MONTHLY SCIENTIFIC REVIEW ON AVIAN INFLUENZA A(H5N1)

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General informations

This section presents a detailed timeline of the outbreak, with significant events related to its progression, current status and case reports.
The content of this document is subject to change as the health situation evolves. All informations comes from a valid and credible source.

Human A(H5N1) infection with exposure to dairy cows in U.S.

Other human infections with A(H5N1) worldwide

Since 2024

May

On 7 July 2024, according to the Ministry of Health, a 3-year-old boy in Takeo province tested positive for the H5N1 bird flu virus on July 5, 2024, confirmed by the National Institute of Public Health and the Institut Pasteur. The boy, who exhibited symptoms like fever, cough, tiredness, and difficulty breathing, has shown improvement and is under intensive care. Investigation revealed that he had contact with a dead chicken brought home for cooking about 10 days prior.

Source: KHMERTIMES. 3 July 2024

On 3 July 2024, the Centers for Disease Control and Prevention (CDC) confirmed the fourth human case of highly pathogenic avian flu in the United States this year and the first in Colorado, as the state reported more infected dairy cows. The person reported eye symptoms only, received oseltamivir treatment, and has recovered.

Source: CIDRAP. 3 July 2024

On 30 May 2024, a 3rd U.S. dairy worker tested positive for bird flu after exposure to infected cows and was the first to suffer respiratory problems.
The infection was the 2nd human case in Michigan, which has confirmed more cases of bird flu in dairy cattle than any other state. It also expands the symptoms for human cases, after the 2 workers who previously tested positive experienced only conjunctivitis, or pink eye, and recovered.

Source: Reuters. 30 May 2024

On 22 May 2024, a Michigan dairy worker has been diagnosed with bird flu, the second human case associated with an outbreak in US dairy cows.
The male worker had been in contact with cows at a farm with infected animals. He experienced mild eye symptoms and has recovered.

Source: APnews. 23 May 2024

On 22 May 2024, the first human case of A(H5N1) highly pathogenic avian influenza (bird flu) has been confirmed in Australia, in a child recently returned from India.
The child who became unwell whilst in India was hospitalized upon return to Australia in March 2024. Influenza A was detected by PCR during admission, and the child was treated with oseltamivir during a prolonged stay in intensive care with severe lower respiratory tract infection and hypoxia with respiratory failure. The child has since been discharged home and has made a complete recovery.

Source: Victoria Health government. 21 May 2024

March

On 28 March 2024, a case of human infection with avian influenza A(H5N1) virus was reported in China. The reported case was a 33-year-old female tested positive for H5N1 in the Guangxi Autonomous Region, China.

Source: WHO. 3 May 2024

On 27 March 2024, a laboratory-confirmed human case of avian influenza A(H5N1) has been detected in the state of Texas.
The case is aged over 18 years, working at a commercial dairy cattle farm and had a history of exposure to dairy cattle (cows). It appears to be the first human infection with A(H5N1) acquired from contact with an infected mammal, although human infections with other influenza subtypes have previously been acquired from mammals.

Source: WHO. 9 April 2024.

On 11 March 2024, a case of human infection with an influenza A(H5N1) virus in a 21-year-old male with no underlying conditions from Viet Nam developed symptoms. Exposure to birds was ascertained to have taken place in the third week of February.
This is the first human infection with an avian influenza A (H5N1) virus reported in Viet Nam since 2022.

Source: WHO. 2 April 2024

February

On 12 February 2024, Cambodia has reported four recent human infections with highly pathogenic avian influenza (HPAI) A(H5N1) (bird flu) virus. These are the first human infections with HPAI A(H5N1) virus identified in Cambodia in 2024.
The four infections occurred in three children, one of whom died, and an adult, all of which were identified in late January and early February. All patients reportedly had a history of recent exposure to sick or dead poultry prior to their illness.

Source: CDC. 12 February 2024

From 1 January 2003 to 21 December 2023, a total of 248 cases of human infection with avian influenza A(H5N1) virus were reported from four countries within the Western Pacific Region (Table 1). Of these cases, 139 were fatal.

Source: WHO.

Scientific articles

This section presents relevant articles published on peer-reviewed scientific journals or pre-print platforms.
The content of this document is subject to change as the health situation evolves. All informations comes from a valid and credible source.

One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland.

Nohynek H, Helve OM.

Published in *Euro Surveillance* on 29 June 2024.
https://doi.org/10.2807/1560-7917.es.2024.29.25.2400383

This article examines the outbreaks of acute illness and mortality among farmed foxes, minks, and raccoon dogs in Finland led to the identification of the highly pathogenic avian influenza (HPAI) H5N1 virus. Initial cases were confirmed through autopsy and real-time PCR testing, revealing that the virus was the cause of increased mortality, especially in young animals born in 2023. Pathological investigations showed gastrointestinal and neurological symptoms. Epidemiological studies highlighted that wild birds, particularly black-headed gulls, were likely the primary source of infection, often facilitated by poor biosecurity measures on farms. Genetic analysis of the virus showed adaptation to mammalian hosts, indicating significant mutations. Control measures included culling approximately 250,000 animals and imposing strict biosecurity regulations. The outbreak emphasized the need for better biosecurity practices to prevent wildlife-to-farm transmission of diseases and underscored the potential pandemic risk posed by avian influenza viruses adapting to mammals. Enhanced virological surveillance and preparedness were recommended to mitigate future outbreaks.

Highly pathogenic avian influenza A(H5N1) virus infections on fur farms connected to mass mortalities of black-headed gulls, Finland, July to October 2023.

Kareinen L, Tammiranta N, Kauppinen A, Zecchin B, Pastori A, Monne I, Terregino C, Giussani E, Kaarto R, Karkamo V, Lähteinen T, Lounela H, Kantala T, Laamanen I, Nokireki T, London L, Helve O, Kääriäinen S, Ikonen N, Jalava J, Kalin-Mänttäri L, Katz A, Savolainen-Kopra C, Lindh E, Sironen T, Korhonen EM, Aaltonen K, Galiano M, Fusaro A, Gadd T.

Published in *Euro Surveillance* on 29 June 2024.
https://doi.org/10.2807/1560-7917.es.2024.29.25.2400063

This article examines the outbreaks of acute illness and mortality among farmed foxes, minks, and raccoon dogs in Finland led to the identification of the highly pathogenic avian influenza (HPAI) H5N1 virus. Initial cases were confirmed through autopsy and real-time PCR testing, revealing that the virus was the cause of increased mortality, especially in young animals born in 2023. Pathological investigations showed gastrointestinal and neurological symptoms. Epidemiological studies highlighted that wild birds, particularly black-headed gulls, were likely the primary source of infection, often facilitated by poor biosecurity measures on farms. Genetic analysis of the virus showed adaptation to mammalian hosts, indicating significant mutations. Control measures included culling approximately 250,000 animals and imposing strict biosecurity regulations. The outbreak emphasized the need for better biosecurity practices to prevent wildlife-to-farm transmission of diseases and underscored the potential pandemic risk posed by avian influenza viruses adapting to mammals. Enhanced virological surveillance and preparedness were recommended to mitigate future outbreaks.

Does pasteurization inactivate bird flu virus in milk?

Cui P, Zhuang Y, Zhang Y, Chen L, Chen P, Li J, Feng L, Chen Q, Meng F, Yang H, Jiang Y, Deng G, Shi J, Chen H, Kong H.

Published in *Emerging Microbes & Infections* on 16 June 2024.
https://doi.org/10.1080/22221751.2024.2364732

An outbreak of highly pathogenic avian influenza A (H5N1) was recently reported in dairy cows in the United States. Currently, little data is available regarding the efficacy of pasteurization against H5N1 virus in raw milk. In this study, authors provide direct evidence that pasteurization is sufficient to inactivate all tested influenza A viruses in raw milk collected from healthy dairy cattles, addressing a common concern among milk consumers and those with food safety concerns.

Antiviral Susceptibility of Highly Pathogenic Avian Influenza A(H5N1) Viruses Circulating Globally in 2022-2023. Andreev K, Jones JC, Seiler P, Kandeil A, Turner JCM, Barman S, Rubrum AM, Webby RJ, Govorkova EA.

Published in *The Journal of Infectious Diseases* on 15 June 2024.
https://doi.org/10.1093/infdis/jiad418

In this study, the antiviral susceptibility of currently circulating (2022–2023) highly pathogenic avian influenza (HPAI) A(H5N1) viruses was assessed by genotypic and phenotypic approaches. The frequency was low for neuraminidase (NA) and polymerase acidic (PA) substitutions associated with reduced inhibition by NA inhibitors (21/2698, 0.78%) or the PA inhibitor baloxavir (14/2600, 0.54%). Phenotypic testing of 22 clade 2.3.2.1a and 2.3.4.4b viruses revealed broad susceptibility to NA inhibitors and baloxavir. Authors therefore concluded that most contemporary HPAI A(H5N1) viruses retain susceptibility to antiviral drugs. Novel NA-K432E and NA-T438I substitutions (N2 numbering) were identified at elevated frequencies in samples (104/2698, 3.85%) and caused reduced zanamivir and peramivir inhibition.

Inactivation of Avian Influenza A(H5N1) Virus in Raw Milk at 63°C and 72°C. Kaiser F, Morris DH, Wickenhagen A, Mukesh R, Gallogly S, Yinda KC, de Wit E, Lloyd-Smith JO, Munster VJ.

Published in *The New England Journal of Medicine* on 14 June 2024.
https://doi.org/10.1093/infdis/jiad418

This article examines the stability of highly pathogenic avian influenza A(H5N1) virus in raw milk when heated to 63°C and 72°C, temperatures commonly used for commercial pasteurization. Samples of raw milk contaminated with the H5N1 virus were subjected to these temperatures, and the presence of the virus was measured. At 63°C, the virus was inactivated in less than two minutes, with an estimated half-life of 4.5 seconds. At 72°C, viral titres fall sharply within five seconds, but traces of infectious virus remain detectable for up to 20 seconds. These results show that pasteurization at 63°C for 30 minutes offers a significant margin of safety. However, at 72°C, a small amount of virus can remain infectious if the initial titre is high. The article highlights the need for further research to confirm these results under commercial pasteurization conditions and to study other dairy products, as the composition of raw milk from infected animals may influence the efficacy of heat inactivation.

Sialic Acid Receptor Specificity in Mammary Gland of Dairy Cattle Infected with Highly Pathogenic Avian Influenza A(H5N1) Virus. Nelli RK, Harm TA, Siepker C, Groeltz-Thrush JM, Jones B, Twu NC, Nenninger AS, Magstadt DR, Burrough ER, Piñeyro PE, Mainenti M, Carnaccini S, Plummer PJ, Bell TM.

Published in *Emerging Infectious Diseases* on 11 June 2024.
https://doi.org/10.3201/eid3007.240689

In March 2024, highly pathogenic avian influenza (HPAI) A(H5N1) virus was detected for the first time in dairy cattle in the United States. This discovery has triggered public health alerts and raised concerns about HPAI H5N1 spread. A key factor of a virus-host range is receptor availability ; however, little is known about the distribution of Influenza A viruses (IAVs) receptors, sialic acids (SA), in dairy cattle, particularly in mammary glands. This study explored the presence and distribution of cellular and receptor factors that enable HPAI H5N1 virus infection in Holstein dairy cattle.

Cow's Milk Containing Avian Influenza A(H5N1) Virus - Heat Inactivation and Infectivity in Mice. Guan L, Eisfeld AJ, Pattinson D, Gu C, Biswas A, Maemura T, Trifkovic S, Babujee L, Presler R Jr, Dahn R, Halfmann PJ, Barnhardt T, Neumann G, Thompson A, Swinford AK, Dimitrov KM, Poulsen K, Kawaoka Y.

Published in *Emerging Infectious Diseases* on 11 June 2024.
https://doi.org/10.1056/nejmc2405495

Highly pathogenic avian influenza virus (HPAI) of the H5N1 subtype was recently detected in nasal swabs and milk of dairy cows, increasing concern that HPAI A(H5N1) viruses may enter the human food chain. In this study, the authors assessed temperature stability and infectivity in mice of HPAI A(H5N1) virus–positive milk samples. Results showed that heat treatment reduced virus titers but did not completely inactivate the virus. At 4°C, HPAI A(H5N1) virus remained infectious for several weeks in raw milk. In addition, high virus titers were detected in the respiratory organs and moderate virus titers in several other organs of mice upon oral inoculation. Collectively, these data indicate that HPAI A(H5N1) virus in untreated milk can infect susceptible animals that consume it.

To respond to the threat of avian influenza, look back at lessons learned from COVID-19.

Published in *Nature Medicine* on 10 June 2024.
https://doi.org/10.1038/s41591-024-03106-3

In January 2020, the World Health Organization declared SARS-CoV-2 a public health emergency with no available vaccines or treatments and limited knowledge about the virus. Today, a new pandemic threat looms with the avian influenza virus H5N1, which has jumped from poultry to dairy cattle and humans in the US. This time, however, we have a better understanding of such threats and the importance of effective communication and public health measures. Recent H5N1 cases in US cattle and subsequent human infections underscore the virus's evolving risk. In response, the US Department of Agriculture has provided support to affected dairy producers, while countries like Mexico and France vaccinate poultry. However, vaccination and culling are short-term solutions, and infrastructural changes are needed to detect and limit the spread of the virus. Key lessons from COVID-19 include the importance of surveillance, protecting agricultural workers, rapid testing, depoliticizing masks, and effective communication. Implementing these lessons can help mitigate the impact of an unpredictable H5N1 evolution.

Avian Influenza A(H5N1) Virus among Dairy Cattle, Texas, USA. Oguzie JU, Marushchak LV, Shittu I, Lednicky JA, Miller AL, Hao H, Nelson MI, Gray GC.

Published in *Emerging Infectious Diseases* on 7 June 2024.
https://doi.org/10.3201/eid3007.240717

During March and April 2024, this study was conducted on dairy cattle specimens from a farm in Texas, revealing that highly pathogenic avian influenza (HPAI) A(H5N1) virus strains were the sole cause of an epizootic. Since the arrival of the H5N1 clade 2.3.4.4b in North America in 2021, there have been frequent mammalian spillover events across various species, including one human infection, though cattle had not been affected until this incident. Samples from 30 cows (24 sick and 6 healthy) were collected and analyzed using molecular screening, cell culture, and metagenomics techniques. The results confirmed the presence of the H5 avian influenza A virus, specifically HPAI H5N1, without other viral co-infections. The virus was more prevalent in nasal swabs than rectal swabs, suggesting respiratory transmission among cattle.
Next-generation sequencing (NGS) of a complete genome from a sick cow's nasal swab indicated high similarity to H5N1 strains from dead birds, other cattle, and a cattle worker in Texas, suggesting a single interconnected multispecies outbreak. A significant mutation (PB2-M631L) in the virus enhances its replication in human cells.
Despite limitations, such as the lack of milk samples, environmental specimens, and a comprehensive farm investigation, this study highlights the necessity of interdisciplinary cooperation under a One Health framework to address complex epizootics. Ensuring that epidemiological investigations do not harm farm owners' businesses is crucial for effective outbreak management.

N-glycosylation on hemagglutinin head reveals inter-branch antigenic variability of avian influenza virus H5-subtypes. Shi K, Feng S, Zhao L, Chen J, Song W, Jia Y, Qu X, Liu Z, Jia W, Du S, Liao M.

Published in *International Journal of Biological Macromolecules* on 5 June 2024.
https://doi.org/10.1016/j.ijbiomac.2024.132901

This article deals with the avian influenza virus subtype H5, which is widespread worldwide and undergoes frequent antigenic drift, necessitating regular vaccine updates. One of the causes of incompatibility between vaccines and epidemic strains is the dynamic modification of glycosylation sites. However, the biological importance of N-glycosylation in viral evolution and antigenic changes remains unclear. A systematic analysis of glycosylation sites on the HA1 subunit of H5N1 has been carried out, highlighting changes in the major glycosylation sites, including 140 N, 156 N and 170 N within the antigenic epitopes of the HA1 protein. Several recombinant viruses based on the HA genes of historical vaccine strains were generated and inactivated to immunize SPF chickens. The inactivated recombinant strains showed antigenicity relatively closer to strains with identical N-glycosylation motifs. The differences in N-glycosylation modification underline the antigenic diversity between branches of H5 viruses and provide an essential basis for improving vaccination strategies.

COBRA HA and NA vaccination elicits long-live protective immune responses against pre-pandemic H2, H5, and H7 influenza virus subtypes. Ge P, Ross TM.

Published in *Virology* on 1 June 2024.
https://doi.org/10.1016/j.virol.2024.110119

In this study, a multivalent pre-pandemic influenza vaccine was evaluated in both naïve and pre-immune mice to mimic immunity in humans. Mice were vaccinated with COBRA H2, H5, and H7 hemagglutinin (HA) and two neuraminidase (NA) proteins, N1 and N2. Vaccinated mice were fully protected against lethal challenge with H5N6 influenza virus. Sera collected after vaccination showed cross-reactive IgG antibodies against a panel of wild-type H2, H5, and H7 HA proteins, and N1 and N2 NA proteins. Mice with pre-existing immunity to H1N1 and H3N2 influenza viruses that were subsequently vaccinated with COBRA HA/NA vaccines had enhanced anti-HA stem antibodies compared to vaccinated mice without pre-existing immunity. Little to no lung injury was observed in the lungs of COBRA HA/NA vaccinated mice following influenza virus challenge. In addition, sera collected after vaccination had hemagglutinin inhibitory activity against a panel of H2Nx, H5Nx, and H7Nx influenza viruses. These protective antibodies were maintained up for up to 4 months after vaccination.

Development of a nucleoside-modified mRNA vaccine against clade 2.3.4.4b H5 highly pathogenic avian influenza virus. Furey C, Scher G, Ye N, Kercher L, DeBeauchamp J, Crumpton JC, Jeevan T, Patton C, Franks J, Rubrum A, Alameh MG, Fan SHY, Phan AT, Hunter CA, Webby RJ, Weissman D, Hensley SE.

Published in *Nature Communications* on 23 May 2024.
https://doi.org/10.1038/s41467-024-48555-z

In this study, an mRNA lipid nanoparticle (LNP) vaccine encoding the hemagglutinin (HA) glycoprotein from a clade 2.3.4.4b H5 isolate was generated. The H5 mRNA-LNP vaccine elicits strong T cell and antibody responses in female mice, including neutralizing antibodies and broadly-reactive anti-HA stalk antibodies. The H5 mRNA-LNP vaccine elicits antibodies at similar levels compared to whole inactivated vaccines in female mice with and without prior H1N1 exposures. Finally, the H5 mRNA-LNP vaccine was immunogenic in male ferrets and prevents morbidity and mortality of animals following 2.3.4.4b H5N1 challenge. Together, our data demonstrate that a monovalent mRNA-LNP vaccine expressing 2.3.4.4b H5 is immunogenic and protective in pre-clinical animal models.

A Chymotrypsin-Dependent Live-Attenuated Influenza Vaccine Provides Protective Immunity against Homologous and Heterologous Viruses. He P, Gui M, Chen T, Zeng Y, Chen C, Lu Z, Xia N, Wang G, Chen Y.

Published in *Vaccines* on 8 May 2024.
https://doi.org/10.3390/vaccines12050512

In this study, using the influenza virus as a model, the authors have established a strategy to quickly obtain a live-attenuated vaccine by mutating the cleavage site of the influenza virus. This mutated influenza virus can be specifically cleaved by chymotrypsin. It has similar biological characteristics to the original strain in vitro, but the safety is improved by at least 100 times in mice. It can effectively protect against lethal doses of both homologous H1N1 and heterologous H5N1 viruses post mucosal administration, confirming that the vaccine generated by this strategy has good safety and broad-spectrum protective activities. Therefore, this study can provide valuable insights for the development of attenuated vaccines for respiratory viruses or other viruses with cleavage sites.

Structures of H5N1 influenza polymerase with ANP32B reveal mechanisms of genome replication and host adaptation. Staller E, Carrique L, Swann OC, Fan H, Keown JR, Sheppard CM, Barclay WS, Grimes JM, Fodor E.

Published in *Nature Communications* on 15 May 2024.
https://doi.org/10.1038/s41467-024-48470-3

Genome replication of avian influenza A viruses (IAVs) in mammalian cells is dependent on host acidic nuclear phosphoprotein 32 (ANP32) proteins and IAV RNA polymerase (FluPol) oligomerisation.This study reveals cryo-electron microscopy structures of monomeric and dimeric avian H5N1 FluPolA with human ANP32B. It provides insight into the molecular mechanisms governing IAV genome replication, while enhancing our understanding of the molecular processes underpinning mammalian adaptations in avian-origin FluPolA.

Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker.

Uyeki TM, Milton S, Abdul Hamid C, Reinoso Webb C, Presley SM, Shetty V, Rollo SN, Martinez DL, Rai S, Gonzales ER, Kniss KL, Jang Y, Frederick JC, De La Cruz JA, Liddell J, Di H, Kirby MK, Barnes JR, Davis CT.

Published in *The New England Journal of Medicine* on 3 May 2024.
https://doi.org/10.1056/nejmc2405371

Conjunctivitis with H5N1 virus in a dairy farm worker in Texas, 03/2024 - close contact with sick cows - H5N1 virus regional cattle epidemic - recovery with oseltamivir - clade 2.3.4.4b (genotype B3.13) identification - PB2 E627K mutation associated with viral adaptation to mammalian hosts - probable sensitivity to two existing clade 2.3.4.4b A(H5N1) candidate vaccine viruses.

The avian and human influenza A virus receptors sialic acid (SA)-α2,3 and SA-α2,6 are widely expressed in the bovine mammary gland.

Kristensen C, Jensen H, Trebbien R, Webby R, Larsen L.

Published in *BioRxiv* on 01 May 2024.
https://doi.org/10.1101/2024.05.03.592326

Cattle were considered almost resistant to IAV infection until recently, when an outbreak of H5N1 highly pathogenic influenza A virus (HPIAV) was detected in dairy cows in the United States. The main aim of this study was to investigate the in situ expression of IAV receptors in the bovine respiratory tract, cerebrum, and mammary glands by lectin histochemistry. The authors demonstrated that duck and human IAV receptors were widely expressed in the bovine mammary gland, whereas chicken receptor dominated the respiratory tract. Only a low expression of IAV receptors was observed in the neurons of the cerebrum. These results provide a mechanistic rationale for the high levels of H5N1 virus reported in infected bovine milk and show that cattle have the potential to act as a mixing vessel for novel IAV generation.

Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus Infection in Domestic Dairy Cattle and Cats, United States, 2024.

Burrough ER, Magstadt DR, Petersen B, Timmermans SJ, Gauger PC, Zhang J, Siepker C, Mainenti M, Li G, Thompson AC, Gorden PJ, Plummer PJ, Main R.

Published in *Emerging Infectious Diseases* on 29 April 2024.
https://doi.org/10.3201/eid3007.240508

This article discusses an outbreak of highly pathogenic avian influenza A virus (H5N1) among dairy cows and cats in the United States. It explores the virus's spread and interspecies transmission. Dairy cows showed decreased milk production, nonspecific illness, and sudden drops in milk yield. Cats fed raw milk from infected cows died. The virus was detected in milk samples, marking the first reported transmission of IAV from livestock to cats through milk consumption. The authors recommend further research into interspecies transmission. Dairy cattle are susceptible to infection with HPAI H5N1 virus and can shed the virus in milk, potentially transmitting infection to other mammals via unpasteurized milk. Clinical signs in affected cows often include reduced milk production and vague systemic illness, while affected domestic cats may rapidly develop neurological signs and death. Veterinarians should consider HPAI virus infection in dairy cattle experiencing unexpected drops in feed intake and milk production, and in cats showing sudden onset of neurological signs and blindness. The recurring global outbreaks of HPAI H5N1 and detection of spillover events in various hosts are concerning, indicating increasing virus adaptation in mammals.

Relevant news

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.

Avian Influenza Weekly Update Number 952

Published in *WHO* on 21 June 2024.
https://cdn.who.int/media/docs/default-source/wpro---documents/emergency/surveillance/avian-influenza/ai_20240621.pdf?sfvrsn=78c8c282_5

On 22 May 2024, the World Health Organization (WHO) was notified of a laboratory-confirmed case of human infection with avian influenza A(H5N1) virus (clade 2.3.2.1a) by the International Health Regulations (IHR) National Focal Point (NFP) of Australia. This is the first confirmed human infection caused by avian influenza A(H5N1) virus detected and reported by Australia. Although the source of exposure to the virus in this case is currently unknown, the exposure likely occurred in India, where the case had travelled, and where this clade of A(H5N1) viruses has been detected in birds in the past. According to the IHR (2005), a human infection caused by a novel influenza A virus subtype is an event that has the potential for high public health impact and must be notified to the WHO. Based on available information, WHO assesses the current risk to the general population posed by this virus as low.

Enhanced influenza surveillance to detect avian influenza virus infections in the EU/EEA during the inter-seasonal period

Published in *ECDC* on 20 June 2024.
https://www.ecdc.europa.eu/en/publications-data/enhanced-influenza-surveillance-detect-avian-influenza-virus-infections-eueea

Highly pathogenic avian influenza A(H5N1) viruses continue to be widespread in wild bird populations across the European Union/European Economic Area (EU/EEA). Viruses circulating in wild birds have spilled over to both wild and domestic/farmed animals, leading to outbreaks in poultry and other animal farms. ECDC encourages national public health authorities to provide messaging to the general public to avoid close contact with or touching of sick or dead birds (especially seabirds and wildfowl) and dead wild mammals.

Commission secures access for Member States to 665,000 doses of zoonotic influenza vaccines to prevent avian flu

Published in *European Commission* on 11 June 2024.
https://ec.europa.eu/commission/presscorner/detail/en/ip_24_3168

The Commission's Health Emergency Preparedness and Response Authority (HERA) as part of its mandate on preparedness, has signed on behalf of participating Member States, a joint procurement framework contract for the supply of up to 665,000 pre-pandemic vaccine doses of the up-to-date Zoonotic Influenza Vaccine Seqirus, as well as an option for a further 40 million doses over the duration of the contract.

Bird flu: Australia records first human case of H5N1

Published in *BMJ* on 10 June 2024.
https://doi.org/10.1136/bmj.q1281

Australia has notified the World Health Organization (WHO) of its first human case of H5N1 influenza (clade 2.3.2.1a), in a 2 year old child who was probably exposed in India. The child has no underlying conditions and had travelled to Kolkata, India, in February before returning to Australia on 1 March. The Victoria Department of Health reported that the child had started to feel unwell in India, with symptoms including loss of appetite, irritability, fever, and vomiting. After two and a half weeks in hospital, she was discharged and is now reported to be “clinically well,”.

Technical Report: June 2024 Highly Pathogenic Avian Influenza A(H5N1) Viruses.

Published in *CDC* on 26 April 2024.
https://www.cdc.gov/bird-flu/php/technical-report/h5n1-06052024.html

This report provides an update to the April 26, 2024, report to include three additional sporadic human cases (1 in Australia and 2 in the United States) and recent activity in wild birds, poultry, and other animals, including the multi-state outbreak in U.S. dairy cattle, and updated information on monitoring for human infections with highly pathogenic avian influenza A(H5N1) virus infections in the United States. CDC continues to believe that the overall risk to human health associated with the ongoing outbreaks of highly pathogenic avian influenza A(H5N1) viruses has not changed and remains low to the U.S. general public at this time.

Avian influenza overview December 2023–March 2024

Published in *European Centre for Disease Prevention and Control* on 23 March 2024.
https://www.ecdc.europa.eu/en/publications-data/avian-influenza-overview-december-2023-march-2024

Compared to previous years, although still widespread, the overall number of HPAI virus detections in birds was significantly lower, among other reasons, possibly due to some level of flock immunity in previously affected wild bird species, resulting in reduced contamination of the environment, and a different composition of circulating A(H5N1) genotypes. Most HPAI outbreaks reported in poultry were primary outbreaks following the introduction of the virus by wild birds. Outside Europe, the majority of outbreaks in poultry were still clustered in North America, while the spread of A(H5) to more naïve wild bird populations on mainland Antarctica is of particular concern. For mammals, A(H5N5) was reported for the first time in Europe, while goat kids in the United States of America represented the first natural A(H5N1) infection in ruminants. Since the last report and as of 12 March 2024, five human avian influenza A(H5N1) infections, including one death, three of which were clade 2.3.2.1c viruses, have been reported by Cambodia. China has reported two human infections, including one fatal case, with avian influenza A(H5N6), four human infections with avian influenza A(H9N2) and one fatal case with co-infection of seasonal influenza A(H3N2) and avian influenza A(H10N5). The latter case was the first documented human infection with avian influenza A(H10N5). Human infections with avian influenza remain rare and no sustained human-to-human infection has been observed. The risk of infection with currently circulating avian H5 influenza viruses of clade 2.3.4.4b in Europe remains low for the general population in the EU/EEA. The risk of infection remains low to moderate for those occupationally or otherwise exposed to infected animals.

Fact sheets

This section provides a short overview of of the epidemiology, virology, clinical features and risk assessment related with the disease.
The content of this document are subject to change as the health situation evolves. All informations comes from a valid and credible source.

Since its first observation in China in 1996, HPAI A(H5N1) has been detected in wild birds and poultry worldwide, causing a highly infectious respiratory disease in birds. Since 2020, a variant of this virus has led to **unprecedented deaths in wild birds and poultry across many countries**. Unlike most other avian influenza viruses, A(H5N1) has infected more than **200 mammal species**, and there has been **an increasing number of deadly reports**. Mammals can contract A(H5N1) avian influenza by consuming infected birds, poultry, or other animals, or by exposure to contaminated environments. While mammal-to-mammal transmission of H5N1 is rare, it is possible. **The virus can also infect humans**, but no sustained human-to-human transmission has been identified. The most commonly identified risk factor for A(H5N1) virus infection is contact with infected birds or contaminated environments.

The incubation period for A(H5N1) infection is typically two to five days after the last known exposure. A(H5N1) influenza virus infection can cause a range of diseases in humans, from mild to severe, and in some cases, it can even be fatal. Symptoms are primarily respiratory, including fever, malaise, cough, sore throat, and muscle aches. Other early symptoms may include conjunctivitis and other non-respiratory symptoms. The infection can quickly progress to severe respiratory illness and neurological changes. A(H5N1) virus has also been detected in asymptomatic individuals.
People presenting with severe respiratory or influenza-like infection and a history of exposure to poultry or wild birds require careful investigation, management, and infection control. Appropriate samples for influenza tests should be rapidly taken and processed from patients with a relevant exposure history within ten days preceding symptom onset. If positive specimens cannot be subtyped, they should be shared with the national reference laboratory.
Influenza patients should be managed properly to prevent severe illness and death. Patients with laboratory-confirmed influenza virus infection with progressive, complicated, or severe illness, or those with asymptomatic or mild disease but who are at increased risk of severe disease, should be treated with antiviral medicines like oseltamivir as soon as possible.
As part of their influenza pandemic preparedness work, some countries have developed and licensed vaccines that could be used for avian influenza viruses, including A(H5N1). Currently, human infections of A(H5N1) are limited, and vaccines have recently been recommended in Finland.

So far, close to 900 human infections have been reported since 2003, over half of which were fatal. **In 2024, four human cases of A(H5N1) infection were reported in the USA** (Texas, Michigan, Colorado) following exposure to dairy cattle, marking **the first detection of these avian influenza viruses in cows**. These individuals **reported exposure to infected cows and eye symptoms**, received oseltamivir treatment, and have recovered. A(H5N1) viruses have been **detected in raw milk** from infected dairy cows in some locations. Due to potential health risks, the consumption of raw milk should be avoided. The WHO advises consuming pasteurized milk.

Source: WHO, Influenza: A(H5N1). 16 May 2024

Guidelines and practical information

This section lists official manuals of recommendations for clinical practice or public health policy published by leading health organizations.

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April 2024	Highly Pathogenic Avian Influenza A(H5N1) Virus: Identification of Human Infection and Recommendations for Investigations and Response (CDC)
June 2024	Prevention and Antiviral Treatment of Avian Influenza A Viruses in People (CDC)
June 2024	Détection des génomes du virus de la grippe A et B et du SARS-CoV-2 par RT-PCR dans un contexte d'exposition à risque à un virus influenza zoonotique (HAS)
May 2024	Avis du COVARS - Point sur la situation liée au virus influenza H5N1 (COVARS)
December 2023	Considerations for emergency vaccination of wild birds against high pathogenicity avian influenza in specific situations (WOAH)
June 2023	Enhanced surveillance of severe avian influenza virus infections in hospital settings in the EU/EEA (ECDC)
2022	Guidelines for the clinical management of severe illness from influenza virus infections (WHO)
December 2021	Avis relatif à la prévention de la transmission à l'homme des virus influenza porcins et aviaires (HCSP)
April 2014	Risk assessment guidelines for infectious diseases transmitted on aircraft (ECDC)