

Highly Pathogenic Avian Influenza A (H5N1) in the United States

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Background

On 1 April 2024, the United States (US) reported a laboratory-confirmed human case of highly pathogenic avian influenza (HPAI) A (H5N1) in Texas¹. HPAI A (H5N1) is part of the influenza A viruses. There are four influenza viruses (A, B, C, and D) belonging to the *Orthomyxoviridae* viral family²⁻⁴. Only influenza A is believed to be capable of causing a global pandemic and has caused four pandemics since 1900 (**Figure 1**)^{2,5-9}. Influenza A pandemics occur when a new virus emerges that can infect humans and sustain human-to-human transmission^{2,9}. There are over 130 subtypes of influenza A viruses categorised according to numerous haemagglutinin (H) and neuraminidase (N) antigens^{3,10}. Some subtypes such as H1N1 and H3N2 routinely circulate among humans however, others such as H5N1 predominantly affect animals with only sporadic human cases^{3,11}.

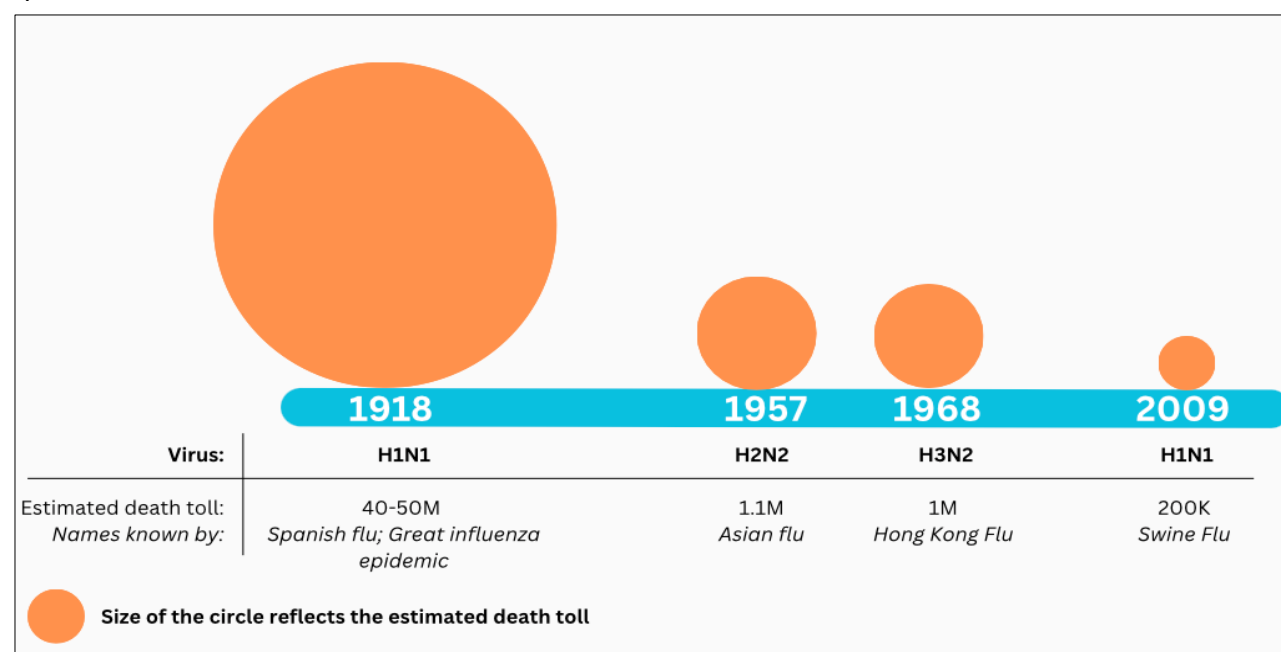


Figure 1:

Pandemics caused by influenza A since 1900

Data used: LePan N. (2020). Visualizing the History of Pandemics. Visual Capitalist. Healthcare. Available from: <https://www.visualcapitalist.com/history-of-pandemics-deadliest/>

Many animals are infected with influenza A viruses, and these do not easily transmit to humans². Animal influenza viruses are named according to the infected host species, for example, avian, swine, or equine influenza (**Figure 2**)². Avian influenzas (also known as bird flu viruses) infect birds globally and can be categorised according to disease severity: low pathogenicity avian influenza (LPAI) and high pathogenicity avian influenza (HPAI)¹². Some HPAI strains can infect humans such as HPAI A (H5N1).

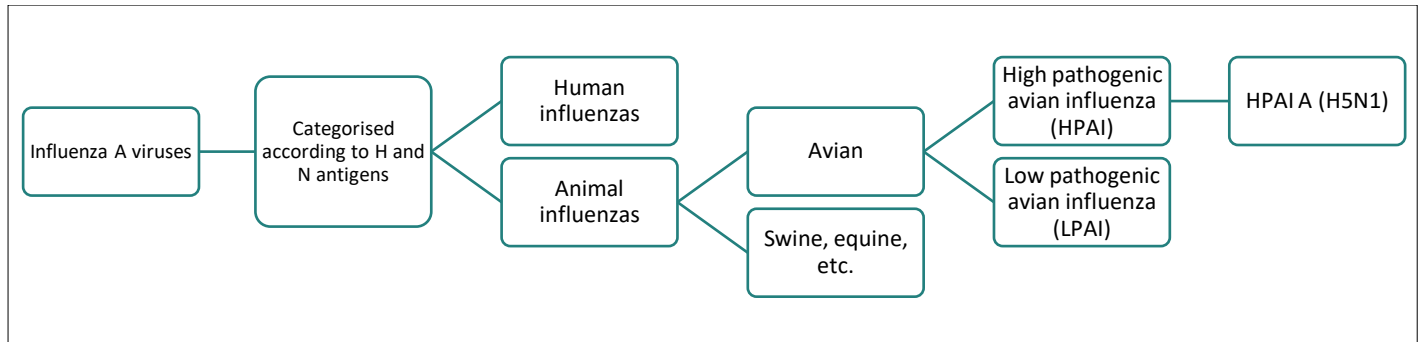


Figure 2: Categorisation of influenza A avian viruses to illustrate the category HPAI A (H5N1) falls under

Transmission, Clinical Presentation, Diagnosis, and Treatment of HPAI A (H5N1)

HPAI A (H5N1) can spread to humans when they come into direct contact with infected poultry or their contaminated environments¹³. Spread from direct contact with infected mammals such as cattle has also been reported however, this is rare¹³. There has been no known sustained human-to-human transmission of the virus yet¹⁴. Humans infected with HPAI A (H5N1) may be asymptomatic or present with mild symptoms of fever, cough, malaise, and a sore throat¹³. In some cases, the disease can become severe and lead to conjunctivitis, respiratory illness, or neurological complications such as seizures^{13,15}. Cases can be treated with antivirals such as oseltamivir and there are four antivirals recommended for use in the US^{13,16}. Vaccination with seasonal flu vaccines does not protect against H5N1¹³.

HPAI A (H5N1) 2024 outbreak in the United States

Infected animals

Since December 2021, poultry, wild birds, and mammals infected with H5N1 have been detected throughout North America¹⁷. Birds are more affected than mammals and wild aquatic birds are considered to be the reservoir host for avian influenza A viruses^{17,18}. Between January 2022 and 30 August 2024, at least 100 million poultry, 9,700 wild birds, and 197 dairy cattle have been infected with HPAI A(H5) viruses across almost all 50 states in the US¹⁹. Genetic sequencing of poultry, where available, confirms infection with H5N1 clade 2.3.4.4²⁰. Infected dairy cattle have only been detected in the US since March 2024 and there is concern that the spread of H5N1 to dairy cattle indicates virus adaptation and the possibility that the virus may become easier to spread to humans^{21,22}.

The first infected cattle in the US were reported on 25 March and involved cattle in two dairy farms in Kansas and one in Texas²³. Since then, infected cattle have been reported from 14/50 states and 22/50 states have implemented restrictions on the importation of dairy cattle²⁴. Infected cattle develop a low appetite, reduced milk production, and produce thickened discoloured milk²⁴. Genetic sequencing so far has confirmed infection with 2.3.4.4b (Eurasian lineage goose/Guangdong clade)²⁴. The virus has spread between cattle in the same herd, but mortality rates have been recorded as low as 2%²⁴. This is less than the high mortality associated with infected birds²⁴. Infected cats have been reported from areas with infected dairy cattle and their illness has been more severe²⁴. Since 2022, sporadic infections have

occurred in various animals and while the virus has been transmitted from mammal to mammal in 2024, testing so far has not found evidence that there have been changes in the virus that could make it more transmissible^{24,25}.

Infected humans

Infection with HPAI A (H5N1) in humans is rare and only sporadic infections have been reported in the US due to close contact with infected animals¹⁴. In 2024, and as of 3 October, 16 human cases of H5 (nine of which have been confirmed as H5N1, however it is likely all are H5N1) have been confirmed in Colorado (n=10), Michigan (n=2), Missouri (n=1), Texas (n=1), and California (n=2)^{26,27}. The most recent cases were reported by California on 3 October²⁷. All cases except for the one case in Missouri had known contact with infected or sick animals^{19,28}. In Missouri, a household contact of the confirmed case became sick but was not tested, and both cases have recovered²⁸. The US Centers for Disease Control and Prevention (CDC) maintains that this is not indicative of person-to-person transmission but likely a common exposure²⁸. Due to low viral RNA levels, the US has not been able to determine the neuraminidase subtype as N1 for all cases²⁹. Before 2024, only one human case of HPAI A (H5N1) infection occurred in 2022 after exposure to infected poultry²⁶. There has not been any case of human-to-human transmission yet although a recent study suggests that the virus can transmit to the upper respiratory tract of humans which could facilitate human transmission^{19,30}. While there is evidence that consumption of untreated raw milk from infected cattle could transmit the disease to other animals and pose a risk to humans, the US Food and Drug Administration (FDA) maintains that the commercial milk supply is safe^{31,32}.

Public Health Response and Risk Assessments

While the spread of H5N1 to cattle and between cattle has caused some concern about the transmissibility of the virus, the US CDC state as of 28 August 2024, that the risk of H5N1 spread to the public is low¹⁹. This is in line with the Food and Agriculture Organization (FAO), the World Health Organization (WHO), and the World Organisation for Animal Health (WOAH) which also state the risk to the public is low however, the risk to persons exposed is low to moderate depending on the nature of the exposure³³.

The US CDC continues to monitor the situation closely to identify any genetic changes that could suggest increased transmissibility, increased disease severity, and reduced susceptibility to antivirals³⁴. They are also conducting wastewater surveillance to complement influenza surveillance systems however this cannot distinguish the subtype or source of influenza A viruses²⁶. Even with a strong surveillance system, there are several barriers to detecting H5N1 in humans and the likely number of infections may be higher than what is reported³⁵. Barriers to detection include asymptomatic infection, limited access to rural farm workers who may be hesitant to seek medical care (especially without health insurance or with concerns about immigration status), and a lack of incentive to report infections in cattle³⁵.

Useful Resources

- Pandemic PACT has a dedicated [H5N1 page](#) in the Outbreak section of the website which provides information and analyses of active mpox research and funding globally since 2020.
- The US CDC published a '[Public Health Science Agenda for Highly Pathogenic Avian Influenza A\(H5N1\)](#)' with strategic priorities to guide research and surveillance activities.
- NIAID published a '[Research Agenda for 2024 H5N1 Influenza – May 2024](#)'.
- The WHO published a '[Summary status of development and availability of A\(H5N1\) candidate vaccine viruses and potency testing reagents](#)' in February 2024.

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