

# Updated joint FAO/WHO/WOAH public health assessment of recent influenza A(H5) virus events in animals and people

Assessment based on data as of 18 November 2024

20 December 2024

## Key points

At the present time, based on available information, FAO-WHO-WOAH assess the global public health risk of influenza A(H5N1) viruses to be low, while the risk of infection for occupationally exposed persons is low to moderate depending on the risk mitigation measures in place and the local avian influenza epidemiological situation. Transmission between animals continues to occur and, to date, a growing yet still limited number of human infections are being reported. Although additional human infections associated with exposure to infected animals or contaminated environments are expected to occur, the overall public health impact of such infections at a global level, at the present time, is minor.

This risk assessment from FAO, WHO, and WOAH updates the assessment of the risk of zoonotic transmission (for example, animal to human) considering additional information made available since the previous [assessment of 14 August 2024](#). This update is limited to the inclusion of additional information being made available globally. Due to the potential risk to human health and the far-reaching implications of the disease on the health of wild birds, poultry, livestock and other animal populations, the use of a One Health approach is essential to tackle avian influenza effectively, to monitor and characterize virus circulation, to prevent within species and to new species transmission, to reduce spread among animals, and to prevent human infections from exposure to animals.

## Infections in animals

In March 2024, influenza A(H5) clade 2.3.4.4b of subtype H5N1 virus was detected in unpasteurized milk samples and oropharyngeal swabs from dairy cattle for the first time in the USA.<sup>1,2</sup> Influenza A(H5N1) virus detections continue to be reported through testing of dairy cattle exhibiting clinical signs and with no apparent disease.<sup>3,4</sup> While H5N1 clade 2.3.4.4b virus was introduced into North America in late 2021, analyses of virus sequence data from infected dairy cows has suggested that the ongoing circulation in dairy herds is linked to a single bird-to-dairy cow transmission event of a B3.13 genotype A(H5N1) virus that occurred in late 2023 or early 2024.<sup>5</sup> Thus far, this genotype has not been detected in cattle outside of the USA under field conditions.<sup>6</sup>

As of 18 November 2024, 599 dairy cattle herds in 15 states of the USA have tested positive for A(H5N1), with a significant surge of confirmed outbreaks in dairy cattle in the State of California reaching 383 herds since the first detection in late August 2024.<sup>7</sup> The average incidence of clinical disease on affected farms ranges between 10 and 20% with main clinical signs including decreased milk production with abnormal milk, decreased feed intake, fever, dehydration, altered faecal

consistency, respiratory distress, and abortions.<sup>8,9,10</sup> Studies have shown that commercial milk pasteurization inactivates the virus making it safe for human consumption.<sup>11,12,13</sup>

The routes and modes of transmission between cattle, the duration of virus shedding as well as the infectious period are under investigation, and while there have been advancements in our understanding, this is still not well understood. Transmission between states in the USA has been linked to cattle movements or possibly through feed and manure handling equipment, or on clothing or footwear of people working or visiting farms.<sup>10</sup>

Experimental studies of lactating dairy cattle and non-lactating heifers have been published and have provided some insight into receptor distribution, viral replication kinetics, and infection routes. Studies have indicated that alpha 2,3 sialic acid receptors (avian virus-type) are abundant in dairy cattle mammary tissue, consistent with the observation of high viral load in raw milk, and such receptors have also been detected in the respiratory tract of dairy cattle.<sup>14,15</sup> However, one study addressing the receptor binding specificity of the mammary gland and respiratory tract of cows to influenza A viruses (IAV) indicated that the upper respiratory tract of cows is devoid of receptors for IAV.<sup>16</sup> The same study demonstrated that the mammary gland of cows abundantly displays avian-type receptors for circulating H5 viruses while lacking human-type receptors. The lack of human-type receptors in mammary tissue contradicts a previous study that solely relied on plant-derived lectins to identify receptors.<sup>15</sup> Experimental inoculations of calves, heifers, and lactating cows demonstrated greater potential of A(H5N1) viruses to infect and replicate in the mammary gland than in the respiratory tract. In calves, intranasal inoculation with A(H5N1) B3.13 genotype virus resulted in poor nasal replication and viral shedding and the observed clinical signs were mild and there was no reported transmission to sentinel calves. While in lactating dairy cows, intramammary inoculation with high doses of A(H5N1) viruses (B3.13 or a representative European wild bird isolate) resulted in severe mammary gland infection with necrotizing mastitis, drastically reduced milk production, with no nasal replication nor systemic infection.<sup>17, 18</sup>

On 29 October 2024, the USDA National Veterinary Services Laboratories confirmed A(H5N1) virus detection in swine from a backyard farm in Oregon State where A(H5N1) virus was also confirmed in poultry on 25 October. The farming operation had a mix of poultry and livestock (including five swine, sheep and goats) that had been in close contact and sharing water sources, housing, and equipment. Although the swine did not express any clinical signs, they were euthanized for further diagnostic analysis.<sup>19</sup> Two of the five swine tested positive for A(H5N1) virus by polymerase chain reaction (PCR). Partial genome sequencing indicated the A(H5N1) belonged to the D1.2 genotype, similarly to the infected poultry on the same farm, and not the B3.13 genotype.<sup>20</sup> The detection of H5N1 virus in two pigs in Oregon State was not unexpected given the close contact between infected poultry and pigs on the farm likely enabling a poultry-to-swine transmission event. Nonetheless, avian influenza detections in pigs warrant attention as they can act as "mixing vessels" for genetic reassortment of avian and human influenza viruses, potentially creating new strains with pandemic potential. The mechanisms underlying A(H5N1) virus adaptation to pigs and the potential for efficient and sustained transmissibility among pigs are yet to be understood. Several experimental infections studies conducted in pigs with A(H5N1) clade 2.3.4.4b viruses showed that mammalian-derived A(H5N1) virus strains demonstrated higher potential for replication, pathogenicity, and transmissibility as compared to avian-derived A(H5N1) virus strains.<sup>21,22</sup> Nonetheless, avian-derived

A(H5N1) virus isolated in the USA in 2022 replicated successfully in the lungs of pigs with pulmonary lesions consistent with IAV infection and A(H5N1) virus transmission to at least one naive pig through direct contact was observed using mammalian isolates (raccoon and red fox) from the USA.<sup>23</sup>

Detections of A(H5) in mammals, other than dairy cattle, and wild and domestic birds continue to be reported in the USA and in other countries worldwide. Since 2021, clade 2.3.4.4b H5 virus circulation in wild and migratory birds and poultry resulted in numerous separate infections of wild carnivorous and scavenging mammals, domestic cats and dogs, marine mammals, and seabirds in various countries and territories. Clade 2.3.4.4b virus infections in mammals in the Americas, Asia and Europe have often resulted in severe disease with neurological signs in some species.<sup>24</sup> Notably, the wild marine mammal populations along the Atlantic and Pacific coastlines of the Americas weathered an important H5N1 epizootic leading to mass mortality events, particularly in Argentina, Chile, and Peru.<sup>25</sup> Amino acid changes potentially associated with increased virulence, transmission, or adaptation to mammalian hosts have been identified in H5N1 viruses responsible for the spillover events in marine mammals, and scientific publications suggested the occurrence of mammal-to-mammal transmission events supported by epidemiological, ecological, and phylogenetic data.<sup>26, 27</sup>

Between August and September 2024, avian influenza outbreaks were reported in captive wild felines in two zoos in southern Viet Nam. These led to the death of at least 47 tigers, three lions and a leopard, and were confirmed to be caused by a reassortant clade 2.3.2.1c A(H5N1) virus containing clade 2.3.4.4b gene segments. None of the zoo staff members in close contact with the infected animals experienced any respiratory symptoms.<sup>28, 29</sup> Previous influenza A(H5N1) outbreaks in felines, characterized by severe pneumonia and high mortality, have been associated with the feeding of infected poultry and likely tiger-to-tiger transmission.<sup>30,31</sup>

For the latest information on avian influenza situation in animals worldwide, see the FAO [Global Avian Influenza Viruses with Zoonotic Potential situation update](#) and the [WOAH situation reports on HPAI](#), as well as [WOAH's World Animal Health Information System](#).

### **Detections in humans**

Since the last joint assessment of August 2024 and as of 27 November 2024, an additional 49 human cases of infection with A(H5) viruses have been reported. Of these, 45 were reported from the USA: 28 in persons with exposure to A(H5N1)-infected dairy cattle in California, 15 in persons with exposure while involved in depopulation of A(H5N1)-infected commercial poultry farms, and two in persons with unknown exposure at the time of reporting. Samples from three cases related to poultry depopulation in the State of Colorado were confirmed to contain A(H5N1) clade 2.3.4.4b, genotype B3.13, virus while cases related to poultry depopulation in the State of Washington contained viruses belonging to the D1.1 genotype.

Intensive epidemiological investigation of the case with unknown exposure in the State of Missouri could not identify any animal or animal product exposure. Five health care workers in contact with the case were shown to be A(H5N1) seronegative, the case and one household contact who reported symptoms with the same onset date were weakly A(H5N1) seropositive. The timing of

symptom onsets supports a single common exposure, which at present remains unknown, rather than human-to-human transmission.<sup>32</sup>

All but one of the detected cases in the USA have reported mild symptoms, including conjunctivitis and mild respiratory symptoms, and recovered without hospitalization. The one exception who had comorbidities reported gastrointestinal symptoms and was hospitalized.<sup>33,34</sup>

A recent sero-study in 115 persons in Colorado and Michigan working on dairy farms during A(H5N1) outbreaks among dairy cattle found that eight (7.0%) had serologic evidence of recent infection (seropositive,  $\geq 40$  antibody titres to H5 2.3.4.4b by both micro-neutralization and hemagglutination inhibition assays). These seropositive individuals reporting working with dairy cattle or in the milking parlour, and four reported being ill when A(H5) was detected among the dairy cattle.<sup>35</sup>

Three human cases of clade 2.3.2.1c A(H5N1) virus infection were reported from Cambodia since the last update of August 2024. All were hospitalized; two recovered and the other died. All three cases had exposure to sick or dead backyard poultry.

On 13 November, one human case of domestically acquired A(H5N1) infection was confirmed by Canadian authorities in a young person without underlying conditions. The condition of the case was reported as critical. There are several ongoing investigations to better understand the exposures of this case, and so far investigations have not been able to identify the source of exposure. The virus from the case belonged to clade 2.3.4.4b, specifically the D1.1 genotype, which was similar to viruses concurrently affecting poultry in the region.<sup>36</sup>

### **Virus characteristics**

Regular monitoring and screening of viral sequences from birds has rarely found markers of mammalian adaptation in clade 2.3.4.4b viruses; those that have been detected are mainly in the polymerase proteins of the virus. These polymerase markers have been more frequently detected in viruses from mammals. As of 4 November 2024, none of the virus sequences from dairy cattle in the USA have well-recognized markers in the HA gene associated with a switch in receptor preference despite continued circulation of the virus. Additional studies on some B3.13 A(H5N1) viruses indicate no differences in receptor binding, pH fusion or thermostability compared to other non-B3.13 avian A(H5N1) viruses, and that these viruses retain their avian influenza virus phenotype.<sup>37</sup>

Available virus sequences from human cases have shown some genetic markers that may reduce susceptibility to neuraminidase inhibitors (antiviral medicines such as oseltamivir) or endonuclease inhibitors (such as baloxavir marboxil). While these changes may reduce antiviral susceptibility in laboratory testing the clinical impact of these genetic changes requires further studies.<sup>38</sup>

Experimental studies with A(H5N1) clade 2.3.4.4b viruses, including a B3.13 virus from the human case in Texas, have shown variable transmission between ferrets by direct contact, but no or inefficient transmission via respiratory droplets in most studies.<sup>39, 40, 41, 42, 43, 44</sup> Ferrets infected with a non-B3.13 A(H5N1) clade 2.3.4.4b virus via the ocular route did experience severe disease and were able to transmit the virus to other ferrets via direct contact; these contact animals also developed severe disease.<sup>45</sup> Currently circulating A(H5N1) viruses would need further genetic

changes to gain the ability to spread efficiently among humans via respiratory droplets, consistent with the current level of risk to public health, which is low.<sup>39</sup>

Other A(H5) virus clades such as 2.3.2.1c<sup>46</sup> and 2.3.2.1a continue to circulate and evolve in poultry in geographically restricted regions. Three A(H5N1) human cases have been detected in Cambodia since the previous assessment. The detected viruses were identified as reassortant influenza A(H5N1) viruses that were also detected in poultry in Cambodia, Lao People's Democratic Republic<sup>47</sup> and Viet Nam, and previously detected in human cases reported from Cambodia since late 2023 and Viet Nam in 2024. This reassortant virus has HA and NA genes from clade 2.3.2.1c viruses, while its internal genes belong to clade 2.3.4.4b viruses.<sup>48,49</sup> The viruses were similar to those detected in captive tigers and leopards in Viet Nam.<sup>50</sup>

Based on limited seroprevalence information available on A(H5) viruses, human population immunity against the HA of H5 viruses is expected to be minimal; human population immunity targeting the N1 neuraminidase is found to be present although the impact of this immunity is yet to be understood.<sup>51</sup>

### **Candidate vaccine viruses (CVV)**

The WHO Global Influenza Surveillance and Response System (GISRS), in collaboration with animal health partners (FAO, WOA, OFFLU (Joint WOA-FAO network of expertise on animal influenza) and others), continue to evaluate candidate vaccine viruses for pandemic preparedness purposes both bi-annually and on an *ad hoc* basis. Regular genetic and antigenic characterization of contemporary zoonotic influenza viruses are published [here](#) with the most recent update on A(H5) CVVs published in September following the WHO Consultation on the Composition of Influenza Virus Vaccines for Use in the 2025 Southern Hemisphere Influenza Season.

While the majority of circulating clade 2.3.4.4b viruses reacted well to at least one of the post-infection ferret antisera raised against the existing CVVs, an increasing proportion of clade 2.3.2.1c viruses from Cambodia and Viet Nam had reduced reactivity with post-infection ferret antiserum raised against an existing CVV. Thus, a new CVV from clade 2.3.2.1c was proposed. The list of available zoonotic influenza candidate vaccine viruses (CVVs) which include A(H5N1) viruses and potency testing reagents is updated on the WHO [website](#).

### **Assessment of current public health risk posed by influenza A(H5N1) viruses<sup>52</sup>**

1. What is the global public health risk of additional human cases of infection with avian influenza A(H5) viruses?

Despite the high and increasing number of A(H5) clade 2.3.4.4b outbreaks and detections in animals and increasing human exposures to the virus at the human-animal-environment interface, there have been relatively few human infections reported to date.

Of the human cases of A(H5) detections reported since the beginning of 2021, the majority were infections in people associated with exposure to A(H5) viruses through direct or indirect contact

with infected animals, or contaminated environments, such as live poultry markets or other premises with infected animals. Severity of illness has ranged from mild to fatal, with the majority of recent cases reporting mild illness. The exception is the recent case reported from Canada, in a young person with no underlying conditions, reported as critical. Thus far, among these cases, there has been no reported or identified human-to-human transmission through follow up epidemiologic, virologic and serologic investigations. Investigations for some of the cases continue.

Current virologic and epidemiologic information indicates that these viruses remain avian influenza viruses without established adaptations to mammalian hosts and have not acquired the capacity for sustained transmission between humans.

The epidemiological situation has changed with the ongoing spread of A(H5) virus in the USA dairy cattle population. Persons exposed to affected dairy cattle and other infected animals may be in prolonged and close contact with potentially contaminated surfaces and animal products. As long as A(H5) viruses continue to be detected in wild and domestic birds and mammals, including dairy cattle, and related environments, including in unpasteurized/raw milk, further human cases are expected, particularly amongst exposed individuals not wearing appropriate personal protective equipment and/or in environments where mitigation measures are not in place. Further studies on the detection of A(H5N1) in two pigs in the USA is needed in order to better understand the risk posed by this finding.

Based on currently available information, FAO-WHO-WOAH assesses the global public health risk of influenza A(H5) viruses as low. Although additional human infections associated with exposure to infected animals or contaminated environments are expected to occur, they remain limited in the general population and the overall current public health impact of such infections at a global level is minor, considering the surveillance, response, mitigation and control measures in place.

However, while the risk of infection to the general public is low, among persons with exposure to infected birds or mammals or contaminated environments, the risk of infection can range from low to moderate, depending on nature of the exposure, the duration of exposure, the consistent and appropriate use of personal protective equipment, and the use of other response, mitigation and control measures particularly in environments where animals are kept.

The pandemic potential of these viruses requires enhanced vigilance, especially in animal populations where animal to animal transmission is known to occur (poultry and dairy cattle), and close monitoring in animals and humans. It remains essential that, while farmers enhance biosecurity on their farms, governments focus efforts on strengthening surveillance in susceptible animal populations and in persons exposure to infected animals, to prevention and mitigation efforts to reduce and/or stop animal to animal transmission and reduce environmental contamination, to prevention efforts to stop animals to human transmission and to improve communication with at risk persons and provide occupationally exposed persons with and train in the use of personal protective equipment.

## 2. What is the likelihood of human-to-human transmission of avian influenza A(H5) viruses?

There has been no reported human-to-human transmission of A(H5) viruses since 2007, although there may be knowledge gaps in investigations around identified human infections. In 2007 and the years prior, small clusters of A(H5) virus infections in humans were reported, including limited human to human transmission from patients to health care workers. At the present time sustained human-to-human transmission has not been reported of A(H5) viruses.<sup>53</sup>

The A(H5) viruses currently detected in mammals, including in human cases, largely retain genomic and biological characteristics of avian influenza viruses and remain well-adapted to spread among birds. Except for in-host obtained amino acid mutations in polymerase proteins, there is still limited evidence for adaptation to mammals and humans even when transmission in mammals has been suspected.<sup>54</sup> No changes in receptor binding tropism have been consistently observed that would increase binding to receptors in the human upper respiratory tract which would increase the probability of transmission to and among people. In addition, available preliminary sero-studies and sero-investigations have not identified human-to-human transmission of A(H5N1) in the USA. Therefore, sustained human-to-human transmission of the currently circulating A(H5N1) viruses is considered unlikely without further genetic changes in the virus. This is actively being assessed by agencies in affected Member States, FAO, WHO, WOA and partners.

WHO, together with FAO and WOA, continues to evaluate A(H5) viruses closely and will re-assess the risk associated with the currently circulating A(H5) viruses as more information becomes available.

Further antigenic characterization of A(H5) viruses, including in relation to the existing CVVs, and development of specific reagents are being prioritized at the WHO Collaborating Centres and Essential Regulatory Laboratories of GISRS in collaboration with public health, animal health, and veterinary sector colleagues.

## **Recommended actions**

It is recommended that Member States and national authorities:

- increase surveillance and vigilance, in human populations, especially amongst occupationally exposed persons, for the possibility of zoonotic infections, particularly through National Influenza Centres (NICs) and other influenza laboratories associated with GISRS;
- assess and reduce the risk among occupationally exposed persons using methods such as active case finding and molecular and serologic methods, reducing environmental exposures, providing adequate and appropriate personal protective equipment;
- conduct active case finding around suspected and confirmed human cases to determine if there are additional cases or indications of human-to-human transmission; and
- work with national agencies and partners to better understand the exposure to and risk from raw/unpasteurized milk and milk products.

Under the International Health Regulations (IHR) (2005),<sup>55</sup> States Parties are required to notify WHO within 24 hours of any laboratory-confirmed case of human influenza caused by a new subtype according to the WHO case definition.<sup>56</sup> WHO has published the case definition for human infections with avian influenza A(H5) virus requiring notification under IHR (2005).<sup>57</sup>

Member States and national authorities are also recommended to:

- increase surveillance and timely reporting efforts for the early detection of A(H5) influenza viruses in domestic birds, wild birds and mammals<sup>58</sup>;
- include infection with an A(H5) influenza virus as a differential diagnosis, in non-avian species, including cattle, swine and other livestock and farmed domestic and wild animal populations, with high likelihood of exposure to A(H5) viruses;
- Implement preventive and early response measures to break the chain of infection among domestic animals (for example, poultry and dairy cattle)
- promptly report high pathogenicity avian influenza (HPAI) events in all animal species, including domestic and wild mammals, to WOAHA and other international organizations such as FAO;
- conduct genetic sequencing and share genetic sequences of influenza viruses and associated metadata in publicly available databases;
- mitigate the risk of introduction and spread of the disease in animals by implementing and/or strengthening biosecurity in livestock holdings/premises and along the value chain;
- employ good production and hygiene practices when handling animals and animal products, and protect persons in contact with suspected/infected animals with appropriate personal protective equipment, information and access to testing; and
- strengthen communication and education on the importance and proper use of personal protective equipment to individuals at risk of exposure to animal influenza viruses.

Additional sets of recommendations related to avian influenza viruses with zoonotic potential can be found in:

- [WOAHA Statement on High Pathogenicity Avian Influenza in Cattle](#), Updated 6 December 2024.
- FAO [Recommendations for the surveillance of influenza A\(H5N1\) in cattle with broader application to other farmed mammals](#), published 27 November 2024
- FAO alert on avian influenza: Risk of upsurge and regional spread through wild birds in Latin America and the Caribbean in [English](#) and [Spanish](#)
- [FAO recommendations for Global Avian Influenza Viruses with Zoonotic Potential](#).
- FAO EMPRES Watch entitled '[A\(H5N1\) influenza in dairy cattle in the United States of America](#)'.
- [WHO Practical interim guidance to reduce the risk of infection in people exposed to avian influenza viruses](#)
- CDC [Information for Workers Exposed to H5N1 Bird Flu](#)



Additional studies/surveillance, applying One Health principles are warranted, which could provide information to enhance confidence in the risk assessment. These may include serological studies in high-risk animal populations, in high-risk human populations, and epidemiological investigations.

Anyone who may have been exposed to infected or potentially infected animals or contaminated environments should be advised to promptly seek health care if they feel unwell, and to inform their health care provider of their possible exposure. Following prompt testing, early and appropriate clinical management should be initiated, and precautionary measures put in place to assess and prevent potential further spread among humans and animals.

Clinicians should also be alerted to potential zoonotic infection in patients with an exposure history to birds or animals especially in areas where A(H5N1) viruses are known or suspected to be circulating in animals but also in areas where surveillance in animals may be limited.

Routine epidemiologic and virologic surveillance for influenza should be conducted ideally year-round using a standard case definition in healthcare facilities according to WHO guidance.<sup>59</sup>

Timely sharing of information and sequence data from both the human and animal health sectors from all regions should continue to be strongly recommended and is critical for rapid and robust joint risk assessment. The rapid sharing of virus materials with WHO Collaborating Centres of GISRS continues to be essential to conduct a thorough risk assessment and develop or adjust targeted response measures. The Tool for Influenza Pandemic Risk Assessment (TIPRA) provides an in-depth assessment of risk associated with some zoonotic influenza viruses – notably the likelihood of the virus gaining human-to-human transmissibility, and the impact should the virus gain such transmissibility. TIPRA maps relative risk amongst viruses assessed using multiple elements.<sup>60</sup> Data pertaining to the risk elements within TIPRA should be generated and shared with WHO.

Efforts to reduce human exposure to birds, livestock, and other mammals infected with or potentially infected with avian and other animal influenza viruses should be implemented and enhanced to minimize the risk of zoonotic infections. Individuals with activities that involve exposure to infected animals and/or contaminated environments are at higher risk and should take necessary precautions to prevent infection.<sup>61</sup>

Those who are exposed to potentially infected animals should have access to, be trained in their use under different environmental conditions, and wear personal protective equipment including eye protection.<sup>62</sup> If they develop respiratory symptoms or conjunctivitis, they should be rapidly tested, and precautionary infection control measures should be put in place to prevent potential further spread among humans and to animals. For detailed guidance on treatment, refer to relevant global and national guidance.<sup>63</sup>

Some manufacturers have initiated production of an A(H5) human vaccine that matches current circulating strains. Although a few countries are procuring vaccine to vaccinate occupationally exposed persons, this is not currently being recommended as a global strategy considering the limited number of human infections with A(H5N1) 2.3.4.4b viruses.

Investigations are ongoing to understand the risk to humans from consuming raw/unpasteurized milk contaminated with A(H5N1) virus. FAO, WHO and WOAHA advise consuming pasteurized milk. Due to the potential health risks from many dangerous zoonotic pathogens, raw/unpasteurized milk consumption should be avoided. If pasteurized milk is not available, heating raw milk until it boils makes it safer for consumption.<sup>64</sup>

More information will be available as investigations are actively ongoing in the USA and elsewhere. WHO and GISRS, jointly with FAO, WOAHA and OFFLU are working closely together to continuously assess the avian influenza situation. This includes increased surveillance and testing to monitor the evolution and geographic spread of avian influenza viruses, including A(H5N1) viruses, to provide timely and updated joint risk assessments.

## References

- <sup>1</sup> Lee D, Bahl J, Torchetti M, Killian M, Ip HS, DeLiberto TJ, et al. Highly Pathogenic Avian Influenza Viruses and Generation of Novel Reassortants, United States, 2014–2015. *Emerg Infect Dis.* 2016;22(7):1283-1285. <https://doi.org/10.3201/eid2207.160048>.
- <sup>2</sup> United States Department of Agriculture (USDA). Federal and State Veterinary, Public Health Agencies Share Update on HPAI Detection in Kansas, Texas Dairy Herds. 25 March 2024. <https://www.aphis.usda.gov/news/agency-announcements/federal-state-veterinary-public-health-agencies-share-update-hpai>
- <sup>3</sup> USDA. Case Definition - Avian Influenza, May 2024. <https://www.aphis.usda.gov/sites/default/files/hpai-livestock-case-definition.pdf>.
- <sup>4</sup> USDA. Highly Pathogenic Avian Influenza H5N1 Genotype B3.13 in Dairy Cattle: National Epidemiologic Brief, 8 June 2024. <https://www.aphis.usda.gov/sites/default/files/hpai-dairy-national-epi-brief.pdf>.
- <sup>5</sup> Nguyen T-Q, Hutter C, Markin A, Thomas M, Lantz K, Killian ML et al. Emergence and interstate spread of highly pathogenic avian influenza A(H5N1) in dairy cattle. *bioRxiv* 2024.05.01.591751; <https://doi.org/10.1101/2024.05.01.591751>.
- <sup>6</sup> FAO. 2024. A(H5N1) influenza in dairy cattle in the United States of America. *EMPRES Watch*, Vol. 38, July 2024. Rome, FAO.
- <sup>7</sup> USDA. Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock. <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock>.
- <sup>8</sup> 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. Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus Infection in Domestic Dairy Cattle and Cats, United States, 2024. *Emerg Infect Dis.* 2024 Jul;30(7):1335-1343. doi: 10.3201/eid3007.240508.
- <sup>9</sup> Caserta, L.C., Frye, E.A., Butt, S.L. *et al.* Spillover of highly pathogenic avian influenza H5N1 virus to dairy cattle. *Nature* 634, 669–676 (2024). <https://doi.org/10.1038/s41586-024-07849-4>
- <sup>10</sup> Animal and Plant Health Inspection Service, USDA, 24 Sept 2024. Highly Pathogenic Avian Influenza H5N1 Genotype B3.13 in Dairy Cattle: National Epidemiologic Brief. <https://www.aphis.usda.gov/sites/default/files/highly-pathogenic-avian-influenza-national-epidemiological-brief-09-24-2024.pdf>.
- <sup>11</sup> United States Food and Drug Administration. Updates on Highly Pathogenic Avian Influenza (HPAI). Ongoing Work to Ensure Continued Effectiveness of the Federal-State Milk Safety System. 28 June 2024. [https://www.fda.gov/food/alerts-advisories-safety-information/updates-highly-pathogenic-avian-influenza-hpai?utm\\_medium=email&utm\\_source=govdelivery](https://www.fda.gov/food/alerts-advisories-safety-information/updates-highly-pathogenic-avian-influenza-hpai?utm_medium=email&utm_source=govdelivery).
- <sup>12</sup> Spackman E, Jones DR, McCoig AM, Colonius TJ, Goraichuk I, Suarez DL. Characterization of highly pathogenic avian influenza virus in retail dairy products in the US. *medRxiv* 2024.05.21.24307706; <https://doi.org/10.1101/2024.05.21.24307706>.
- <sup>13</sup> Spackman E, Anderson N, Walker S, Suarez DL, Jones DR, McCoig A et al. Inactivation of Highly Pathogenic Avian Influenza Virus with High-temperature Short Time Continuous Flow Pasteurization and Virus Detection in

Bulk Milk Tanks, *Journal of Food Protection*, Volume 87, Issue 10, 2024, 100349, ISSN 0362-028X, <https://doi.org/10.1016/j.jfp.2024.100349>.

- <sup>14</sup> Nelli RK, Harm TA, Siepker C, Groeltz-Thrush JM, Jones B, Twu N, et al. Sialic Acid Receptor Specificity in Mammary Gland of Dairy Cattle Infected with Highly Pathogenic Avian Influenza A(H5N1) Virus. *Emerg Infect Dis*. 2024;30(7):1361-1373. doi.org/10.3201/eid3007.240689.
- <sup>15</sup> Kristensen C, Jensen HE, Trebbien R, Webby RJ, Larsen LE. Avian and Human Influenza A Virus Receptors in Bovine Mammary Gland. *Emerg Infect Dis*. 2024;30(9):1907-1911. doi.org/10.3201/eid3009.240696.
- <sup>16</sup> Ríos Carrasco M, Gröne A, van den Brand JMA, de Vries RP. O. The mammary glands of cows abundantly display receptors for circulating avian H5 viruses. *J Virol* 0:e01052-24. doi.org/10.1128/jvi.01052-24.
- <sup>17</sup> Halwe NJ, Cool K, Breithaup A, Schön J, Trujillo JD, Nooruzzaman M et al. H5N1 clade 2.3.4.4b dynamics in experimentally infected calves and cows. *Nature* (2024). doi.org/10.1038/s41586-024-08063-y.
- <sup>18</sup> Baker AL, Arruda B, Palmer MV, Boggiatto P, Davila KS, Buckley A et al. Dairy cows inoculated with highly pathogenic avian influenza virus H5N1. *Nature* (2024). <https://doi.org/10.1038/s41586-024-08166-6>.
- <sup>19</sup> USDA. Federal and State Veterinary Agencies Share Update on HPAI Detections in Oregon Backyard Farm, Including First H5N1 Detections in Swine, 30 October 2024. <https://www.aphis.usda.gov/news/agency-announcements/federal-state-veterinary-agencies-share-update-hpai-detections-oregon>.
- <sup>20</sup> USDA. USDA Animal and Plant Health Inspection Service Shares Update on H5N1 Detection in Oregon Swine, Bovine Vaccine Candidate Progression, 6 November 2024. <https://www.aphis.usda.gov/news/agency-announcements/usda-animal-plant-health-inspection-service-shares-update-h5n1-detection>.
- <sup>21</sup> Graaf A, Piesche R, Sehl-Ewert J, et al. Low Susceptibility of Pigs against Experimental Infection with HPAI Virus H5N1 Clade 2.3.4.4b. *Emerg Infect Dis*. 2023;29(7):1492-1495. 10.3201/eid2907.230296.
- <sup>22</sup> Kwon T, Trujillo JD, Carossino M, et al. Pigs are highly susceptible to but do not transmit mink-derived highly pathogenic avian influenza virus H5N1 clade 2.3.4.4b. *Emerg Microbes Infect*. 2024;13(1):2353292. 10.1080/22221751.2024.2353292.
- <sup>23</sup> Arruda B, Baker A, Buckley A, et al. Divergent Pathogenesis and Transmission of Highly Pathogenic Avian Influenza A(H5N1) in Swine. *Emerging Infectious Diseases*. 2024;30(4):738-751. 10.3201/eid3004.231141.
- <sup>24</sup> Plaza PI, Gamarra-Toledo V, Euguí J, Lambertucci SA. Recent Changes in Patterns of Mammal Infection with Highly Pathogenic Avian Influenza A(H5N1) Virus Worldwide. *Emerg Infect Dis*. 2024;30(3):444-452. doi.org/10.3201/eid3003.231098.
- <sup>25</sup> OFFLU. Continued expansion of high pathogenicity avian influenza H5 in wildlife in South America and incursion into the Antarctic region, 21 December 2023. <https://www.offlu.org/wp-content/uploads/2023/12/OFFLU-wildlife-statement-no.-ii.pdf>.
- <sup>26</sup> Puryear W, Sawatzki K, Hill N, et al. Highly Pathogenic Avian Influenza A(H5N1) Virus Outbreak in New England Seals, United States. *Emerg Infect Dis*. 2023;29(4):786-791. 10.3201/eid2904.221538.
- <sup>27</sup> Uhart, M.M., Vanstreels, R.E.T., Nelson, M.I. et al. Epidemiological data of an influenza A/H5N1 outbreak in elephant seals in Argentina indicates mammal-to-mammal transmission. *Nat Commun* 15, 9516 (2024). doi.org/10.1038/s41467-024-53766-5.
- <sup>28</sup> Voice of Viet Nam [media]. Test results of 20 tigers that died in Dong Nai due to A/H5N1 flu infection, 1 November 2024. <https://vov.gov.vn/ket-qua-xet-nghiem-vu-20-con-ho-chet-o-dong-nai-do-nhiem-cum-ah5n1-dtnew-1035996>.
- <sup>29</sup> World Organization for Animal Health (WOAH). 2024. Report from World Animal Health Information System (WAHIS): Report ID 169715. <https://wahis.woah.org/#/in-review/5944?fromPage=event-dashboard-url>.
- <sup>30</sup> Thanawongnuwech R, Amonsin A, Tantilertcharoen R, et al. Probable tiger-to-tiger transmission of avian influenza H5N1 [published correction appears in *Emerg Infect Dis*. 2005 Jun;11(6):976]. *Emerg Infect Dis*. 2005;11(5):699-701. 3201/eid1105.050007.
- <sup>31</sup> Keawcharoen J, Oraveerakul K, Kuiken T, et al. Avian influenza H5N1 in tigers and leopards. *Emerg Infect Dis*. 2004;10(12):2189-2191. 10.3201/eid1012.040759.
- <sup>32</sup> United States Centers for Disease Control and Prevention (US CDC). CDC Report on Missouri H5N1 Serology Testing, 24 October 2024. <https://www.cdc.gov/bird-flu/spotlights/missouri-h5n1-serology-testing.html>.
- <sup>33</sup> World Health Organization (9 April 2024). Disease Outbreak News; Avian Influenza A (H5N1) – the United States of America. <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON512>.
- <sup>34</sup> US CDC. CDC A(H5N1) Bird Flu Response Update September 13, 2024. <https://www.cdc.gov/bird-flu/spotlights/h5n1-response-09132024.html>.

- <sup>35</sup> Mellis AM, Coyle J, Marshall KE, Frutos AM, Singleton J, Drehoff C et al. Serologic Evidence of Recent Infection with Highly Pathogenic Avian Influenza A(H5) Virus Among Dairy Workers — Michigan and Colorado, June–August 2024. *MMWR Morb Mortal Wkly Rep* 2024;73:1004–1009. <http://dx.doi.org/10.15585/mmwr.mm7344a3>.
- <sup>36</sup> Public Health Agency of Canada. Statement from the Public Health Agency of Canada: Update on Avian Influenza and Risk to Canadians, 13 November 2024. <https://www.canada.ca/en/public-health/news/2024/11/update-on-avian-influenza-and-risk-to-canadians.html>.
- <sup>37</sup> Yang J, Qureshi M, Kolli R, Peacock TP, Sadeyen J-R, Carter T et al. The Haemagglutinin Gene of Bovine Origin H5N1 Influenza Viruses Currently Retains an Avian Influenza Virus. Phenotype. Available at: [bioRxiv 2024.09.27.615407](https://doi.org/10.1101/2024.09.27.615407); <https://doi.org/10.1101/2024.09.27.615407>.
- <sup>38</sup> US CDC. CDC A(H5N1) Bird Flu Response Update November 18, 2024. <https://www.cdc.gov/bird-flu/spotlights/h5n1-response-11152024.html>.
- <sup>39</sup> US CDC. CDC Reports A(H5N1) Ferret Study Results. 7 June 2024. <https://www.cdc.gov/bird-flu/spotlights/ferret-study-results.html>.
- <sup>40</sup> Pulit-Penalosa JA, Brock N, Belser JA, Sun X, Pappas C, Kieran TJ, Thakur PB, Zeng H, Cui D, Frederick J, Fasce R, Tumpey TM, Maines TR. Highly pathogenic avian influenza A(H5N1) virus of clade 2.3.4.4b isolated from a human case in Chile causes fatal disease and transmits between co-housed ferrets. *Emerg Microbes Infect.* 2024 Mar 17:2332667.
- <sup>41</sup> Eisfeld AJ, Biswas A, Guan L, Gu C, Maemura T, Trifkovic S et al. Pathogenicity and transmissibility of bovine H5N1 influenza virus. *Nature* (2024). doi.org/10.1038/s41586-024-07766-6.
- <sup>42</sup> Restori KH, Septer KM, Field CJ, Patel DR, VanInsberghe D, Raghunathan V et al. Risk assessment of a highly pathogenic H5N1 influenza virus from mink. *Nat Commun* 15, 4112 (2024). <https://doi.org/10.1038/s41467-024-48475-y>.
- <sup>43</sup> Pulit-Penalosa JA, Belser JA, Brock N, et al. Transmission of a human isolate of clade 2.3.4.4b A(H5N1) virus in ferrets. *Nature*. Published online October 28, 2024. <https://doi.org/10.1038/s41586-024-08246-7>.
- <sup>44</sup> Gu C, Maemura T, Guan L, Eisfeld AJ, Biswas A, Kiso M et al. A human isolate of bovine H5N1 is transmissible and lethal in animal models. *Nature* (2024). doi.org/10.1038/s41586-024-08254-7 (2024).
- <sup>45</sup> Belser JA, Sun X, Pulit-Penalosa JA, Maines TR. Fatal Infection in Ferrets after Ocular Inoculation with Highly Pathogenic Avian Influenza A(H5N1) Virus. *Emerg Infect Dis.* 2024;30(7):1484-1487. doi.org/10.3201/eid3007.240520.
- <sup>46</sup> World Health Organization/World Organisation for Animal Health/Food and Agriculture Organization (WHO/OIE/FAO) H5N1 Evolution Working Group (2014) Revised and updated nomenclature for highly pathogenic avian influenza A (H5N1) viruses. *Influenza and Other Respiratory Viruses* 8(3), 384–388.
- <sup>47</sup> World Health Organization. Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness, February 2024. [https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2024-2025/202402\\_zoonotic\\_vaccinivirusupdate.pdf?sfvrsn=70150120\\_4](https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2024-2025/202402_zoonotic_vaccinivirusupdate.pdf?sfvrsn=70150120_4).
- <sup>48</sup> Food and Agriculture Organization of the United Nations (FAO) Viet Nam (5 April 2024). Stay vigilant with Highly Pathogenic Avian Influenza A(H5N1). <https://www.fao.org/vietnam/news/detail-events/ru/c/1680337/>.
- <sup>49</sup> Siegers JY, Ruopeng X, Byrne AM, Edwards KM, Hu S, Yann S et al. Emergence of a Novel Reassortant Clade 2.3.2.1c Avian Influenza A/H5N1 Virus Associated with Human Cases in Cambodia. *medRxiv* 2024.11.04.24313747. doi.org/10.1101/2024.11.04.24313747.
- <sup>50</sup> Government Electronic Newspaper, Viet Nam [machine translation]. Dong Nai has controlled the outbreak of avian influenza A/H5N1, 31 Oct 2024. <https://baochinhphu.vn/dong-nai-da-khong-che-duoc-o-dich-cum-gia-cam-a-h5n1-102241031184954402.htm>.
- <sup>51</sup> Daulagala P, Cheng S, Chin A, Luk L, Leung K, Wu JT, et al. Avian Influenza A(H5N1) Neuraminidase Inhibition Antibodies in Healthy Adults after Exposure to Influenza A(H1N1)pdm09. *Emerg Infect Dis.* 2024;30(1):168-171. doi.org/10.3201/eid3001.230756.
- <sup>52</sup> World Health Organization. (2012). Rapid risk assessment of acute public health events. <https://iris.who.int/handle/10665/70810>.
- <sup>53</sup> US CDC. Past Examples of Probable Limited, Non-Sustained, Person-to-Person Spread of Avian Influenza A Viruses. [https://www.cdc.gov/bird-flu/php/avian-flu-summary/h5n1-human-infections.html?CDC\\_AAref\\_Val=https://www.cdc.gov/flu/avianflu/h5n1-human-infections.htm](https://www.cdc.gov/bird-flu/php/avian-flu-summary/h5n1-human-infections.html?CDC_AAref_Val=https://www.cdc.gov/flu/avianflu/h5n1-human-infections.htm).

- <sup>54</sup> US CDC. Technical Update: Summary Analysis of Genetic Sequences of Highly Pathogenic Avian Influenza A(H5N1) Viruses in Texas, 2 April 2024. <https://www.cdc.gov/bird-flu/spotlights/h5n1-analysis-texas.html>.
- <sup>55</sup> International Health Regulations (2005). Third edition. Geneva: World Health Organization; 2016. <https://iris.who.int/handle/10665/246107>.
- <sup>56</sup> Case definitions for the four diseases requiring notification to WHO in all circumstances under the IHR (2005). Geneva: World Health Organization; 2009. [https://www.who.int/publications/m/item/case-definitions-for-the-four-diseases-requiring-notification-to-who-in-all-circumstances-under-the-ihp-\(2005\)](https://www.who.int/publications/m/item/case-definitions-for-the-four-diseases-requiring-notification-to-who-in-all-circumstances-under-the-ihp-(2005)).
- <sup>57</sup> WHO case definition for human infections with avian influenza A(H5) virus requiring notification under IHR (2005). Geneva: World Health Organization; 2024. <https://www.who.int/teams/global-influenza-programme/avian-influenza/case-definitions>.
- <sup>58</sup> El Masry I, Delgado AH, Silva GOD, Dhingra M, Lyons NA. 2024. Recommendations for the surveillance of influenza A(H5N1) in cattle – With broader application to other farmed mammals. FAO Animal Production and Health Guidelines, No. 37. Rome, FAO. <https://doi.org/10.4060/cd3422en>
- <sup>59</sup> End-to-end integration of SARS-CoV-2 and influenza sentinel surveillance, revised interim guidance, 31 January 2022. Geneva: World Health Organization; 2022. <https://iris.who.int/bitstream/handle/10665/351409/WHO-2019-nCoV-Integrated-sentinel-surveillance-2022.1-eng.pdf?sequence=1>.
- <sup>60</sup> World Health Organization. Tool for influenza pandemic risk assessment. [http://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-\(tipra\)](http://www.who.int/teams/global-influenza-programme/avian-influenza/tool-for-influenza-pandemic-risk-assessment-(tipra)).
- <sup>61</sup> US CDC. Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations. <https://www.cdc.gov/bird-flu/prevention/hpai-interim-recommendations.html>.
- <sup>62</sup> Animal and Plant Health Inspection Service, USDA (12 April 2024). APHIS Recommendations for Highly Pathogenic Avian Influenza (HPAI) H5N1 Virus in Livestock For Workers. <https://www.aphis.usda.gov/sites/default/files/recommendations-workers-hpai-livestock.pdf>.
- <sup>63</sup> Guidelines for the clinical management of severe illness from influenza virus infections. Geneva: World Health Organization; 2022. <https://apps.who.int/iris/handle/10665/352453>.
- <sup>64</sup> Joint FAO/WHO Codex Alimentarius Commission. Codex Alimentarius: Code of hygienic practice for milk and milk products. [https://www.fao.org/fileadmin/user\\_upload/livestockgov/documents/CXP\\_057e.pdf](https://www.fao.org/fileadmin/user_upload/livestockgov/documents/CXP_057e.pdf).

#### DISCLAIMER

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) or of the World Organisation for Animal Health (WOAH) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. All reasonable precautions have been taken by WHO, FAO and WOAH to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO, FAO and WOAH be liable for damages arising from its use.