

Background and summary of human infection with avian influenza A(H7N9) virus – as of 31 January 2014

The influenza A(H7N9) virus is one subgroup among the larger group of H7 viruses, which normally circulate among birds.

Human infections with other subgroups of H7 influenza viruses (H7N2, H7N3, and H7N7) have previously been reported in Australia, Canada, Italy, Mexico, the Netherlands, the United Kingdom and the United States of America. Most of these infections occurred in association with poultry outbreaks. The infections mainly resulted in conjunctivitis and mild upper respiratory symptoms, with the exception of one death, which occurred in the Netherlands.

Since the first notification at the end of March 2013, China has been reporting to WHO cases of human infection with H7N9 virus. This is the first time infection with this virus has been found in humans.

Epidemiology

The laboratory-confirmed cases have been reported from 13 provinces/municipalities in eastern mainland China, Hong Kong, Special Administrative Region, China, and the Taipei Centers for Disease Control (Taipei CDC). Most cases are presumed to have contracted the infection directly from infected animals or their environment, particularly as a result of visiting live animal markets. Only a few small clusters with possible human-to-human transmission have occurred among family members, but there has been no evidence of sustained human-to-human transmission to date.

As of 28 January 2014, the case fatality rate of all confirmed cases is 22%, but many cases are still hospitalized. Of all cases, 67% were male. The median age of reported cases is 58 years and that of fatal cases is 66 years.

Cases occurred in a first wave (n=133) from February through May 2013. Reports of human infection decreased during the summer, with only two cases reported; they have increased since October, demonstrating a second wave, likely in conjunction with cooler temperatures.

For the latest information on cases and outcomes, see:

- [Disease Outbreak News \(DONs\)](#)

Virology

Thus far the H7N9 viruses detected in China are homologues. The HA gene is most similar to that of A(H7N3) viruses detected in ducks in Eastern China. The NA gene is most similar to N9 NA genes from viruses circulating recently in domestic ducks in China and Korea. The six internal genes are derived from influenza A(H9N2) viruses circulating in poultry in eastern Asia. 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.

Human-Animal Interface

The source of infection is assumed to be infected poultry or contaminated environments. Many of the human cases have reported visiting markets where live poultry were sold. This virus has been detected in both poultry and in markets that patients reported visiting. However, because this virus does not appear to cause clinical signs in infected poultry, clear links between infections in poultry and human cases have been difficult to establish.

Clinical presentation

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. Severe illness is more likely to occur in older persons with underlying chronic conditions.

Treatment

Laboratory testing conducted so far has shown that the H7N9 viruses are sensitive to the anti-influenza drugs known as neuraminidase inhibitors (oseltamivir and zanamivir) but resistant to adamantanes (amantadine and rimantadine). 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 case of non-response to the antiviral therapy in such patients, health care workers are reminded to reassess and reinforce infection prevention and control measures and consider clinical sampling for antiviral sensitivity testing. Clinicians may need to adjust their treatment strategies accordingly.

Published WHO guidance on treatment of A(H5N1) virus infection is applicable to A(H7N9) infection (link: <http://www.who.int/influenza/resources/documents/ClinicalManagement07.pdf>).

Intervention strategies directly targeting the virus include higher dose or combination antiviral therapy, intravenous formulations of antivirals and convalescent plasma therapy. Evidence to support these therapies is still insufficient and requires further clinical studies.

Patients with severe or progressive illness should be managed in a hospital and given timely supportive therapies, especially for ARDS and sepsis. Lung-protective ventilation strategies and conservative fluid management are important for ARDS case management (link: http://www.who.int/csr/disease/coronavirus_infections/InterimGuidance_ClinicalManagement_NovelCoronavirus_11Feb13u.pdf).

Systemic high-dose corticosteroids in severely ill patients has been reported to be harmful and should not be given unless otherwise indicated.

Prevention

No vaccines are commercially available and of proven efficacy. In September 2013 WHO recommended that an A/Anhui/1/2013-like virus be used for the development of H7N9 vaccines for the purpose of pandemic preparedness. Several high-growth candidate vaccine viruses have now been developed by the WHO Global Influenza Surveillance and Response System (GISRS) and are available to interested entities, including vaccine manufactures. Clinical trials are ongoing in some countries to ascertain immunogenicity and establish the optimal vaccination regimen and dose.

Although the source of infection and the mode of transmission have not yet been determined, it is prudent to follow good hygiene practices to prevent infection. For advice on infection prevention, contact with animals and food preparation, see:

- [Frequently Asked Questions on human infection caused by the avian virus](#)

Guidance for infection prevention and control in health care settings is available at:

- [Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care](#)

Current evidence does not support sustained human-to-human transmission of this virus.

However, given the potential risk of transmission, basic infection prevention and control measures (Standard Precautions) should be applied in all health-care settings for all patients, which include hand hygiene and use of personal protective equipment (PPE) to avoid direct contact with patients' blood, body fluids, secretions (including respiratory secretions) and non-intact skin. Droplet precautions should be added when providing care to all patients with symptoms of acute respiratory infection, and contact precautions plus eye protection should be added when caring for confirmed or probable cases of H7N9 infection. Airborne precautions are indicated when performing aerosol generating procedures.

Neither quarantine nor isolation of asymptomatic contacts seems necessary at this time. Persons (including health-care workers) who may have been exposed to individuals with confirmed or probable H7N9 infection, should be advised to monitor their health for 7 days from the last day of possible contact and seek immediate medical attention if they develop symptoms, particularly fever and respiratory symptoms such as coughing or shortness of breath. [If a contact develops symptoms, antiviral treatment with a neuraminidase inhibitor should be started immediately.](#)

Current activities

WHO has been closely monitoring the situation since detection of the first case and has been working with partners to ensure a high degree of preparedness should the new virus be found to be sufficiently transmissible to cause community outbreaks. WHO has also been working with animal health partners to investigate possible circulation in animals and possible reservoirs.

- Actions taken by WHO in coordination with national authorities and technical partners include the following: iterative public health risk assessments in collaboration with China and the region.
- Rapid information sharing with countries under the International Health Regulations (IHR), and communications through WHO websites, Disease Outbreak News, and social media.
- Coordination of enhanced surveillance for pneumonia cases of unknown origin to ensure early detection and laboratory confirmation of new cases, and epidemiological investigation, including assessment of suspected cases and contacts of known cases.
- Support to H7N9 vaccine development and production with candidate vaccine viruses developed and made available, and ongoing continuous efforts on developing higher-growth candidates and using classical reassortment technology.
- Close collaboration with animal health partners, specifically the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO) and the OIE/FAO Network of Expertise on Animal Influenza (OFFLU), to share information, assess public health risks at the human-animal interface, and ensure that materials and information, including laboratory test reagents, are shared among animal health and public health laboratories.
- Continuous risk assessment of the situation in collaboration with the WHO Global Influenza Surveillance and Response System (GISRS); with animal health laboratories, coordinated by the WHO-OFFLU collaboration; and with other technical partners.
- Technical support to China for clinical management guidance development and update with the WHO clinical network, clinical research collaboration and training workshop for critical care.
- In collaboration with FAO partners, enhanced and targeted public health surveillance to identify possible incursions of the virus in neighbouring countries at risk.

WHO recommendations

Based on the current situation and available information, WHO advises the following:

- Any new human infection of H7N9 virus should continue to be reported rapidly under IHR 2005.
- The WHO GISRS laboratories continue to maintain high levels of alertness. Unsubtypable influenza viruses should be sent immediately to a WHO Collaborating Centre of GISRS for further analysis.
- The same surveillance strategy applies as for human infections with highly pathogenic avian influenza A(H5N1) virus.
- Clinicians and laboratory specialists should consider the possibility of human infection with influenza in patients presenting with severe acute respiratory disease.
- Health care workers (clinicians and other personnel) should apply Standard Precautions for infection control in all health-care settings for all patients. If H7N9 virus infection is suspected, apply relevant additional precautions, conduct contact tracing around such cases and treat the patient immediately with a neuraminidase inhibitor (oseltamivir or zanamivir).
- Standard guidance should also be applied to rigorous investigation of clusters of severe respiratory infections and such infections in health care workers who have been caring for patients with severe acute respiratory disease.

- WHO does not advise special screening at points of entry with regard to this event nor does it recommend that any travel or trade restrictions be applied.

WHO will continue working closely with national authorities and technical partners to gain a better understanding of the virus and the disease in humans, assess the situation as it evolves, and provide updated information and guidance accordingly.