Influenza at the human-animal interface

Summary and risk assessment, from 29 March to 3 May 2024[1]

- **New infections[2]:** From 29 March to 3 May 2024, one human case of infection with an influenza A(H5N1) virus, one human case of infection with an A(H9N2) virus, one human case of infection with an influenza A(H10N3) virus and one human case of infection with an influenza A(H1N2) variant virus were reported officially.
- **Risk assessment[3]:** The overall public health risk from currently known influenza viruses at the human-animal interface has not changed, and sustained human-to-human transmission of the viruses from these cases is currently considered unlikely. Although human infections with viruses of animal origin are unusual, they 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).[4] 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:

A(H5N1), United States of America (USA)

Since the last risk assessment of 28 March 2024, one human case of infection with an A(H5N1) influenza virus was notified to WHO from the USA on 1 April 2024.

The case is an adult aged over 18 years residing in the state of Texas. On 27 March, the case developed conjunctivitis while working at a commercial dairy cattle farm. The case had direct contact to apparently healthy dairy cattle and dairy cattle presumed to be infected with influenza A(H5N1) virus and the case did not wear any respiratory or eye protection when working with the dairy cattle. There was no reported exposure to sick or dead birds or other animals.[5]

[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 (2012). Rapid risk assessment of acute public health events. World Health Organization. Available at: https://iris.who.int/handle/10665/70810.

[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).

[5] Uyeki TM, Milton S, Abdul Hamid C, Reinoso Webb C, Presley SM, Shetty V et al. Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker. N Engl J Med. 2024 May 3.

On 28 March, respiratory and conjunctival specimens were collected from the case and tested at a local laboratory. Reverse transcription-polymerase chain reaction (RT-PCR) analysis indicated that both specimens were presumptive positive for influenza A(H5) virus. The specimens were then sent to the United States Centers for Disease Control and Prevention (US CDC) for further testing. They were received and tested at the US CDC on 30 March and confirmed as high pathogenicity avian influenza (HPAI) A(H5N1) virus clade 2.3.4.4b by RT-PCR and sequencing. On 28 March, the patient was advised to isolate and given antiviral treatment (oseltamivir) following US CDC guidance. The patient did not report symptoms other than conjunctivitis, was not hospitalized, and at the time of reporting, was recovering. Household contacts of the patient did not report illness and have been provided influenza antiviral prophylaxis as per US CDC recommendations. No additional cases of human infection with influenza A(H5N1) associated with this case have been identified.[6]

Further details are included in a joint FAO/WHO/WOAH preliminary assessment of recent influenza A(H5N1) viruses was published on 23 April 2024 here.[7]

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.

Risk Assessment:

1. What is the public health risk of additional sporadic human cases of infection with avian influenza A(H5) viruses?
Most human cases so far were sporadic infections in people exposed to A(H5) viruses, for example through contact with infected poultry or contaminated environments, including live poultry markets, and occasionally infected mammals and contaminated environments. While the viruses continue to be detected in animals and related environments humans are exposed to, further human cases are expected but unusual. The impact for public health if additional sporadic cases are detected is minimal. The overall public health risk of additional sporadic human cases is low.

2. What is the likelihood of sustained human-to-human transmission of avian influenza A(H5) viruses?
No sustained human-to-human transmission was identified associated with the events described above. In the past, small clusters of A(H5) virus infections were reported, including those involving health care workers, but without evidence of sustained human-to-human transmission. Current epidemiological and virological evidence suggests that contemporary influenza A(H5) viruses have not acquired the ability of sustained transmission among humans, therefore sustained human-to-human transmission is thus currently considered unlikely.

3. What is the likelihood 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 current evidence suggests these viruses have not acquired the ability to transmit easily among humans.

[6] World Health Organization (9 April 2024). Disease Outbreak News; Avian Influenza A (H5N1) – the United States of America. Available at: http://www.who.int/emergencies/disease-outbreak-news/iten/2024-DON512.
[7] World Health Organization (23 April 2024). Global Influenza Programme; Joint FAO/WHO/WOAH preliminary assessment of recent influenza A(H5N1) viruses. Available at: https://www.who.int/publications/m/item/joint-fao-who-woah-preliminary-assessment-of-recent-influenza-a(h5n1)-viruses.

A(H9N2), Viet Nam

Since the last risk assessment of 28 March 2024, one human case of infection with an A(H9N2) influenza virus was notified to WHO from Viet Nam on 9 April 2024.

A 37-year-old male from Tien Giang Province, Viet Nam, who had underlying conditions, developed a fever on 10 March 2024 and was admitted to the hospital on 16 March. Following a diagnosis of severe pneumonia, he was transferred to the intensive care unit (ICU) on 21 March and received treatment with oseltamivir and antibiotics. As of 15 April, the patient was in severe condition and under intensive care.

The patient was detected through severe viral pneumonia surveillance (SVP). A nasopharyngeal swab collected on 21 March tested positive by RT-PCR at the Pasteur Institute in Ho Chi Minh City (PI HCMC) for avian influenza A(H9) virus on 1 April. Subsequently, the virus was confirmed to be an avian influenza A(H9N2) virus on 8 April.

Case investigation identified that the patient lives near a poultry market, where poultry trade occurs daily in front of his house. There have been no reports of dead or sick poultry near the patient's residence or of consumption of sick, dead, or uncooked poultry products from his household or neighbouring households. On 2 April, seven poultry samples were collected from two live bird trading points within the same commune of the case's residence. One sample was positive A(H5N1), and the remaining were negative for avian influenza A(H5N1), A(H5N6), A(H5N8), A(H7N9), and A(H9) viruses. On 4 April, samples taken from two geese at the patient's house tested negative for A(H5) and A(H9) viruses.

Fifteen close contacts of the case were requested to self-monitor their health at home. As of 15 April, there were no reports of additional cases with respiratory symptoms among contacts of the case or outbreaks in the community where the case resides.

This is the first human infection with avian influenza A(H9N2) reported in Viet Nam.[8]

Avian influenza A(H9N2) viruses are enzootic in poultry in Asia including in Viet Nam.

Risk Assessment:

1. What is the public health risk of additional sporadic human cases of infection with avian influenza A(H9N2) viruses?

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. A few cases have been severe or fatal, mostly in persons with underlying conditions. Since the virus continues to be detected in poultry populations, further human cases can be expected but remain unusual. The impact to public health if additional sporadic cases are detected is minimal. The overall public health risk of additional sporadic human cases is low.

2. What is the likelihood of sustained human-to-human transmission of avian influenza A(H9N2) viruses?

No sustained human-to-human transmission has been identified associated with the event described above. Current epidemiologic and virologic evidence suggests that contemporary influenza A(H9N2) viruses assessed by the Global Influenza Surveillance and response System (GISRS) have not acquired

[8] World Health Organization (19 April 2024). Disease Outbreak News; Avian Influenza A(H9N2) in Viet Nam. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON514.

the ability of sustained transmission among humans, therefore sustained human-to-human transmission is thus currently considered unlikely.

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 current evidence suggests the A(H9N2) virus subtype has not acquired the ability to transmit easily among humans.

A(H10N3), China

Since the last risk assessment of 28 March 2024, one human case of infection with an influenza A(H10N3) virus was reported from China on 2 April 2024.

A 51-year-old male from Yunnan province, China, with no underlying conditions, had onset of illness on 28 February 2024. He developed fever, cough and shortness of breath, which progressed to respiratory failure, and he was admitted to hospital on 6 March with severe pneumonia. A sample collected from the patient tested positive for influenza A, and he was treated with antiviral medication starting on 6 March. On 16 March, testing of a sample collected on 15 March confirmed the sample was positive for A(H10N3). At the time of reporting, the patient was in severe condition in the intensive care unit. The patient is a poultry and livestock farmer who had exposure to poultry and a poultry-related environment prior to illness onset. No family members or close contacts had developed symptoms at the time of reporting. Samples collected from close contacts and the environment tested negative for A(H10N3) virus.

This is the third case of human A(H10N3) virus infection detected in China and globally to date.

Risk Assessment:

1. What is the public health risk of additional human cases of infection with avian influenza A(H10N3) viruses will occur?
Human infections with avian influenza A(H10) viruses have been detected and reported previously. The extent of circulation and epidemiology of these viruses in birds is unclear. Avian influenza A(H10N3) viruses with different genetic characteristics have been detected previously in migratory and other wild birds since the 1970s. As long as the virus continues to circulate in birds, further human cases can be expected but remain unusual. The impact to public health if additional sporadic cases are detected is minimal. The overall public health risk of additional sporadic human cases is low.

2. What is the likelihood of sustained human-to-human transmission of avian influenza A(H10N3) viruses?
No sustained human-to-human transmission has been identified associated with the event described above. Current epidemiologic and virologic evidence suggests that contemporary influenza A(H10N3) viruses assessed by the Global Influenza Surveillance and response System (GISRS) have not acquired the ability of sustained transmission among humans, therefore sustained human-to-human transmission is thus currently considered unlikely.

3. What is the likelihood of international spread of avian influenza A(H10N3) 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 based on current limited evidence.

Swine Influenza Viruses

Current situation:

Influenza A(H1N2) variant viruses [A(H1N2)v], USA

Since the risk assessment of 28 March 2024, one human infection with an influenza A(H1N2v) virus was reported from the USA on 29 March 2024.

A child under 18 years of age from the state of Pennsylvania, who had comorbidities and no travel history outside of the state, developed acute respiratory illness with fever, vomiting, cough, and rhinorrhea on 5 March, and sought emergency medical care that same day. An upper respiratory specimen collected from the patient that same day tested positive for influenza A virus. The patient was hospitalized, received influenza antiviral treatment, and has recovered from their illness.

The specimen was tested at the Pennsylvania Department of Health on 7 March where RT-PCR analysis indicated it was positive for influenza A virus but negative for contemporary human influenza A viruses representing either H1pdm09 or H3 subtypes. The specimen was then sent to the Centers for Disease Control and Prevention (CDC) and received on 26 March. That same day, CDC RT-PCR testing confirmed the sample was positive for an influenza A(H1N2)v virus. Additional virologic characterization was underway at the time of reporting.

Investigation by local public health officials identified swine exposure by the patient within ten days prior to their illness onset; these swine were not tested for influenza. Additional investigation identified mild illness in two of the patient's close contacts that began prior to the patient's onset of symptoms and have since resolved. Specimens were not collected from these individuals for testing.

This is the first influenza A(H1N2)v virus infection identified in the United States during 2024.

Risk Assessment:

1. What is the public health risk of additional sporadic human cases of infection with swine influenza viruses?

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 but remain unusual. The impact for public health if additional sporadic cases are detected is minimal. The overall risk of additional sporadic human cases is low.

2. What is the likelihood of sustained human-to-human transmission of swine influenza viruses?

No sustained human-to-human transmission was identified associated with the event described above. Current evidence suggests that contemporary swine influenza viruses have not acquired the ability of sustained transmission among humans, therefore sustained human-to-human transmission is thus currently considered unlikely.

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 current evidence suggest that 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 in poultry, wild birds and some wild and domestic mammals, the public should avoid contact with animals that are sick or dead from unknown causes, including wild animals, and should report dead birds and mammals or request their removal by contacting local wildlife or veterinary authorities.
- Eggs, poultry meat and other poultry food products should be properly cooked and properly handled during food preparation. Due to the potential health risks to consumers, raw milk should be avoided. WHO advises consuming pasteurized milk. If pasteurized milk isn't available, heating raw milk until it boils makes it safer for consumption.
- 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).[9] State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed[10] case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic[11]. 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

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

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

[11] World Health Organization. Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits, 2nd edition. Available at: https://iris.who.int/handle/10665/341850

with pandemic potential on a **timely basis**[12] with a WHO Collaborating Centre for Influenza of GISRS. The viruses are used by the public health laboratories to assess the risk of pandemic influenza and to develop candidate vaccine viruses.

- When there has been human exposure to a known outbreak of an influenza A virus in domestic poultry, wild birds or other animals – or when there has been an identified human case of infection with such a virus – enhanced surveillance in potentially exposed human populations becomes necessary. Enhanced surveillance should consider the health care seeking behaviour of the population, and could include a range of active and passive health care and/or community-based approaches, including: enhanced surveillance in local influenza-like illness (ILI)/severe acute respiratory infection (SARI) systems, active screening in hospitals and of groups that may be at higher occupational risk of exposure, and inclusion of other sources such as traditional healers, private practitioners and private diagnostic laboratories.
- 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 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
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
WHO Public health resource pack for countries experiencing outbreaks of influenza in animals:
https://www.who.int/publications/i/item/9789240076884
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 United Nations (FAO) webpage: Avian Influenza
https://www.fao.org/animal-health/avian-flu-qa/en/
OFFLU
http://www.offlu.org/

[12] 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