment, mostly from animal markets which sell poultry.

- Most human cases (approximately three out of four patients) report a history of exposure to birds, mostly chickens.
- The virus has been detected in poultry in live animal markets, which sell poultry.
- The number of new case reports of the disease has decreased after the implementation of public health measures, which included closure of live poultry markets and increasing public awareness.

The existence of other virus reservoirs, such as domestic or wild bird and mammalian species, has not yet been determined.

Evidence regarding human-to-human transmission

Although four small human clusters have been reported, evidence does not support sustained human-to-human transmission.

- Monitoring and testing of contacts (>2000 people) of confirmed cases has detected few infections.
- Testing of more than 20,000 people with influenza-like illness (ILI) in March and April has confirmed only six infections with H7N9. An additional case of influenza-like illness was seen in May. This suggests that milder cases of H7N9 infection are not occurring in large numbers.

Virus characteristics

Genetic and laboratory analysis of H7N9 viruses isolated from humans indicates that:

- The virus contains genes of multiple avian origin.
- Genetic analysis indicates that this H7N9 virus may have greater ability to infect mammals, including humans, than other avian influenza viruses. In addition, in laboratory testing, ferrets became infected, shed the virus, and transmitted it by direct contact.
- Sequence variations among the genes of the isolates suggest that the H7N9 virus has been introduced from animals into humans more than once.
- These viruses are in general expected to be sensitive to the neuraminidase inhibitors oseltamivir and zanamivir, but resistant to the antiviral drugs amantadine and rimantadine. Testing of one H7N9 strain (A/Shanghai/1/2013) in the neuraminidase inhibition assay yielded discrepant results. A small study has shown that the virus can develop resistance during treatment.
- The isolates have a haemagglutinin structure that is associated with low pathogenicity in birds. This has been confirmed in laboratory studies.

Risk assessment

This 7 June 2013 risk assessment has been prepared in accordance with WHO's published recommendations for rapid risk assessment of acute public health events and will be updated as more information becomes available. The risk has not changed since the previous assessment published on 10 May.

What is the risk that more human cases will occur in the affected areas?
The understanding of the epidemiology of the virus and this outbreak , including the main reservoirs of infection and the extent of geographic spread among animals, remains limited. However, it is likely that most human H7N9 infections have been associated with contacts with live animal markets that sell poultry. Further sporadic human cases should be expected in affected and possibly neighboring areas.

Other avian influenza viruses such as H5N1 have demonstrated a seasonal pattern in which animal outbreaks and human cases have been less frequent in summer months and more frequent in winter months in temperate zones. The number of newly reported cases has decreased over the past few weeks, but it remains to be seen whether H7N9 infections will follow the same seasonal pattern. Most human cases have resulted in clinically severe illness.

What is the risk of human-to-human transmission?
Evidence does not support sustained human-to-human transmission. However, four small clusters suggest that limited human-to-human transmission may occur where there is close contact between cases and non-infected people, as occurs in families and in healthcare settings. Moreover, the genetic changes seen among these viruses suggest that adaptation to mammals is of concern, and further adaptation may occur. Should sustained human-to-human transmission occur with an increased number of clinically severe cases, health systems are likely to be strained. WHO is providing coordination and guidance regarding provisional vaccine candidates; there are currently no recommendations on the large-scale manufacture of H7N9 vaccine.

What is the risk of international spread of H7N9 by travelers?
There is no indication that international spread has occurred, although when infected people from affected areas travel, their infection may be detected in another country. However, as the virus does not appear to cause sustained human-to-human transmission, extensive community spread is unlikely. If transmissibility were to increase, then the possibility of spread would likewise increase.

Does WHO recommend any travel and trade precautions related to H7N9?
WHO does not advise special screening at points of entry with regard to this event, nor does it currently recommend any travel or trade restrictions.

What should countries do?
WHO advises countries to continue surveillance, reporting as applicable under the IHR (2005) and other preparedness actions. Current technical information as well as guidance related to avian influenza

A(H7N9) can be found at the WHO website, http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/.

Resources

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WHO. Rapid Risk Assessment of Acute Public Health Events. World Health Organization, 2012 (WHO/HSE/GAR/ARO/2012.1). http://www.who.int/csr/resources/publications/HSE_GAR_ARO_2012_1/en/

Additional Information

Most recent disease outbreak news can be found at: http://www.who.int/csr/don/en/index.html
Frequently Asked Questions and other information on human infections with avian influenza A(H7N9) are available at: http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html

Public health relevant virological features of influenza A(H7N9) causing human infection in China: http://www.euro.who.int/en/what-we-do/health-topics/communicable-diseases/influenza/publications/2013/public-health-relevant-virological-features-of-influenza-ah7n9-causing-human-infection-in-china