Influenza at the human-animal interface

Summary and assessment, 20 July to 3 October 2016

- **New infections**[1]**:** Since the previous update, new human infections with A(H5N1), A(H7N9), A(H9N2), A(H1N2)v and A(H3N2)v viruses were reported.
- **Risk assessment:** The overall public health risk from currently known influenza viruses at the human-animal interface has not changed. Further human infections with viruses of animal origin can be expected, but the likelihood of sustained human-to-human transmission remains low.
- **Risk management:** Status of the development of candidate vaccine viruses (CVVs) and selection of new CVVs of zoonotic influenza for influenza pandemic preparedness purposes were reviewed in a recent WHO consultation.[2]
- **IHR compliance:** All human infections caused by a new influenza subtype are reportable under the International Health Regulations (IHR, 2005).[3] This includes any animal and non-circulating seasonal viruses. Information from these notifications will continue to inform risk assessments for influenza at the human-animal interface.

Avian Influenza Viruses

Avian influenza A(H5) viruses

Current situation:

Since the last update[4], two new laboratory-confirmed human cases of avian influenza A(H5N1) virus infection were reported to WHO. A 3-year-old male resident of Fayoum Governorate, Egypt, had onset of symptoms on 7 May 2016, was hospitalized and treated with antivirals for pneumonia, but passed away on 20 May 2016. Prior to his illness, the case was exposed to domestic poultry that appeared healthy. The second case was a 3-year-old female resident of Giza Governorate, Egypt, who had onset of symptoms on 24 July 2016, was hospitalized and treated with antivirals for pneumonia, but passed away on 31 July 2016. Prior to her illness, the case was exposed to poultry purchased from a market that later died. Investigation and follow up of contacts of the two cases took place for 14 days with no further cases detected. Avian influenza A(H5N1) viruses are enzootic in poultry in Egypt.[5]

[1] For epidemiological and virological features of human infections with animal influenza viruses not reported in this assessment, see the yearly report on human cases of influenza at the human-animal interface published in the Weekly Epidemiological Record. www.who.int/wer/en/

[2] http://www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

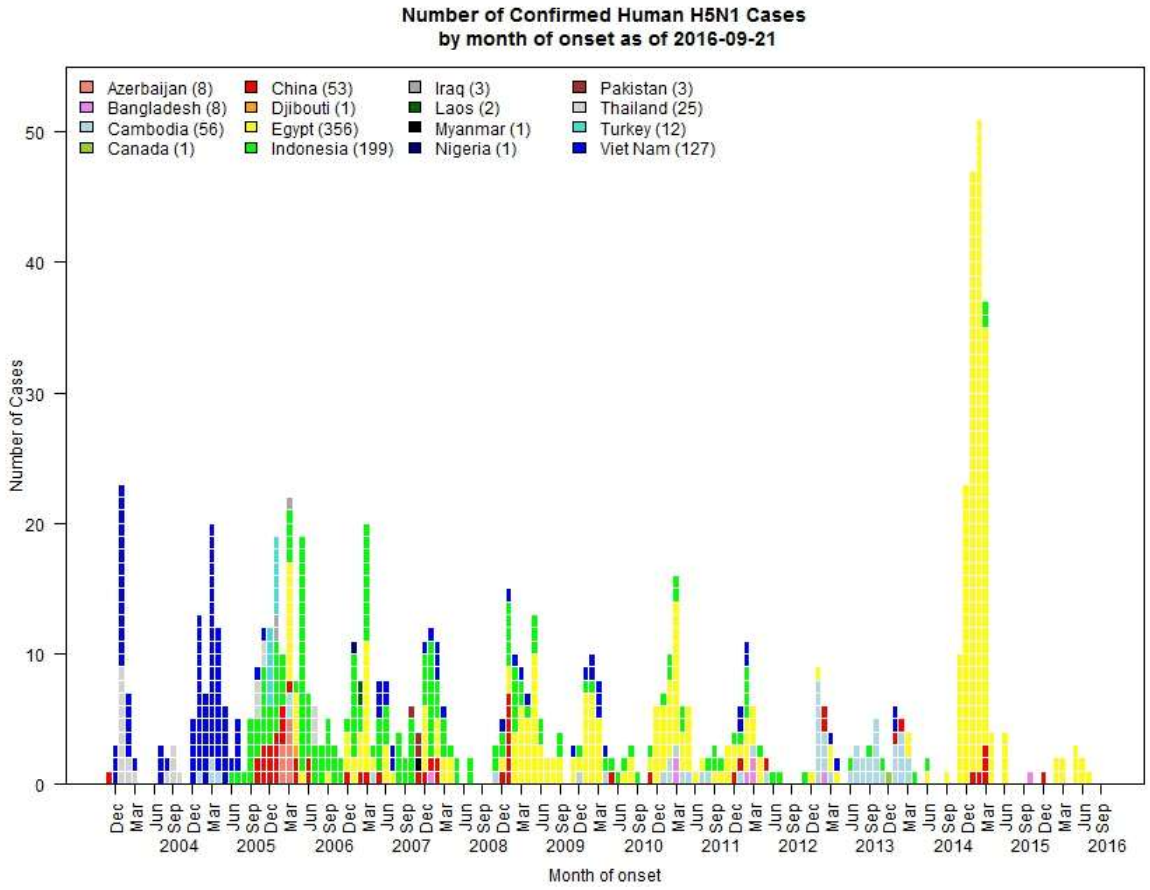
[3] World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005). www.who.int/ihr/Case_Definitions.pdf

[4] www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_07_19_2016.pdf

[5] www.emro.who.int/images/stories/Executive_Summary_14_May_2015.pdf

Since 2003, a total of 856 laboratory-confirmed cases of human infection with avian influenza A(H5N1) virus, including 452 deaths, have been reported to WHO from 16 countries (see Figure 1).

Figure 1: Epidemiological curve of avian influenza A(H5N1) cases in humans by week of onset, 2003-2016



Although other influenza A(H5) subtype viruses have the potential to cause disease in humans, no human cases, other than those with influenza A(H5N1) and A(H5N6), have been reported so far. According to reports received by the World Organisation for Animal Health (OIE), various influenza A(H5) subtypes continue to be detected in birds in West Africa, Europe and Asia. The A(H5N1) virus outbreaks in poultry in West Africa continue since 2014 with a newly-affected country, Togo, now reporting outbreaks. No human infections associated with these outbreaks in Western and Central Africa have been identified to date, despite surveillance and testing of human samples.

Influenza A(H5) viruses are highly diverse and continue to evolve. Further details about these viruses can be found in the September 2016 WHO report of the antigenic and genetic characteristics of zoonotic influenza viruses, including the development of two new candidate vaccine viruses for pandemic preparedness.[6]

[6] www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

Risk Assessment:

1. **What is the likelihood that additional human cases of infection with avian influenza A(H5) viruses will occur?** Most human cases were exposed to A(H5) viruses through contact with infected poultry or contaminated environments, including live poultry markets. Since the viruses continue to be detected in animals and environments, further human cases can be expected.
2. **What is the likelihood of human-to-human transmission of avian influenza A(H5) viruses?** Even though small clusters of A(H5) virus infections have been reported previously including those involving healthcare workers, current epidemiological and virological evidence suggests that this and other A(H5) viruses have not acquired the ability of sustained transmission among humans, thus the likelihood is low.
3. **What is the risk of international spread of avian influenza A(H5) viruses by travellers?** Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as evidence suggests these viruses have not acquired the ability to transmit easily among humans.

Avian influenza A(H7N9) viruses

Current situation:

During this reporting period, China reported five laboratory-confirmed human cases of A(H7N9) virus infection to WHO on 11 August 2016, including one fatal case. One cluster of three cases was reported for which the possibility of human-to-human transmission for two cases in the cluster cannot be excluded. For more details on these cases, see Table 1 below and the Disease Outbreak News.

Table 1: Human cases of avian influenza A(H7N9) reported from 20 July to 3 October 2016

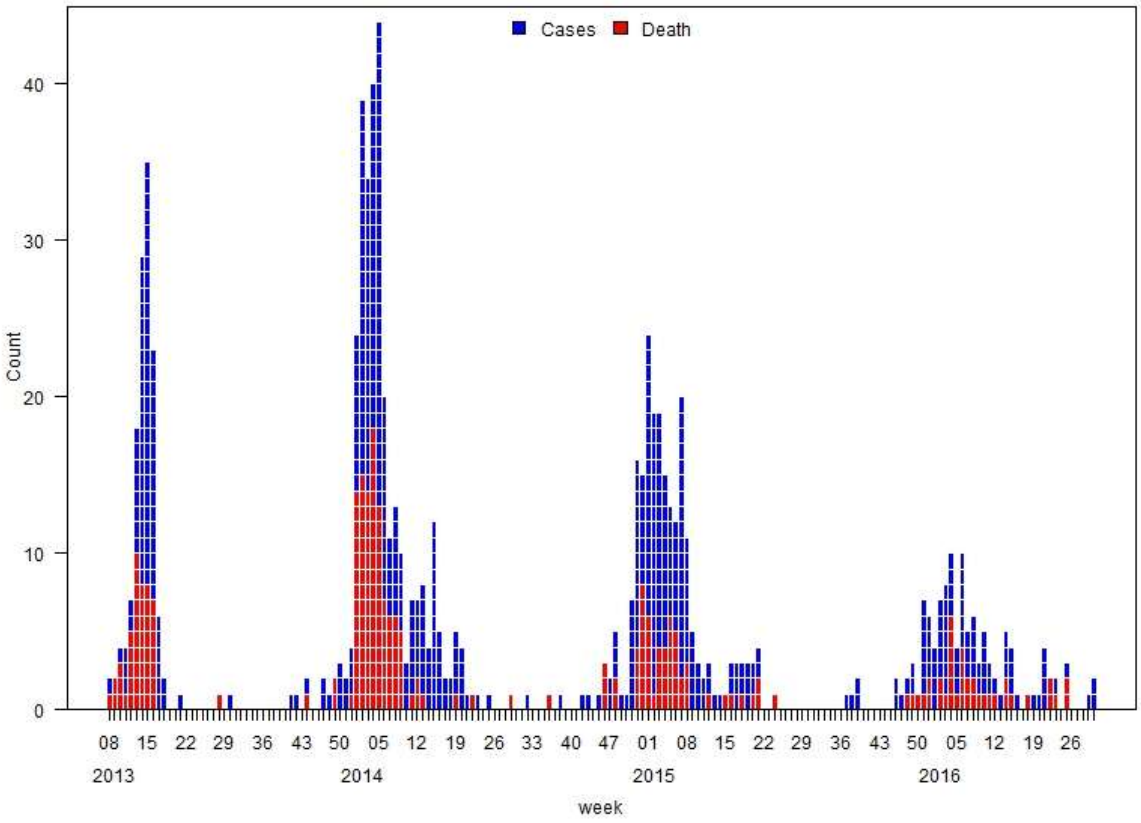
Province or region reporting (province of assumed exposure, if different from reporting province or region)	Age	Sex	Date of onset (yyyy/mm/dd)	Case condition at time of reporting	Exposure history
Fujian	79	M	2016/06/25	Died	Visited a market
Fujian	78	M	2016/06/24	Severe	Live poultry
Beijing (Jiangxi)	35	M	2016/07/18	Severe	Live poultry
Hebei (Jiangxi)	13	F	2016/07/26	Mild	Resided with case above
Hebei	68	F	2016/07/29	Mild	Resided with above two cases

A total of 798 laboratory-confirmed cases of human infection with avian influenza A(H7N9) viruses, including at least 320 deaths[7], have been reported to WHO (Figure 2). According to reports received

[7] Total number of fatal cases is published on a monthly basis by China National Health and Family Planning Commission.

by the Food and Agriculture Organization (FAO) on surveillance activities for avian influenza A(H7N9) viruses in China[8], positives among virological samples continue to be detected mainly from live bird markets, vendors and some commercial or breeding farms.

Figure 2: Epidemiological curve of avian influenza A(H7N9) cases in humans by week of onset, 2013-2016



Virology data from recent human cases as well as from viruses detected in animals and the environment indicate that there have been few genetic and antigenic changes in recent influenza A(H7N9) viruses. Thus, based on this information as well as the epidemiology of human infections with this virus, no new A(H7N9) candidate vaccine viruses have been proposed.[9]

Risk Assessment:

1. **What is the likelihood that additional human cases of infection with avian influenza A(H7N9) viruses will occur?** Most human cases are exposed to the A(H7N9) virus through contact with infected poultry or contaminated environments, including live poultry markets. Since the virus continues to be detected in animals and environments, further human cases can be expected.

[8] Food and Agriculture Organization. H7N9 situation update. www.fao.org/ag/againfo/programmes/en/empres/H7N9/situation_update.html

[9] www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

Additional sporadic human cases of influenza A(H7N9) in other provinces in China that have not yet reported human cases are also expected.

2. **What is the likelihood of human-to-human transmission of avian influenza A(H7N9) viruses?** Even though small clusters of cases have been reported, including those involving healthcare workers, current epidemiological and virological evidence suggests that this virus has not acquired the ability of sustained transmission among humans, thus the likelihood is low.
3. **What is the risk of international spread of avian influenza A(H7N9) virus by travellers?** Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as this virus has not acquired the ability to transmit easily among humans.

Avian influenza A(H9N2) viruses

Current situation:

Since the last update[10], two laboratory-confirmed human cases of A(H9N2) virus infection were reported to WHO from China. No abnormalities were observed among close contacts of these cases at the time of reporting. In addition, four other cases were identified in China over the past six months, including one retrospectively diagnosed case from 2015. For more details on these cases, see Table 2 below. The outcome of a previously reported case, a 57-year-old woman with underlying conditions from Sichuan province in China, was recently reported as fatal. This would be the first fatality associated with influenza A(H9N2) virus infections in humans. Avian influenza A(H9N2) viruses are enzootic in poultry in China.

Table 2: Information on additional human cases of avian influenza A(H9N2) identified in China

Province or region reporting (province of assumed exposure, if different from reporting province or region)	Age	Sex	Date of onset (yyyy/mm/dd)	Case condition at time of reporting	Exposure history
Guangdong	29	F	2016/08/08	Recovered	Poultry exposure
Yunnan	10 m	M	2016/08/07	Recovered	Poultry exposure
Guangdong	84	F	2015/02/04	Unknown	Poultry exposure
Henan	5	F	2016/02/01	Unknown	No poultry exposure
Guangdong	3	M	2016/07/09	Unknown	Poultry exposure
Jiangxi	4	F	2016/08/02	Unknown	No poultry exposure

[10] www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_07_19_2016.pdf?ua=1

Virology data from recent human cases as well as from viruses detected in animals indicate that there have been few genetic and antigenic changes in recent influenza A(H9N2) viruses. Thus, based on this information as well as the epidemiology of human infections with this virus, no new A(H9N2) candidate vaccine viruses have been proposed.[11]

Risk Assessment:

1. **What is the likelihood that additional human cases of infection with avian influenza A(H9N2) viruses will occur?** Most human cases are exposed to the A(H9N2) virus through contact with infected poultry or contaminated environments. Human infection tends to result in mild clinical illness. Since the virus continues to be detected in poultry populations, further human cases can be expected.
2. **What is the likelihood of human-to-human transmission of avian influenza A(H9N2) viruses?** No case clusters have been reported. Current epidemiological and virological evidence suggests that this virus has not acquired the ability of sustained transmission among humans, thus the likelihood is low.
3. **What is the risk of international spread of avian influenza A(H9N2) virus by travellers?** Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as this virus has not acquired the ability to transmit easily among humans.

Swine Influenza Viruses

Current situation:

Influenza A(H1N2)v viruses

WHO was notified of one new laboratory-confirmed human infection with an A(H1N2) variant virus in Brazil. The infection occurred in an adolescent in November 2015, in the southern region of Brazil, and was detected through surveillance for influenza-like illness. The virus was similar to A(H1N2) swine influenza viruses isolated in 2011 and 2013 from pigs in that region, and the case did report contact with swine prior to illness onset. No further cases were detected at the time, and retrospective analyses of samples collected in the same area have not revealed any additional cases. Genetically, this virus does not resemble the influenza A(H1N2)v viruses detected in the United States this year.

Influenza A(H3N2)v viruses

On 10 August 2016, the United States IHR National Focal Point (NFP) reported the first case of human infection with an influenza A(H3N2)v virus in 2016 in a child from the state of Ohio. The child developed an acute respiratory illness on 28 July 2016 and a sample from the patient was confirmed positive for influenza A(H3N2)v virus. The patient did not require hospitalization and swine contact at an agricultural fair was reported in the week preceding illness onset.

[11] www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

Following this case, an additional 17 laboratory-confirmed human cases of A(H3N2)v virus infection have been detected in the USA (in Michigan and Ohio) over the summer. Most infections were in children under 19 years and hospitalization was not required except for one case. All cases had exposure to swine at agricultural fairs and no human-to-human transmission was reported. Viruses from the cases were closely related to viruses circulating in the local swine populations. Since reporting of novel influenza A viruses became nationally notifiable in 2005, 372 human infections with influenza A(H3N2)v viruses have been reported to the U.S. CDC.[12]

The haemagglutinin (HA) gene in the viruses from 16 of the 18 cases detected this summer in the USA differed from previously detected influenza A(H3N2)v viruses. Given the number of cases which occurred over a short period this summer, and the genetic and antigenic changes, a new A(H3N2)v candidate vaccine virus for pandemic preparedness has been proposed.[13]

Additionally, since February 2016, a human case of infection with an influenza A(H3N2)v virus was retrospectively detected in Viet Nam. The infection occurred in June 2015 and the exposure history of the case is unknown. The virus isolate from this case was also closely related to swine influenza viruses circulating in the local swine population.[14]

Risk Assessment:

1. **What is the likelihood that additional human cases of infection with swine influenza viruses will occur?** Influenza A(H1N2) and A(H3N2) viruses circulate in swine populations in many regions of the world. Depending on geographic location, the genetic characteristics of these viruses differ. Most human cases are exposed to swine influenza viruses through contact with infected swine or contaminated environments. Human infection tends to result in mild clinical illness. Since these viruses continue to be detected in swine populations, further human cases can be expected.
2. **What is the likelihood of human-to-human transmission of swine influenza viruses?** No case clusters have been reported. Current evidence suggests that these viruses have not acquired the ability of sustained transmission among humans, thus the likelihood is low.
3. **What is the risk of international spread of swine influenza viruses by travellers?** Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as these viruses have not acquired the ability to transmit easily among humans.

Overall Risk Management Recommendations:

- WHO does not advise special traveller screening at points of entry or restrictions with regard to the current situation of influenza viruses at the human-animal interface. For recommendations on safe trade in animals from countries affected by these influenza viruses, refer to OIE guidance.
- WHO advises that travellers to countries with known outbreaks of animal influenza should avoid farms, contact with animals in live animal markets, entering areas where animals may be slaughtered, or contact with any surfaces that appear to be contaminated with animal faeces.

[12] www.cdc.gov/flu/swineflu/variant-cases-us.htm
[13] www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/
[14] www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

Travellers should also wash their hands often with soap and water. Travellers should follow good food safety and good food hygiene practices.

- Due to the constantly evolving nature of influenza viruses, WHO continues to stress the importance of global surveillance to detect virological, epidemiological and clinical changes associated with circulating influenza viruses that may affect human (or animal) health. Continued vigilance is needed within affected and neighbouring areas to detect infections in animals and humans. As the extent of virus circulation in animals is not clear, epidemiological and virological surveillance and the follow-up of suspected human cases should remain high.
- All human infections caused by a new influenza subtype are notifiable under the International Health Regulations (IHR, 2005).[15] State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed[16] case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic.[6] Evidence of illness is not required for this report.
- It is critical that influenza viruses from animals and people are fully characterized in appropriate animal or human health influenza reference laboratories and reported according to international standards. Under WHO's Pandemic Influenza Preparedness (PIP) Framework, Member States are expected to share their influenza viruses with pandemic potential on a regular and timely basis with the Global Influenza Surveillance and Response System (GISRS), a WHO-coordinated network of public health laboratories. The viruses are used by the public health laboratories to assess the risk of pandemic influenza and to develop candidate vaccine viruses.

Links:

WHO Human-Animal Interface web page
http://www.who.int/influenza/human_animal_interface/en/
Cumulative Number of Confirmed Human Cases of Avian Influenza A(H5N1) Reported to WHO
http://www.who.int/influenza/human_animal_interface/H5N1_cumulative_table_archives/en/
Avian Influenza A(H7N9) Information
http://who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html
WHO Avian Influenza Food Safety Issues
http://www.who.int/foodsafety/areas_work/zoonose/avian/en/
World Organisation of Animal Health (OIE) web page: Web portal on Avian Influenza
http://www.oie.int/animal-health-in-the-world/web-portal-on-avian-influenza/
Food and Agriculture Organization of the UN (FAO) webpage: Avian Influenza
http://www.fao.org/avianflu/en/index.html
OFFLU
http://www.offlu.net/index.html

[15] World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005). www.who.int/ihr/Case_Definitions.pdf
[16] World Health Organization. Manual for the laboratory diagnosis and virological surveillance of influenza (2011). www.who.int/influenza/gisrs_laboratory/manual_diagnosis_surveillance_influenza/en/