Influenza at the human-animal interface

Summary and risk assessment, from 1 June to 14 July 2023[1]

- **New infections[2]:** From 1 June to 14 July 2023, one human case of infection with an influenza A(H1N1) variant virus, two human cases with positive influenza A(H5N1) detections, one human case of infection with an influenza A(H5N6) virus, and one human case of infection with an influenza A(H9N2) virus were reported officially.
- **Risk assessment:** The overall public health risk from currently known influenza viruses at the human-animal interface has not changed, and the likelihood of sustained human-to-human transmission of these viruses remains low. Human infections with viruses of animal origin are not unexpected at the human-animal interface wherever these viruses circulate in animals.
- **IHR compliance:** All human infections caused by a new influenza subtype are required to be reported under the International Health Regulations (IHR, 2005).[3] This includes any influenza A virus that has demonstrated the capacity to infect a human and its haemagglutinin gene (or protein) is not a mutated form of those, i.e. A(H1) or A(H3), circulating widely in the human population. Information from these notifications is critical to inform risk assessments for influenza at the human-animal interface.

Avian Influenza Viruses

Current situation:

Avian influenza A(H5) viruses

In late-June, the United Kingdom of Great Britain and Northern Ireland reported to the World Health Organization (WHO) the detection of avian influenza A(H5) virus in a poultry worker at a farm in England where poultry was infected with high pathogenicity avian influenza (HPAI) A(H5N1) viruses and not the same farm linked to previous human cases.[4] The case was detected as part of an ongoing enhanced surveillance study of asymptomatic workers exposed to poultry infected with avian influenza. A sample collected the first day of recruitment was negative for influenza. The case self-collected three samples on different days and one of these samples was A(H5) positive. The case also reported having a sore throat and myalgia one week after exposure to the infected poultry. However, the date of collection of the positive sample is unknown and it is unclear if the symptoms resulted from infection. The case is currently well, and no further detections were reported among

[1] This summary and assessment covers information confirmed during this period and may include information received outside of this period.

[2] For epidemiological and virological features of human infections with animal influenza viruses not reported in this assessment, see the reports on human cases of influenza at the human-animal interface published in the Weekly Epidemiological Record here.

[3] World Health Organization. Case definitions for the 4 diseases requiring notification to WHO in all circumstances under the International Health Regulations (2005). Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005).

[4] World Health Organization. Influenza at the human-animal interface summary and assessment, 31 May 2023. https://www.who.int/publications/m/item/influenza-at-the-human-animal-interface-summary-and-assessment--31-may-2023

the case's contacts or among other workers participating in the study. Thus far, a determination if this is a contamination event or representative of a true infection has not been made.

In mid-July, the United Kingdom of Great Britain and Northern Ireland reported to the World Health Organization (WHO) the detection of avian influenza A(H5) virus in another poultry worker at a farm in England where poultry was infected with high pathogenicity avian influenza (HPAI) A(H5N1) viruses. This farm is different from those linked with previous human cases. The case was also detected as part of an ongoing enhanced surveillance study of asymptomatic workers exposed to poultry infected with avian influenza. A sample collected the first day of recruitment (the same day the case was involved in culling operations at the farm) was A(H5) positive. A subsequent self-collected sample 2 days later was negative for influenza. The case had no symptoms, and no further detections were reported among the case's contacts or among other workers at the farm linked with this event who are participating in the study. In this case, the detection was likely due to temporary contamination of the nasopharynx rather than infection.

Genetic sequencing of samples from these two cases identified influenza A(H5N1) viruses belonging to the H5 clade 2.3.4.4b. These would be the fourth and fifth reported detections of influenza A(H5N1) viruses in humans in the United Kingdom.[5]

On 12 July 2023, China reported to WHO one human case of infection with an influenza A(H5N6) virus in a 64-year-old male from Guangxi province. He had an onset of illness on 3 July 2023 and was hospitalized on 4 July in severe condition. He had exposure to live backyard poultry. Samples collected from his close contacts and the environment tested negative for influenza. No family members had developed symptoms at the time of reporting.

According to reports received by the World Organisation for Animal Health (WOAH), various influenza A(H5) subtypes continue to be detected in wild and domestic birds in Africa, Asia, Europe and the Americas. Infections in non-human mammals are also reported. The Food and Agriculture Organization of the United Nations (FAO), WHO, and WOAH released a situation analysis on the public health risk of ongoing avian influenza outbreaks in animals.

Risk Assessment:

1. What is the likelihood that additional human cases of infection with avian influenza A(H5) viruses will occur?
The overall risk assessment is unchanged. Most human cases so far were sporadic infections 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 related environments, further human cases can be expected. In some cases, the confirmation of infection with influenza A(H5) versus transient contamination of the nasopharynx/oropharynx with virus particles after exposure to infected birds or contaminated environment remains inconclusive.

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 were reported in the past, including those involving health care workers, so far, epidemiological and virological evidence suggests that influenza A(H5) viruses have not acquired the ability of sustained transmission among humans, thus the likelihood is low.

[5] Investigation into the risk to human health of avian influenza (influenza A H5N1) in England: technical briefing 5 (Updated 14 July 2023). Available at: https://www.gov.uk/government/publications/avian-influenza-influenza-a-h5n1-technical-briefings/investigation-into-the-risk-to-human-health-of-avian-influenza-influenza-a-h5n1-in-england-technical-briefing-5

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(H9N2) viruses

Since the last risk assessment on 31 May 2023, one human case of influenza A(H9N2) virus infection was reported from China.

On 9 June 2023, China notified WHO of one laboratory-confirmed A(H9N2) virus infection in a six-year-old girl from Sichuan province. She had onset of mild illness on 30 May 2023, was detected through routine influenza-like illness surveillance and was not hospitalized. She had suspected exposure to a live poultry market. No further cases have been reported among family members.

Avian influenza A(H9N2) viruses are enzootic in poultry in Asia and increasingly reported in poultry in Africa.

Risk Assessment:

1. What is the likelihood that additional human cases of infection with avian influenza A(H9N2) viruses will occur?
Most human cases follow exposure to the A(H9N2) virus through contact with infected poultry or contaminated environments. Human infection tends to result in mild clinical illness in most cases. 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 epidemiologic and virologic evidence suggests that influenza A(H9N2) viruses assessed by GISRS have not acquired the ability of sustained transmission among humans, thus the likelihood is low.

3. What is the likelihood 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 the A(H9N2) virus subtype has not been confirmed to have acquired the ability to transmit easily among humans.

Swine Influenza Viruses

Current situation:

Influenza A(H1N1) variant viruses [A(H1N1)v]

Since the last risk assessment on 31 May 2023, one human case of infection with an influenza A(H1N1)v virus was reported by Brazil.

On 7 June 2023, Brazil notified WHO of one laboratory-confirmed A(H1N1)v virus infection in a 42-year-old woman from the state of Paraná. She developed symptoms on 1 May 2023, was hospitalized on 3 May with a severe acute respiratory infection, was admitted to the Intensive Care Unit (ICU) on 4 May, and she passed away on 5 May. The patient had underlying medical conditions

and lived near a swine farm. Ongoing investigations reported that the patient did not have any direct contact with pigs, however, two of her close contacts worked at the swine farm. The two contacts did not develop respiratory disease and tested negative for influenza. To date, no human-to-human transmission associated with this case has been identified.

During her hospitalization, a nasopharyngeal swab sample was collected from the patient for influenza and SARS-CoV-2 testing, as part of regular respiratory virus surveillance activities. Real-time Polymerase Chain Reaction (RT-PCR) was conducted at the State of Paraná Central Public Health Laboratory, where the sample was subtyped as an influenza A/H1 virus. The sample also tested positive for a swine influenza A virus marker by RT-PCR. The specimen was forwarded to the National Influenza Centre (NIC) Oswaldo Cruz Foundation, in Rio de Janeiro, where further complementary analyses and genomic sequencing were performed. Samples received at the NIC on 25 May were confirmed to be an influenza A(H1N1)v virus by sequence analysis on 30 May. The recovered genome has a high identity (99%) with the haemagglutinin (HA) of other Influenza A(H1N1)v viruses previously detected in the municipality of Toledo state of Paraná in 2022. In addition, it has 96% identity with the HA of viruses collected from pigs in Brazil in 2015. The patient's samples were shared with a WHO Collaborating Centre for further characterization.[6]

Risk Assessment:

1. What is the likelihood that additional human cases of infection with swine influenza viruses will occur?
Swine influenza 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 animals or contaminated environments. Human infection tends to result in mild clinical illness in most cases. 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?
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 likelihood of international spread of swine influenza viruses by travelers?
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 regards to the current situation of influenza viruses at the human-animal interface. For recommendations on safe trade in animals and related products from countries affected by these influenza viruses, refer to WOAH guidance.
- Given the observed extent and frequency of avian influenza cases in wild birds and some wild mammals, the public should avoid contact with animals that are sick or dead from unknown causes, including wild animals, and should report dead wild birds and mammals or request their removal by contacting local wildlife or veterinary authorities.

[6] World Health Organization. Disease Outbreak News. Influenza A(H1N1) variant virus – Brazil, 16 June 2023. https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON473

- 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 excreta. Travelers should also wash their hands often with soap and water. All individuals should follow good food safety and hygiene practices.
- Due to the constantly evolving nature of influenza viruses, WHO continues to stress the importance of global surveillance to detect virologic, epidemiologic 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. Collaboration between the animal and human health sectors is essential. As the extent of influenza viruses circulation in animals is not clear, epidemiologic and virologic surveillance and the follow-up of suspected human cases should continue systematically. Guidance on investigation of non-seasonal influenza and other emerging acute respiratory diseases has been published on the WHO website here: https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2.
- Vigilance for the emergence of novel influenza viruses of pandemic potential should be maintained at all times including during a non-influenza emergency. In the context of the co-circulation of SARS-CoV-2 and influenza viruses, WHO has developed practical guidance for integrated surveillance. The guidance is available here: https://www.who.int/publications/i/item/WHO-2019-nCoV-Integrated_sentinel_surveillance-2022.1
- All human infections caused by a new subtype of influenza virus are notifiable under the International Health Regulations (IHR, 2005).[7] State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed[8] case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic[9]. Evidence of illness is not required for this report.
- It is critical that these influenza viruses from animals or from people are fully characterized in appropriate animal or human health influenza reference laboratories. Under WHO's Pandemic Influenza Preparedness (PIP) Framework, Member States are expected to share influenza viruses with pandemic potential on a **timely basis**[10] 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.
- The Tool for Influenza Pandemic Risk Assessment (TIPRA) provides an in-depth assessment of risk associated with some zoonotic influenza viruses – notably the likelihood of the virus gaining human-to-human transmissibility, and the impact should the virus gain such transmissibility. TIPRA maps relative risk amongst viruses assessed using multiple elements. The results of TIPRA complement those of the risk assessment provided here, and those of prior TIPRA analyses will soon be published at http://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-(tipra).

Links:

WHO Human-Animal Interface web page

[7] World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005).

[8] World Health Organization. Manual for the laboratory diagnosis and virological surveillance of influenza (2011). Available at: https://apps.who.int/iris/handle/10665/44518

[9] World Health Organization. Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits. Available at: https://apps.who.int/iris/handle/10665/44796

[10] World Health Organization. Operational guidance on sharing influenza viruses with human pandemic potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework (2017). Available at: https://apps.who.int/iris/handle/10665/25940

https://www.who.int/teams/global-influenza-programme/avian-influenza
WHO Influenza (Avian and other zoonotic) fact sheet
https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic)
WHO Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases
https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2
Cumulative Number of Confirmed Human Cases of Avian Influenza A(H5N1) Reported to WHO
https://www.who.int/teams/global-influenza-programme/avian-influenza
Avian Influenza A(H7N9) Information
https://www.who.int/teams/global-influenza-programme/avian-influenza/avian-influenza-a-(h7n9)-virus
World Organisation of Animal Health (WOAH) web page: Avian Influenza
https://www.woah.org/en/home/
Food and Agriculture Organization of the UN (FAO) webpage: Avian Influenza
https://www.fao.org/animal-health/avian-flu-qa/en/
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