

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

Last updated: 01 Nov 2024

Prepared by the GloPID-R Research and Policy team with support from the Pandemic PACT programme

Table of Contents

Background	1
Transmission, Clinical Presentation, Diagnosis, and Treatment of HPAI A (H5N1)	2
HPAI A (H5N1) 2024 outbreak in the United States	2
Infected animals.....	2
Infected humans	3
Public Health Response and Risk Assessments	3
Useful Resources.....	4
References	4

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}.

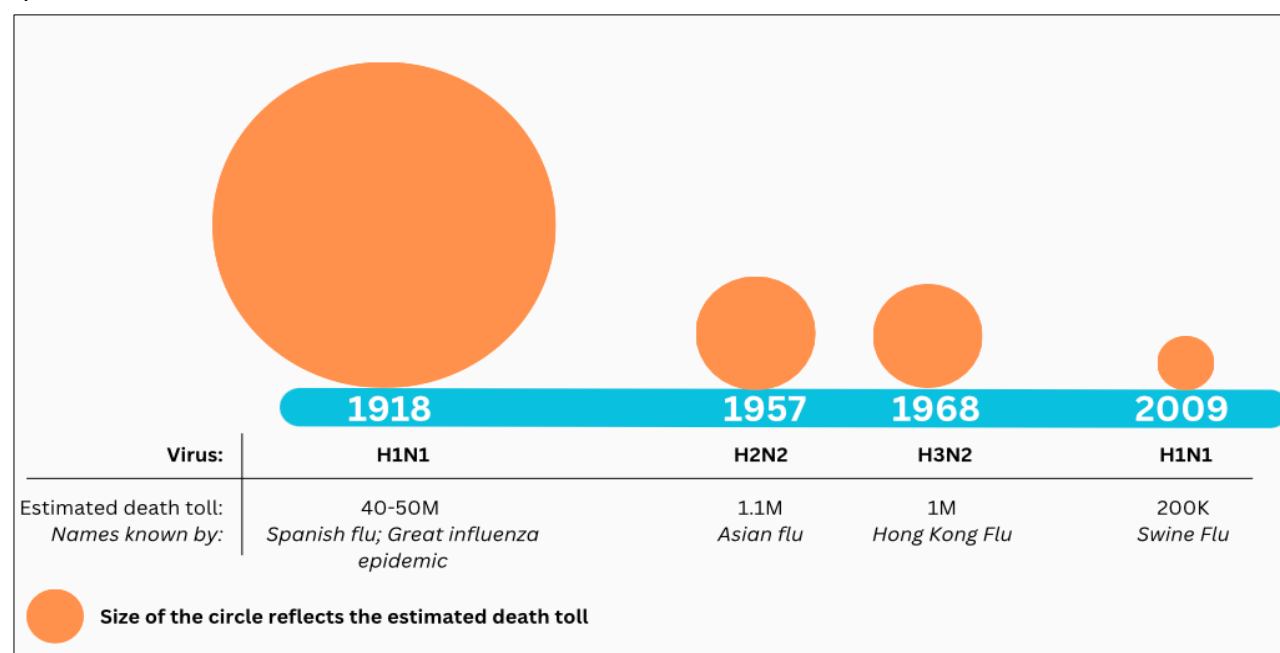


Figure 1: Pandemics caused by influenza A since 1900

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).

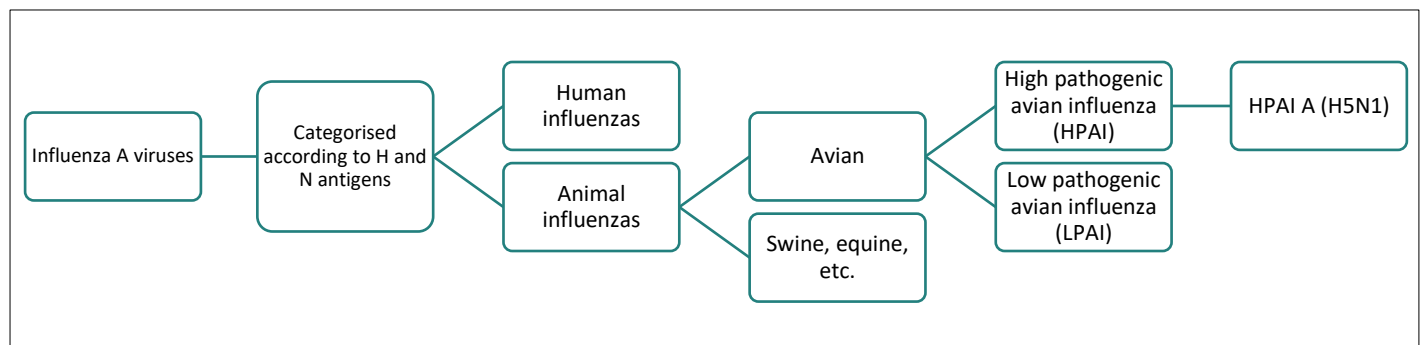


Figure 2: Categorisation of influenza A avian viruses to illustrate the category HPAI A (H5N1) falls under

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 31 October 2024, at least 100 million poultry, 10,000 wild birds, 403 dairy cattle, and one pig have been infected with HPAI A(H5) viruses across almost all 50 states in the US^{19–21}. Genetic sequencing of poultry, where available, confirms infection with H5N1 clade 2.3.4.4²². 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^{20,23}.

The first infected cattle in the US were reported on 25 March and involved cattle in two dairy farms in Kansas and one in Texas²⁴. Since then, infected cattle have been reported from 14/50 states and 22/50 states have implemented restrictions on the importation of dairy cattle²⁵. California has the highest number of affected dairy cattle²⁰. On 3 October, there were 56 affected herds in California, which increased to 100 by 11 October and 203 by 29 October. Colorado is the second most affected state with 64 herds affected as of 13 August²⁰. Infected cattle develop a low appetite, reduced milk production, and produce thickened, discoloured milk²⁵. Genetic sequencing so far has confirmed infection with 2.3.4.4b (Eurasian lineage goose/Guangdong clade)²⁵. The virus has spread between cattle in the same herd, but mortality rates have been recorded as low as 2%²⁵. This is less than the high mortality associated with infected birds²⁵. Infected cats have been reported from areas with infected dairy cattle and their illness has been more severe²⁵. 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^{25,26}.

On 29 October, H5N1 was reported in a pig on a non-commercial farm in Oregon. This is the first time that H5N1 has been confirmed in a pig in the US²¹. There were four other pigs on the farm all of which had been euthanised²¹. Two of these pigs have tested negative for H5N1 and two are awaiting test results²¹. As the farm is non-commercial, the US Department of Agriculture (USDA) maintains that the national pork supply remains safe²¹.

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 30 October, 39 human cases of H5 (some of which have been confirmed as H5N1, however it is likely all are H5N1) have been reported from Colorado (n=10), Michigan (n=2), Missouri (n=1), Texas (n=1), Washington (n=9), and California (n=16)^{27,28}. Most cases developed eye redness and conjunctivitis but some reported mild respiratory symptoms²⁹. No case has been hospitalised²⁹. All cases except for the one case in Missouri had known contact with infected or sick animals^{19,30}. In Missouri, a household contact of the confirmed case became sick but was not tested, and both cases have recovered³⁰. The US Centers for Disease Control and Prevention (CDC) maintains that this is not indicative of person-to-person transmission but likely a common exposure³⁰. Similarly, while California has the highest number of human infections, epidemiological investigation suggests that this is occurring due to sporadic animal-to-human transmission³¹. Due to low viral RNA levels, the US has not been able to determine the neuraminidase subtype as N1 for all cases³². Before 2024, only one human case of HPAI A (H5N1) infection occurred in 2022 after exposure to infected poultry²⁷. 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^{19,33}. 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^{34,35}. To gain a better understanding of the prevalence of H5N1 in raw cow's milk, a double-blind study for gathering purposes only intends to begin on 28 October. This study will sample Grade "A" raw cow's milk from dairy processing facilities for detection of H5N1³⁴.

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 states 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 exposure³⁶.

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 antivirals³⁷. They are also conducting wastewater surveillance to complement influenza surveillance systems however this cannot distinguish the subtype or source of influenza A viruses²⁷. 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 reported³⁸. 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 cattle³⁸.

As part of a CDC initiative, over 100,000 seasonal influenza vaccine doses have been administered to individuals from 12 states with infected dairy cattle³¹. The vaccine does not protect against H5N1 however, it could reduce illness severity³¹. Further, with a reduction in seasonal influenza, HPAI (H5) cases may be

better detected³¹. In addition, the USDA has approved two vaccine candidates for research trials to develop vaccines that protect cattle from H5N1²¹.

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.

References

1. US Centers for Disease Control and Prevention. Highly Pathogenic Avian Influenza A (H5N1) Virus Infection Reported in a Person in the U.S. CDC Newsroom [Internet]. 2024 Apr 1 [cited 2024 Aug 14]; Available from: <https://www.cdc.gov/media/releases/2024/p0401-avian-flu.html>
2. World Health Organization. Influenza (Avian and other zoonotic) [Internet]. Fact sheets. 2023 [cited 2024 Aug 14]. Available from: [https://www.who.int/news-room/fact-sheets/detail/influenza-\(avian-and-other-zoonotic\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic))
3. US Centers for Disease Control and Prevention. Types of Influenza Viruses [Internet]. Influenza (Flu). 2023 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/flu/about/viruses/types.htm>
4. Donchet A, Oliva J, Labaronne A, Tengo L, Miloudi M, C.A. Gerard F, et al. The structure of the nucleoprotein of Influenza D shows that all Orthomyxoviridae nucleoproteins have a similar NPCORE, with or without a NPTAIL for nuclear transport. *Sci Rep*. 2019 Jan 24;9(1):600.
5. US Centers for Disease Control and Prevention. 2000-2009 Highlights in the History of Avian Influenza (Bird Flu) Timeline [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/bird-flu/avian-timeline/2000-2009.html>
6. US Centers for Disease Control and Prevention. 1960-1999 Highlights in the History of Avian Influenza (Bird Flu) Timeline [Internet]. Avian Flu (Bird Flu). 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/bird-flu/avian-timeline/1960-1999.html>
7. US Centers for Disease Control and Prevention. 1880-1959 Highlights in the History of Avian Influenza (Bird Flu) Timeline [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/bird-flu/avian-timeline/1880-1959.html>
8. LePan N. Visualizing the History of Pandemics [Internet]. Visual Capitalist. Healthcare. 2020 [cited 2024 Aug 14]. Available from: <https://www.visualcapitalist.com/history-of-pandemics-deadliest/>
9. US Centers for Disease Control and Prevention. About Pandemic Influenza [Internet]. Pandemic Flu. 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/pandemic-flu/basics/index.html>
10. US Centers for Disease Control and Prevention. About Influenza A in Animals [Internet]. Influenza in Animals. 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/flu-in-animals/about/index.html>
11. US Centers for Disease Control and Prevention. Avian Influenza Type A Viruses [Internet]. Avian influenza (Bird Flu). 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/bird-flu/about/index.html>
12. World Organisation for Animal Health. Avian Influenza [Internet]. 2024 [cited 2024 Aug 14]. Available from: <https://www.woah.org/en/disease/avian-influenza/>
13. World Health Organization. Influenza: A(H5N1) [Internet]. Questions and answers. 2024 [cited 2024 Aug 14]. Available from: <https://www.who.int/news-room/questions-and-answers/item/influenza-h5n1>
14. US Centers for Disease Control and Prevention. Current U.S. Bird Flu Situation in Humans [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/bird-flu/situation-summary/inhumans.html>
15. PAHO. Avian Influenza [Internet]. [cited 2024 Aug 14]. Available from: <https://www.paho.org/en/topics/avian-influenza#:~:text=The%20Highly%20Pathogenic%20Avian%20Influenza,in%20birds%20are%20not%20zoonotic.>
16. Garg S, Reed C, Davis CT, Uyeki TM, Behraves CB, Kniss K, et al. Outbreak of Highly Pathogenic Avian Influenza A(H5N1) Viruses in U.S. Dairy Cattle and Detection of Two Human Cases — United States, 2024. *MMWR Morb Mortal Wkly Rep*. 2024 May 30;73(21):501–5.
17. National Wildlife Health Center. Distribution of Highly Pathogenic Avian Influenza in North America, 2021/2022 [Internet]. USGS. 2022 [cited 2024 Aug 28]. Available from: <https://www.usgs.gov/centers/nwhc/science/distribution-highly-pathogenic-avian-influenza-north-america-20212022#overview>
18. US CDC. Avian Influenza in Birds: Causes and How It Spreads [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 28]. Available from: <https://www.cdc.gov/bird-flu/virus-transmission/avian-in-birds.html#:~:text=Wild%20aquatic%20birds%20include%20waterbirds,for%20avian%20influenza%20A%20viruses.>
19. US CDC. H5 Bird Flu: Current Situation [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 28]. Available from: https://www.cdc.gov/bird-flu/situation-summary/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fflu%2Favianflu%2Favian-flu-summary.htm
20. USDA. HPAI Confirmed Cases in Livestock [Internet]. 2022-2024 Detections of Highly Pathogenic Avian Influenza. 2024 [cited 2024 Aug 28]. Available from: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/hpai-confirmed-cases-livestock>
21. US Department of Agriculture. Animal and Plant Health Inspection Service. Federal and State Veterinary Agencies Share Update on HPAI Detections in Oregon Backyard Farm, Including First H5N1 Detections in Swine. USDA [Internet]. 2024 Oct 30 [cited 2024 Oct 31];

- Available from: <https://www.aphis.usda.gov/news/agency-announcements/federal-state-veterinary-agencies-share-update-hpai-detections-oregon>
22. US CDC. USDA Reported H5N1 Bird Flu Detections in US Backyard and Commercial Poultry [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 28]. Available from: <https://www.cdc.gov/bird-flu/situation-summary/data-map-commercial.html>
 23. Katella K. H5N1 Bird Flu: What You Need to Know. Yale Medicine [Internet]. 2024 Jul 30 [cited 2024 Aug 28]; Available from: <https://www.yalemedicine.org/news/h5n1-bird-flu-what-to-know#:~:text=Almost%2025%20years%20later%2C%20in,species%20in%20all%2050%20states>
 24. USDA. Federal and State Veterinary, Public Health Agencies Share Update on HPAI Detection in Kansas, Texas Dairy Herds [Internet]. Agency Announcements. 2024 [cited 2024 Aug 28]. Available from: <https://www.aphis.usda.gov/news/agency-announcements/federal-state-veterinary-public-health-agencies-share-update-hpai>
 25. American Veterinary Medical Association. Avian influenza virus type A (H5N1) in U.S. dairy cattle [Internet]. Avian Influenza. 2024 [cited 2024 Aug 28]. Available from: <https://www.avma.org/resources-tools/animal-health-and-welfare/animal-health/avian-influenza/avian-influenza-virus-type-h5n1-us-dairy-cattle>
 26. USDA. Detections of Highly Pathogenic Avian Influenza in Mammals [Internet]. 2022-2024 Detections of Highly Pathogenic Avian Influenza. 2024 [cited 2024 Aug 28]. Available from: <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/mammals>
 27. US Centers for Disease Control and Prevention. How CDC is monitoring influenza data among people to better understand the current avian influenza A (H5N1) situation [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 14]. Available from: <https://www.cdc.gov/bird-flu/h5-monitoring/index.html>
 28. US CDC. CDC Confirms New Human Cases of H5 Bird Flu in California. CDC Newsroom [Internet]. 2024 Oct 3 [cited 2024 Oct 3]; Available from: <https://www.cdc.gov/media/releases/2024/s1003-birdflu-case-california.html>
 29. US CDC. CDC A(H5N1) Bird Flu Response Update October 29, 2024. Bird Flu [Internet]. 2024 [cited 2024 Oct 31]; Available from: <https://www.cdc.gov/bird-flu/spotlights/bird-flu-response-10-29-24.html>
 30. US CDC. CDC A(H5N1) Bird Flu Response Update September 13, 2024 [Internet]. Avian Influenza (BirdFlu). 2024 [cited 2024 Sep 18]. Available from: <https://www.cdc.gov/bird-flu/spotlights/h5n1-response-09132024.html>
 31. US CDC. CDC A(H5N1) Bird Flu Response Update October 11, 2024 [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Oct 16]. Available from: <https://www.cdc.gov/bird-flu/spotlights/h5n1-response-10112024.html>
 32. US CDC. CDC A(H5N1) Bird Flu Response Update, July 12, 2024 [Internet]. Avian Influenza (Bird Flu). 2024 [cited 2024 Aug 28]. Available from: <https://www.cdc.gov/bird-flu/spotlights/h5n1-response-07122024.html>
 33. Eisfeld AJ, Biswas A, Guan L, Gu C, Maemura T, Trifkovic S, et al. Pathogenicity and transmissibility of bovine H5N1 influenza virus. *Nature*. 2024 Jul 8;
 34. U.S. Food & Drug Administration. Updates on Highly Pathogenic Avian Influenza (HPAI) [Internet]. Alerts, Advisories & Safety Information. 2024 [cited 2024 Aug 28]. Available from: <https://www.fda.gov/food/alerts-advisories-safety-information/updates-highly-pathogenic-avian-influenza-hpai>
 35. Guan L, Eisfeld AJ, Pattinson D, Gu C, Biswas A, Maemura T, et al. Cow's Milk Containing Avian Influenza A(H5N1) Virus — Heat Inactivation and Infectivity in Mice. *New England Journal of Medicine*. 2024 Jul 4;391(1):87–90.
 36. Food and Agriculture Organization of the United Nations, World Health Organization, World Organisation for Animal Health. Updated joint FAO/WHO/WOAH assessment of recent influenza A(H5N1) virus events in animals and people. Assessment based on data as of 18 July 2024. 2024 Aug.
 37. US CDC. Frequently Asked Questions about Avian Influenza (Bird Flu) [Internet]. CDC Archive. 2024 [cited 2024 Aug 28]. Available from: <https://archive.cdc.gov/#/details?url=https://www.cdc.gov/flu/avianflu/avian-flu-faq.htm>
 38. Stone W. The U.S. may be missing human cases of bird flu, scientists say. *npr* [Internet]. 2024 May 2 [cited 2024 Aug 28]; Available from: <https://www.npr.org/sections/health-shots/2024/05/02/1248538298/the-u-s-may-be-missing-human-cases-of-bird-flu-scientists-say>