



## Preliminary FAO/WHO/WOAH Joint Rapid Risk Assessment

# Human infection with influenza A(H5N1), Cambodia (2023)

### Background

As of 27 March 2023, two human cases of infection with avian influenza virus A(H5N1) virus have been confirmed in Cambodia. On 23 February 2023, Cambodia reported to WHO one confirmed fatal case of human infection with avian influenza A(H5N1) virus in a child. A second case, the father of the first case, was reported on 24 February 2023 and had mild illness. Both cases had onset of illness on the same day, and both had exposure to sick and dead backyard poultry. No further cases associated with this event or through other surveillance activities have been detected. There is no evidence of human-to-human transmission associated with this event given the information available at this time.

Limited, non-sustained human-to-human transmission of zoonotic influenza A(H5N1) viruses has been observed in past events and appears to be unusual.<sup>1</sup> Sustained human-to-human transmission of influenza A(H5N1) viruses has not been documented.

### Summary of the assessment of current risk to humans posed by A(H5N1) virus

As long as influenza A(H5N1) viruses are circulating in animals, further human infections with A(H5N1) viruses cannot be excluded. The likelihood of sustained human-to-human transmission of these current viruses is low based on the information obtained to date. The Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Organisation for Animal Health (WOAH) will re-assess the risk associated with the influenza A(H5N1) viruses as more information becomes available.

### Human infections

Between 2005 and 2014, sporadic human cases of infection with influenza A(H5N1) viruses due to poultry-to-human transmission (directly or indirectly through the contaminated environment) were reported in Cambodia. The cases described above are the first two cases reported in Cambodia since 2014. Globally, 873 human cases of infection with avian influenza A(H5N1) viruses, including 458 fatal cases, have been reported from 22 countries. Occasional spillover of avian influenza A(H5N1) viruses into humans has occurred when this virus is circulating in birds. Most people who have been infected with these viruses have had direct contact with infected birds or indirect contact via exposure to environments contaminated with the viruses.

### Findings in animals

Avian influenza viruses are persistently circulating in poultry in Cambodia. Longitudinal surveillance in Cambodia reveals high levels of avian influenza viruses, including A(H5N1) viruses and other subtypes, are regularly detected in poultry. Since 2017, Cambodia has reported 8462 cases of A(H5N1) in poultry to (WOAH), and the number of cases in wild birds is unknown (although the disease has been reported present in this population to WOA).<sup>2</sup> Previous outbreaks were reported in backyard, farms or village poultry, with the most recently reported poultry outbreak occurring in January 2021. Specimens collected from chickens and ducks near the residence of the child

<sup>1</sup> United States Centers for Disease Control and Prevention. Past Examples of Probable Limited, Non-Sustained, Person-to-Person Spread of Avian Influenza A Viruses. <https://www.cdc.gov/flu/avianflu/h5n1-human-infections.htm>

<sup>2</sup> <https://wahis.woah.org/#/home>

(the first case described above) on 23 Feb were negative for influenza A(H5N1) viruses. Most recently, on 6 March 2023, an outbreak in wild birds was reported to WOAHA.<sup>2</sup> It began on 24 February in the same province as the two human cases mentioned above.

## Understanding of the virus

The A/goose/Guangdong/96 (Goose/Guangdong)-like virus lineage of influenza A(H5N1) viruses first emerged in birds in 1996-97 and later re-emerged in 2003-04. Viruses from this lineage continue to evolve and cause outbreaks in domestic and wild birds. The continuous evolution of the hemagglutinin (HA) protein gene of these viruses has resulted in the designation of different influenza A(H5) genetic clades (groups).<sup>3</sup>

In Cambodia, surveillance in poultry indicates different clades have circulated. Influenza A(H5) viruses of clade 1.1.2 were predominant in poultry in 2013 and were detected in a number of human infections. In 2014, these viruses were replaced by clade 2.3.2.1c viruses in poultry and were detected in one human case. Since 2014, influenza A(H5N1) viruses belonging to clade 2.3.2.1c have circulated persistently in poultry. Starting in 2018, A(H5N6) viruses of clade 2.3.4.4g and 2.3.4.4h were detected, and A(H5N8) viruses belong to clade 2.3.4.4b started to be detected in poultry at live bird markets in late 2021.<sup>4</sup>

The viruses from the two human cases mentioned above belonged to the influenza A(H5) genetic clade 2.3.2.1c.

Influenza A(H5N1) viruses of the 2.3.2.1c clade have been detected in other countries in Africa, Asia, Europe and the Middle East in domestic and wild birds.<sup>5</sup>

## Recommended actions

It is strongly recommended that countries remain vigilant for potential human infections with avian influenza viruses, particularly through National Influenza Centers (NICs), other national laboratories, national and sub-national surveillance systems associated with the Global Influenza Surveillance and Response System (GISRS).

All human samples that are confirmed influenza A-positive but negative for the HAs of seasonal viruses, together with any additional information, should be expedited for shipment to a WHO Collaborating Center of GISRS.

As avian influenza is persistently circulating in Cambodia, epidemiological and virological surveillance, and the follow-up of any suspected human and animal cases should be implemented systematically. Collaboration between the animal and human health sectors is essential. Procedures to reduce human exposure to potentially infected birds with avian influenza viruses should be considered and implemented to minimize the risk of zoonotic infections.

FAO, WOAHA, WHO and OFFLU are closely working together to monitor the avian influenza situation, including the detection and geographic spread of avian influenza viruses, and their evolution, and to provide timely updated risk assessments.

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<sup>3</sup> WHO/OIE/FAO H5N1 Evolution Working Group. Toward a unified nomenclature system for highly pathogenic avian influenza virus (H5N1) [conference summary]. *Emerg Infect Dis* [serial on the Internet]. 2008 Jul. Available at: <http://www.cdc.gov/EID/content/14/7/e1.htm>.

<sup>4</sup> Edwards KM, Siegers JY, Wei X, Aziz A, Deng Y, Yann S, et al. Detection of Clade 2.3.4.4b Avian Influenza A(H5N8) Virus in Cambodia, 2021. *Emerg Infect Dis*. 2023;29(1):170-174. Available at: <https://doi.org/10.3201/eid2901.220934>.

<sup>5</sup> Suttie A, Tok S, Yann S, Keo P, Horm SV, Roe M, et al. (2019) Diversity of A(H5N1) clade 2.3.2.1c avian influenza viruses with evidence of reassortment in Cambodia, 2014-2016. *PLoS ONE* 14(12): e0226108. Available at: <https://doi.org/10.1371/journal.pone.0226108>.