

Influenza at the human-animal interface

Summary and assessment, from 30 January to 15 April 2021¹

- **New infections²:** Since the previous update on 29 January 2021, two human infections with avian influenza A(H5N6) viruses, seven human infections with avian influenza A(H5N8) viruses, three human infections with avian influenza A(H5) viruses, 10 human infections with avian influenza A(H9N2) viruses, two human infections with influenza A(H1N1) variant viruses, and one human infection with an influenza A(H3N2) variant virus were reported officially.³
- **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 expected 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 (HA) 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

Since the last risk assessment on 29 January 2021, two new laboratory-confirmed human cases of influenza A(H5N6) virus infection were reported to WHO.

On 2 March 2021, China notified WHO of a 50-year-old male farmer from Guangxi Province infected with an influenza A(H5N6) virus and who had exposure to backyard poultry prior to the onset of his illness. He developed symptoms on 16 February 2021, was hospitalized on 17 February with severe pneumonia and passed away on 2 March. Environmental samples taken from around the patient's domestic poultry tested positive for influenza A(H5N6) viruses.

On 15 March 2021, Lao People's Democratic Republic (LPDR) notified WHO of a human case of infection with an influenza A(H5) virus in a five-year-old boy from Luang Prabang province who had exposure to backyard poultry (one of which was sick) prior to the onset of his illness. He developed symptoms on 28 February 2021 and a sample was collected on 1 March as part of routine influenza-like illness. On 12 March, the sample tested positive for influenza A(H5) and on 18 March, the N6

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 yearly report on human cases of influenza at the human-animal interface published in the Weekly Epidemiological Record. Available at: www.who.int/wer/en/

³ Standardization of terminology for the influenza virus variants infecting humans: Update. Available at: https://www.who.int/influenza/gisrs_laboratory/terminology_variant/en/

⁴ World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005). Available at: www.who.int/ihr/Case_Definitions.pdf

subtype was confirmed. The patient recovered on 8 March. As part of the investigation, no further cases of infection with influenza viruses were detected upon testing of close contacts. Influenza A(H5N6) virus was detected in samples from poultry in a neighboring village and there were deaths reported among backyard poultry from neighboring houses.

A total of 31 laboratory-confirmed cases of human infection with influenza A(H5N6) virus have been reported to WHO since 2014, with 30 reported from China and one reported from LPDR.

On 18 February 2021, the Russian Federation notified WHO of the detection of avian influenza A(H5N8) virus in seven human clinical specimens in December 2020. Positive nasopharyngeal clinical specimens were collected from poultry farm workers who participated in a response operation to contain an avian influenza A(H5N8) outbreak detected in a poultry farm in Astrakhan Oblast in the Russian Federation. The laboratory investigation of the seven specimens was performed by the State Research Centre for Virology and Biotechnology VECTOR (WHO H5 Reference Laboratory). The age of the seven cases ranged between 29 to 60 years and five were female. The cases remained asymptomatic for the whole follow-up duration (several weeks). Follow-up nasopharyngeal swabs were collected during the medical observation period and tested negative for influenza A(H5N8) virus. No obvious clinical manifestations were reported from any farm workers under medical surveillance, their family members, or other close contacts of the seven cases.⁵

To date, for the investigated human cases, one virus (A/Astrakhan/3212/2020) has been laboratory-confirmed as A(H5N8) clade 2.3.4.4b by sequencing. This virus and those from poultry were nearly identical to each other and were closely related to other A(H5) clade 2.3.4.4b viruses detected in poultry and wild birds in other parts of Eurasia. Further laboratory investigation of samples is ongoing.

This is the first reported human infection with an avian influenza subtype A(H5N8) virus. Based on the risk assessment, WHO recommended the development of a new candidate vaccine virus (CVV) to provide a H5 clade 2.3.4.4b CVV with a neuraminidase (NA) gene more representative of currently circulating viruses.⁶

On 4 March 2021, Nigeria notified WHO of the detection of human cases of infection with avian influenza A(H5) viruses associated with outbreaks of avian influenza A(H5N1) in poultry. According to the IHR notification, on 29 January and 3 February 2021, the Nigeria Centre for Disease Control (NCDC) received reports of confirmed avian influenza outbreaks among poultry in Kano and Plateau States, respectively. A joint team from NCDC and the Department of Veterinary Services and Pest Control were deployed to both states.

As of 17 March, 64 nasopharyngeal/oropharyngeal swabs were collected from bird handlers, who had been exposed to avian influenza A(H5N1) positive birds. Seven of the 64 samples tested positive for influenza A virus (four in Kano State, three in Plateau State), three of which were positive for influenza A(H5) at the NCDC National Reference Laboratory (NRL). All of the seven influenza A-positive cases were asymptomatic.

Samples from the seven influenza A-positive human cases were shipped to the WHO Collaborating Centre at the United States Centers for Disease Control and Prevention (US CDC) for further characterization. Only fragments from three samples were able to be sequenced and the results indicated the influenza (H5) virus in the samples was from the H5 2.3.4.4b clade, and the HA gene

⁵ <https://www.who.int/csr/don/26-feb-2021-influenza-a-russian-federation/en/>

⁶ https://www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

sequences were similar to those from influenza A(H5N8) viruses recently reported in wild birds and poultry outbreaks in Africa, Asia, Europe, and the Middle East. NA gene sequences could not be generated; thus, the NA subtype could not be confirmed. The confirmation of infection with influenza A(H5) versus transient contamination of the nasopharynx/oropharynx after exposure to infected birds or contaminated environment, in these persons remains inconclusive. Additional information may be gained through the collection and analysis of serological samples.

Outbreaks of avian influenza A(H5N1) in poultry in Nigeria were first reported in February 2006. One human case of infection with an influenza A(H5N1) virus was reported from Nigeria in 2007. Influenza A(H5N8) virus infections in poultry were reported in 2016 in several states including Plateau, Bauchi, and Kano. In 2019, Nigeria reported the first occurrence of influenza A(H5N6) virus outbreaks in birds at a live poultry market in Sokoto state.

According to reports received by the OIE, various influenza A(H5) subtypes continue to be detected in birds in Africa, Europe and Asia.

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 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. The detection of influenza A(H5) virus in nasopharyngeal/oropharyngeal samples collected from individuals in close contact with infected poultry or other birds, whether the individuals are symptomatic or not, is not unexpected. Good quality serological investigations may be useful in differentiating infection from contamination in these cases and allow for a better assessment of the risk of human infection.

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 influenza 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

There have been no publicly available reports from animal health authorities in China or other countries on influenza A(H7N9) virus detections in animals in recent months.⁷

Overall, the risk assessment has not changed.

⁷ Food and Agriculture Organization of the United Nations. H7N9 Situation Update. www.fao.org/ag/againfo/programmes/en/empres/H7N9/situation_update.html

Avian influenza A(H9N2) viruses

Between 3 February and 15 April 2021, China notified WHO of the detection of nine human cases of infection with influenza A(H9N2). All were detected through ILI surveillance and all except one case reportedly had mild illnesses (the 54-year-old woman was hospitalized with severe pneumonia and underlying conditions), and all except one (the six-year-old boy) are reported to have recovered. Additionally, no clusters of cases have been reported. More details are included in Table 1.

Table 1. Human cases of influenza A(H9N2) reported to WHO from China from 30 January to 15 April 2021.

Date reported to WHO	Onset date	Reporting province*	Gender	Age (years)	Live poultry exposure
3 Feb 2021	26 Jan 2021	Guangdong	M	6	Yes
5 Feb 2021	22 Jan 2021	Hunan	F	8	Unknown
8 Feb 2021	2 Feb 2021	Guangdong	M	2	Yes
10 Feb 2021	17 Jan 2021	Anhui	F	5	Unknown
10 Feb 2021	30 Nov 2020	Sichuan	F	1	Yes
10 Feb 2021	18 Jan 2021	Jiangxi	F	2	Unknown
18 Feb 2021	20 Oct 2020	Anhui	F	54	Yes
9 April 2021	28 Jan 2020	Fujian	M	10	No
9 April 2021	7 Feb 2021	Hubei	F	2	Yes

*Potential exposure location is same as reporting province for all these cases.

On 17 March, Cambodia notified WHO of the detection of one human case of infection with an avian influenza A(H9N2) virus. The virus was detected in a three-year-old boy from Siem Reap province who developed mild illness on 26 February 2021. A sample was collected on 28 February as a part of routine influenza-like illness surveillance and was confirmed to be positive for influenza A(H9) on 4 March with the N2 subtype determined thereafter. The patient had exposure to domestic live poultry prior to the onset of illness. As part of the investigation, no further cases of infection with influenza A(H9N2) were detected upon testing of close contacts. Testing results on samples from poultry in the patient's backyard as well as from poultry from a nearby live bird market and a poultry wholesaler in Siem Reap are pending.

This is the first case of human infection with an influenza A(H9N2) virus reported from Cambodia.

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 the Global Influenza Surveillance and Response System (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 virus (A(H1N1)v)

On 4 February 2021, Denmark notified WHO of a human case of infection with a swine influenza A(H1N1)v virus. The patient, a 73-year old female with underlying conditions, developed symptoms of a respiratory tract infection on 19 January 2021. The patient was admitted to hospital on 20 January and a sample was collected on 21 January as part of routine surveillance. The patient was discharged on 26 January. The patient lives in a rural area with a pig farm nearby although the patient had not been near the farm prior to illness onset. As part of the investigation, samples from the pigs from the nearby farm were tested and all were negative for influenza viruses. There is no clinical evidence of onward transmission among the patient's close contacts and no other human infections with swine influenza viruses were detected among samples tested in Denmark in January 2021.

Whole genome sequencing of the patient's sample indicated that all of the genes except one were derived from an influenza A(H1N1)pdm09 virus, with highest similarity to those circulating in swine. The remaining gene had highest similarity to avian-like influenza A(H1N1) and A(H1N2) swine viruses. All genes were distinct from the seasonal influenza vaccine virus A/Brisbane/02/2018.

On 24 March 2021, the United States of America (USA) notified WHO of a human infection with a swine influenza A(H1N1)v virus. The patient, an adult over 18 years of age old with no underlying medical conditions that would convey increased risk for severe influenza, developed an influenza-like illness in North Carolina on 17 November 2020. On 24 November, the patient sought medical care and a sample was collected. Real-time RT-PCR testing at the North Carolina State Public Health Laboratory indicated an influenza A(H1N1)pdm09 virus infection. The specimen was forwarded to the National Influenza Reference Center in New York on 23 February 2021 for inclusion in the national influenza virus strain surveillance program where whole genomic sequencing was performed. On 22 March 2021, analysis of the sequence data by the Influenza Division of the Centers for Disease Control and Prevention confirmed an A(H1N1)v virus infection. Retrospective investigation into the source of the infection revealed that the patient worked with and had daily contact with swine. No human-to-human transmission has been identified associated with this patient. The patient was not hospitalized and has recovered from illness. This is the first influenza A(H1N1)v virus identified from a specimen collected in the United States in 2020.

Influenza A(H3N2) variant virus (A(H3N2)v)

On 9 April 2021, Australia reported to WHO the detection of a human case of infection with an influenza A(H3N2)v. The virus was detected in a sample from a 10-year-old boy from South Australia. He developed respiratory and gastrointestinal symptoms on 26 January 2021 and sought healthcare as an outpatient. The respiratory sample was taken on 27 January and was reported as influenza A

positive and then forwarded to the WHO Collaborating Centre for Reference and Research on Influenza Victorian Infectious Diseases Reference Laboratory. Sequencing and phylogenetic analysis of the HA and NA genes of the virus showed that the virus was an A(H3N2)v virus that was nearly identical to a virus detected in a sample from a person in Australia in 2018. Both these viruses grouped with other variant swine influenza viruses detected in Australia and USA over the last decade. The remaining internal genes were contributed by influenza A(H1N1)pdm09 viruses that had been previously circulating in swine prior to this reassortant virus being generated. The patient has recovered and there was no identified possible source of exposure to the virus.

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 traveler 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 from countries affected by these influenza viruses, refer to OIE guidance.
- WHO advises that travelers 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. Travelers 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 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 virus circulation in animals is not clear, epidemiological and virological surveillance and the follow-up of suspected human cases should remain high. Guidance on investigation of non-seasonal influenza and other emerging acute respiratory diseases has been published on the WHO website here www.who.int/influenza/resources/publications/outbreak_investigation_protocol/en/.
- In the current COVID-19 pandemic, vigilance for the emergence of novel influenza viruses of pandemic potential should be maintained. WHO is developing practical guidance to prepare for

the upcoming influenza season and influenza emergencies in the context of the cocirculation of SARS-CoV-2 and influenza viruses.

- All human infections caused by a new subtype of influenza virus are notifiable under the International Health Regulations (IHR, 2005).⁸ State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory-confirmed⁹ case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic¹⁰. 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 regular and **timely basis**¹¹ 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/

WHO Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases

http://www.who.int/influenza/resources/publications/outbreak_investigation_protocol/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://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/

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>

⁸ World Health Organization. Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005). Available at: www.who.int/ihr/Case_Definitions.pdf

⁹ World Health Organization. Manual for the laboratory diagnosis and virological surveillance of influenza (2011). Available at: www.who.int/influenza/gisrs_laboratory/manual_diagnosis_surveillance_influenza/en/

¹⁰ https://www.who.int/influenza/resources/pip_framework/en/

¹¹ World Health Organization. Operational guidance on sharing influenza viruses with human pandemic potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework (2017). Available at: www.who.int/influenza/gisrs_laboratory/ivpp_sharing_guidance/en/