Public health risk of avian influenza A(H5N1) detected recently in dairy cattle

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World Health Organization

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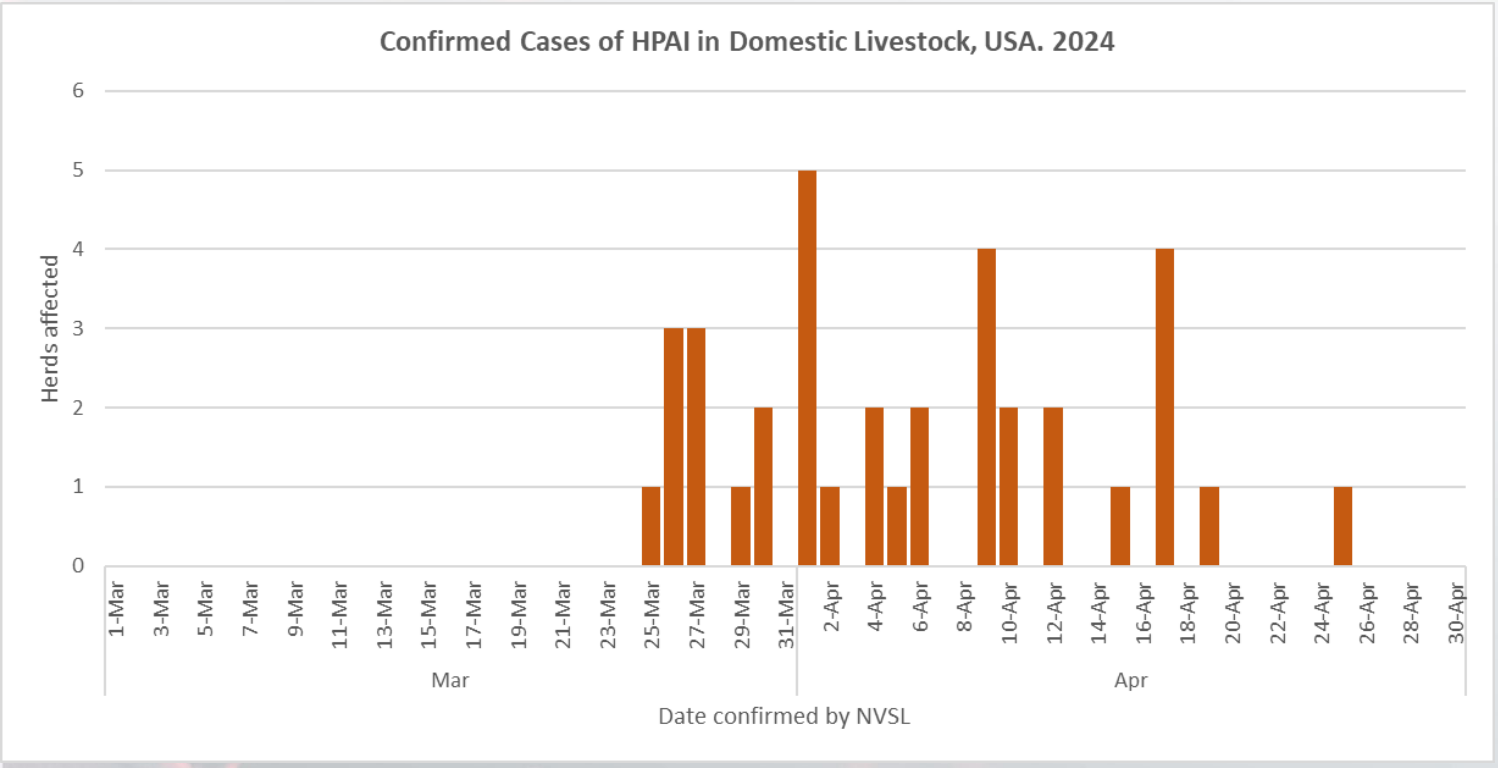
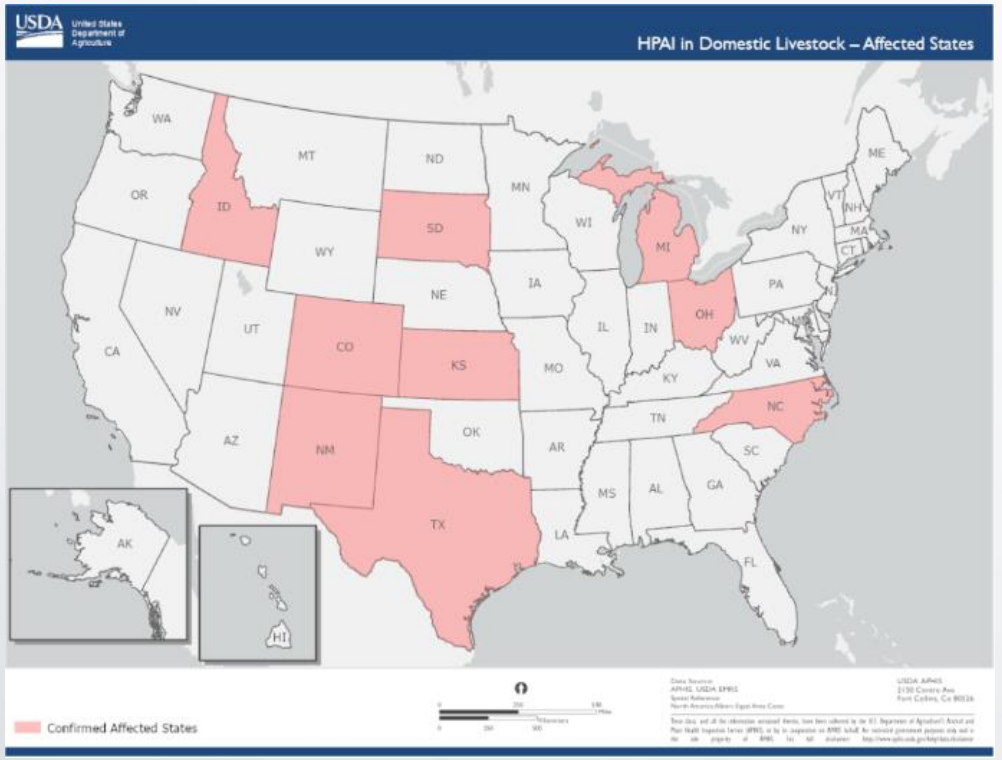
A(H5N1) in dairy cattle in United States of America (USA), 2024

- **January 2024:** unexplained illness in dairy cattle causing drop in milk production, among other non-specific signs, in multiple states
- **25 March**: detection of influenza A(H5N1) in cows reported
- **1 April:** human case notified to WHO
- **24 April:** presence of HPAI using qPCR in pasteurized retail milk samples; further studies underway on milk, meat and other products
- As of **3 May**: detections in 36 dairy cattle herds in 9 states
- Cats, raccoons, birds (wild and domestic) also affected near infected dairy cattle herds
- **Risk assessment**:
  - At the present time, based on available information, WHO assesses the overall public health risk posed by A(H5N1) to be low, and for those with exposure to infected birds or animals or contaminated environments, the risk of infection is considered low-to-moderate. This risk requires close monitoring and WHO and partners will continue to regularly assess and publish public health risk assessments for avian influenza.

https://www.aphis.usda.gov/aphis/newsroom/news/sa_by_date/sa-2024/hpai-cattle
https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON512
https://www.fda.gov/food/alerts-advisories-safety-information/updates-highly-pathogenic-avian-influenza-hpai
https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock
https://wwwnc.cdc.gov/eid/article/30/7/24-0508_article
https://www.usda.gov/media/press-releases/2024/04/24/usda-actions-protect-livestock-health-highly-pathogenic-h5n1-avian
https://www.who.int/publications/m/item/joint-fao-who-woah-preliminary-assessment-of-recent-influenza-a(h5n1)-viruses
Nguyen et al. bioRxiv 2024.05.01.591751

HPAI in domestic livestock (cows) in the USA





As of 3 May: 36 herds in 9 states

https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock

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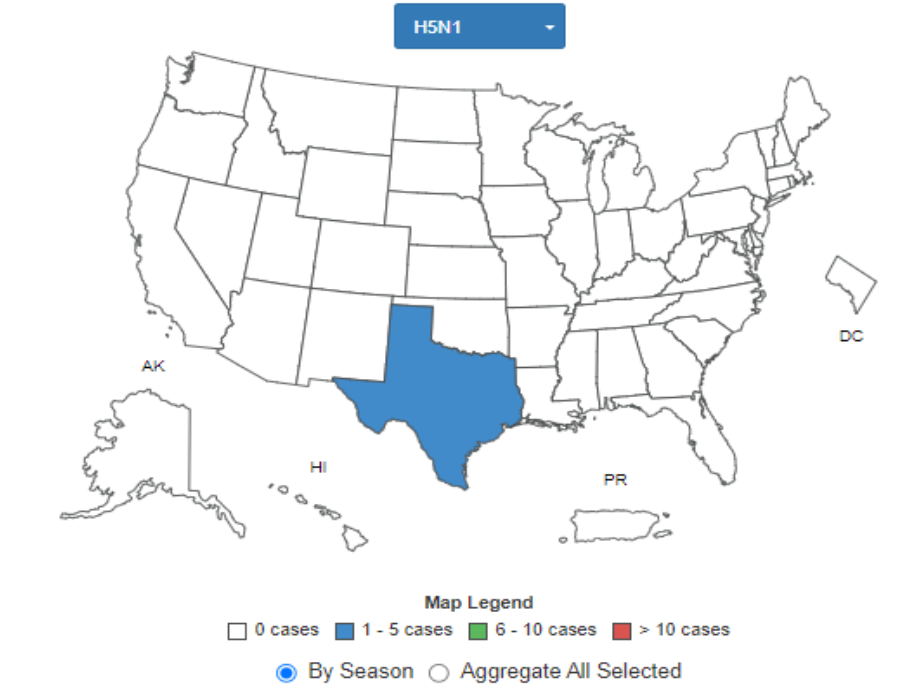
A(H5N1) in dairy cattle in the USA

- High viral load in milk from affected cows and low viral load in nasal swabs of cows
- Asymptomatic cows have tested positive and evidence of virus in lungs at slaughterhouse from asymptomatic herd
- Spread between cows within the same herd and spread between dairies associated with cattle movements identified
  - Cattle to cattle transmission likely through mechanical means but under investigation
- Previously, influenza A was thought to occur on a very infrequent basis in cows
- As of 24 April, U.S. Department of Agriculture (USDA) has put in place
  - mandatory testing for interstate movement of dairy cattle
  - mandatory reporting on testing for influenza A in livestock

https://www.usda.gov/media/press-releases/2024/04/24/usda-actions-protect-livestock-health-highly-pathogenic-h5n1-avian
https://www.mdpi.com/1999-4915/11/6/561

Human case of A(H5N1), USA



- 1 human case of conjunctivitis in a dairy farm worker in direct contact (without eye or respiratory protection) with cattle presumed to be infected
- Onset of symptoms 27 March
- Laboratory confirmation on 30 March by U.S. CDC
- Case notified to WHO on 1 April
- No additional cases of human infection with influenza A(H5N1) associated with this case have been identified thus far
- Active monitoring of exposed workers and monitoring influenza using routine surveillance data
  - No further human cases detected

https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-analysis-texas.htm
https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/one-health-situation-update.htm
https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON512
https://www.cdc.gov/flu/avianflu/what-cdc-doing-h5n1.htm
Uyeki TM et al.. Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker. N Engl J Med. 2024 May 3

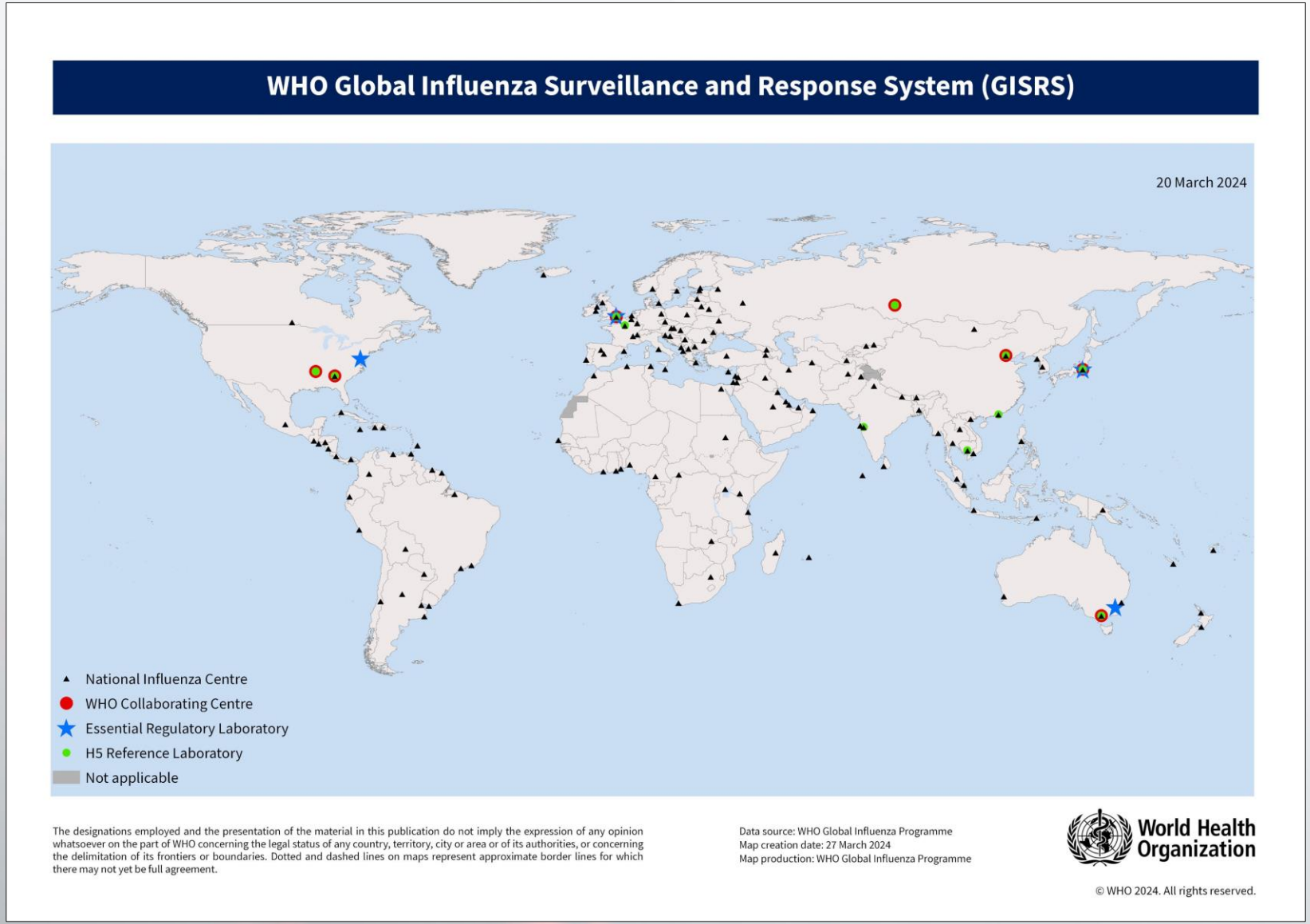
Virus characteristics

- **These viruses are primarily avian viruses**
- **No changes in the virus receptor binding tropism have been observed that would increase transmission to and among people**
- **Genetic analysis**
  - H5 clade 2.3.4.4b, genotype B3.13, which has not been detected outside the USA thus far
  - PB2: E627K mutation detected in the virus from human, and in one virus from cattle with a mixed E & K (31% K)
  - No known markers for reduced susceptibility to neuraminidase inhibitors (NIs) (antiviral medicines such as oseltamivir) or endonuclease inhibitors (such as baloxavir), except in one virus with a change in NA (T438I) associated with reduced susceptibility to (NIs)
- **Antigenic analysis**
  - Data from Hemagglutination Inhibition Assays conducted in WHO CC CDC US showed that the human virus was well covered by existing Candidate Vaccine Viruses (CVVs) (IDCDC-RG71A, IDCDC-RG78A, IDCDC-RG80A)
  - Viruses from cows are also expected to be covered well by the CVVs considering almost identical genetic sequences

https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-analysis-texas.htm
Uyeki TM et al.. Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker. N Engl J Med. 2024 May 3

Broader context

For over 70 years, the **Global Influenza Surveillance and Response System (GISRS)** has been in place to protect people from the threat of influenza (seasonal, zoonotic and pandemic)



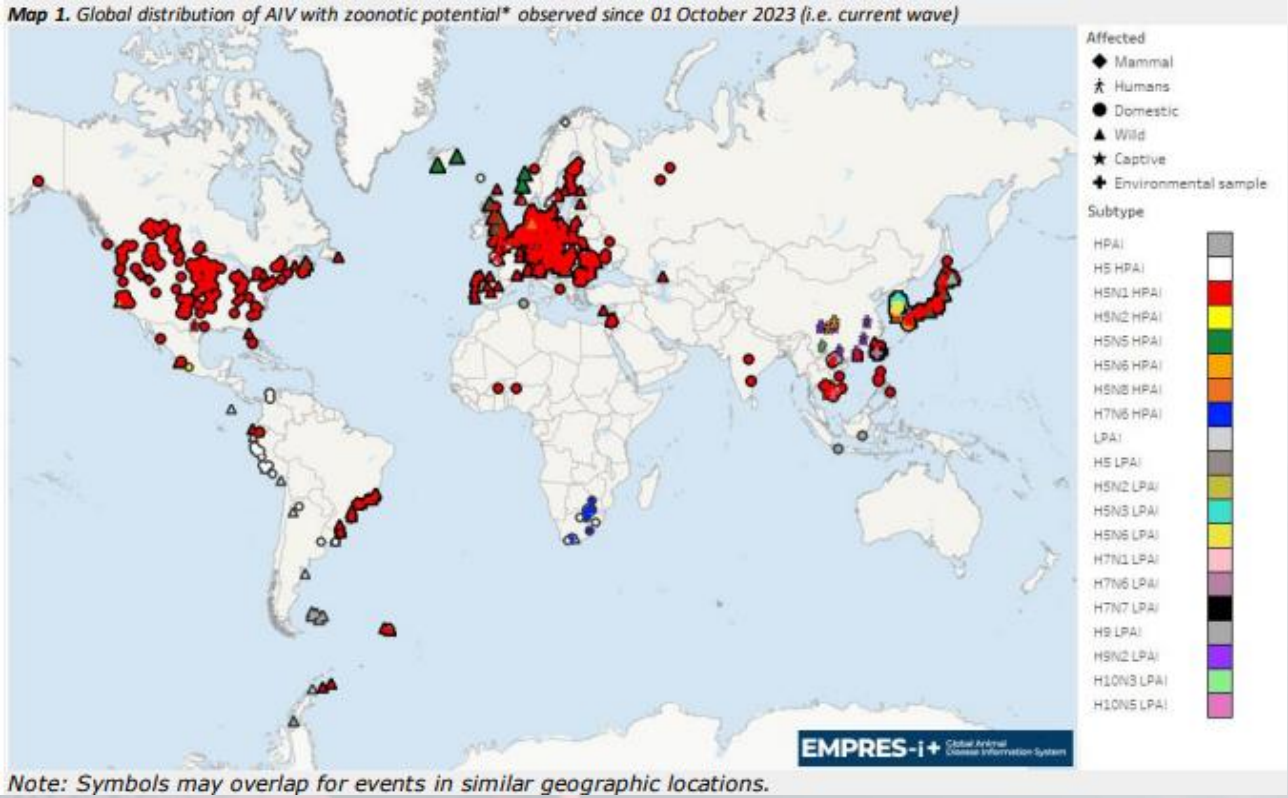
https://www.who.int/initiatives/global-influenza-surveillance-and-response-system

Broader context

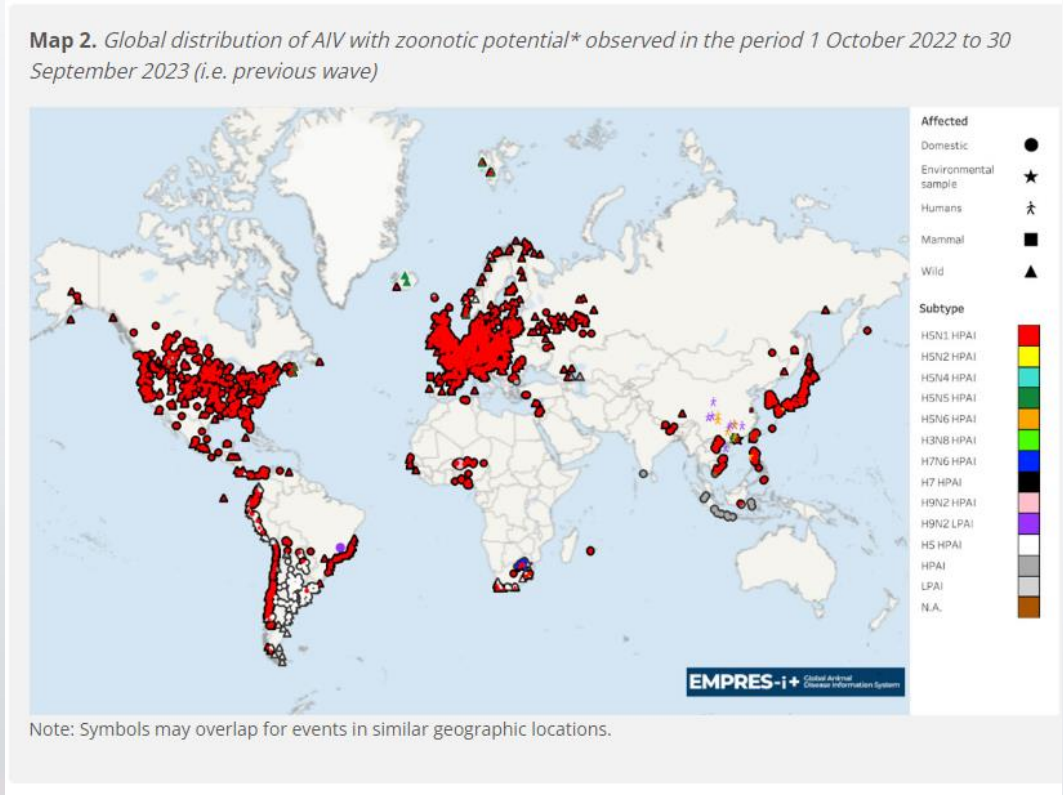
- Over 800 detections of **A(H5N1) in humans** reported from over 20 countries since 2003.
- Avian influenza A(H5N1) viruses, especially those of clade 2.3.4.4b, continue to **diversify genetically** and **spread geographically**.
  - Since 2022, a **broader range of wild bird species** has been infected globally which has had deleterious ecological consequences and caused mass die-offs in some species. The situation with **wild mammals** is also worrying, with some species suffering significant mortality events.
- Despite the high number of A(H5N1) clade 2.3.4.4b outbreaks and detections in animals, and human exposures to the virus at the human-animal-environment interface, relatively **few human infections** have been reported to date.
  - 28 human cases of A(H5N1) detections reported 2021-all were sporadic infections in people exposed to A(H5N1) viruses through direct or indirect contact with infected animals or contaminated environments.
  - Among these cases, there has been **no reported human-to-human transmission** based on investigations thus far.
- **Swine influenza viruses** circulate in pigs in many countries and human infections with swine influenza viruses have been reported.

Global circulation of avian influenza in animals

1 Oct 2023 to 25 April 2024



1 Oct 2022 to 30 Sept 2023



https://www.fao.org/animal-health/situation-updates/global-aiv-with-zoonotic-potential

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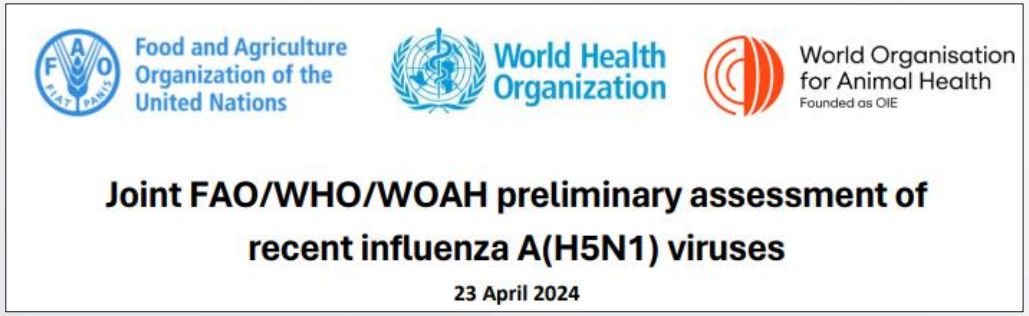
Assessment of current global public health risk to humans posed by influenza A(H5N1) viruses



- At the present time, based on available information, WHO assesses the overall public health risk posed by A(H5N1) to be **low**.
- For those with exposure to infected birds or animals or contaminated environments, the risk of infection is considered **low-to-moderate**.
- There has been **no reported human-to-human transmission** of A(H5N1) viruses since 2007, although there may be gaps in investigations. Prior to 2007, small clusters of A(H5) virus infections in humans were reported, including some involving health care workers, where limited human-to-human transmission could not be excluded; however, sustained human-to-human transmission was not reported.
- This risk requires close monitoring and WHO and partners will continue to regularly assess and publish public health risk assessments for avian influenza.

Joint FAO/WHO/WOAH preliminary assessment of recent influenza A(H5N1) viruses

Assessment of current global public health risk to humans posed by influenza A(H5N1) viruses

- 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.
- As long as people are in contact with infected animals (including dairy cattle) without appropriate personal protective equipment, there is a risk for human infections.
- The risk can be mitigated by measures to reduce exposure to the virus, such as the use of recommended personal protective equipment, appropriate personal hygiene and other risk-based biosecurity measures.

Joint FAO/WHO/WOAH preliminary assessment of recent influenza A(H5N1) viruses

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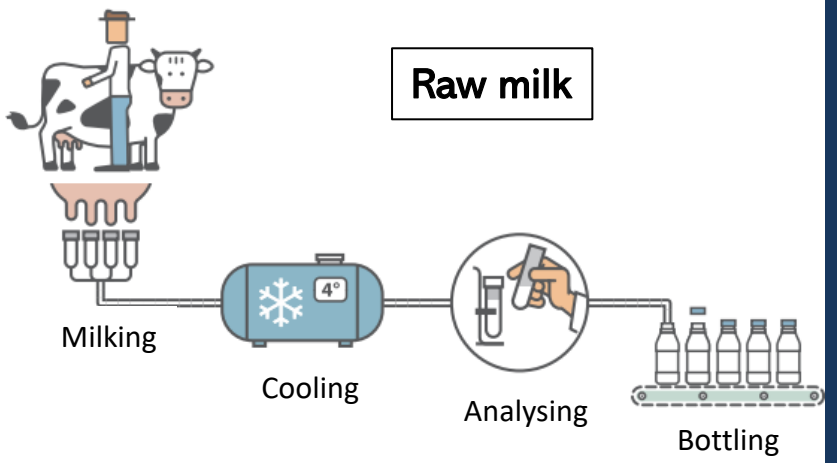
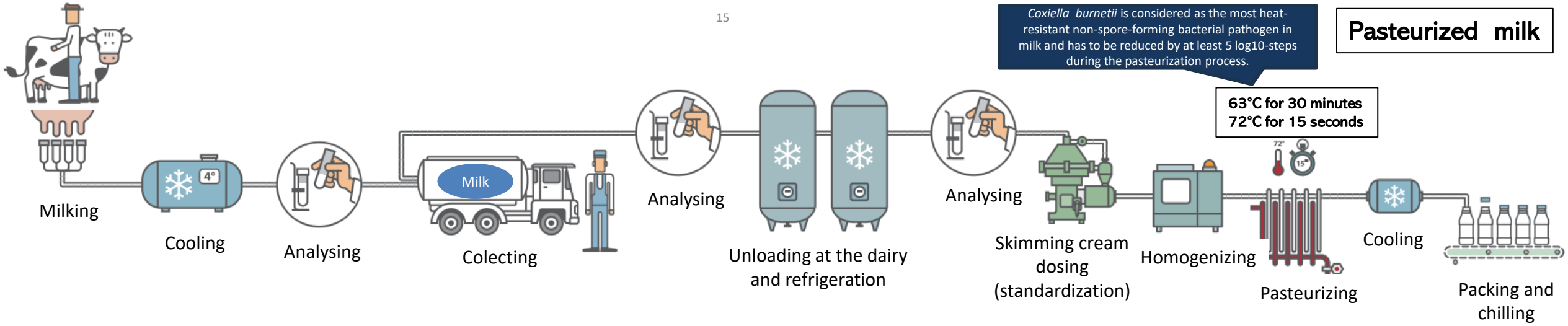
Food Safety Aspects

Raw milk vs Pasteurized milk



Good Hygiene Practices

1. sick cows are milked separately
2. abnormal milk is redirected
3. milk from farms with zoonotic diseases is collected in a special stream



Testing of Commercialized Pasteurized milk

1

20% of samples of commercially sold pasteurized milk tested positive on q-RT-PCR → sampling Plan? Representativity?

2

16

As of May 2, 2024, no live infectious virus has been detected in these positive samples

The available information supports the argument that pasteurization effectively inactivates the A(H5N1) virus.

Pasteurization's efficacy to inactivate A(H5N1) in milk

1

Two elements:

- Initial viral load → expected to be high → US FDA –USDA
- A(H5N1) survival capacity to heat treatment → no data in milk → ongoing studies

2

- The preliminary results are encouraging. The virus is inactivated by heat treatment conditions similar to milk pasteurization.
- Waiting for additional studies with higher initial virus load and varied temperatures

Consuming raw milk, eggs, or meat is not recommended, especially in places where influenza outbreaks have occurred on farms. Make sure to consume pasteurized or properly boiled milk and pasteurized milk products*, and thoroughly cook meat and eggs. Also, if you are handling raw products, make sure to wash your hands before and after, and follow other food safety precautions. This is our consistent advice, with or without avian influenza, because these practices protect you from a variety of diseases.

* *In general, it is not recommended to consume raw milk products. However, some cheese-making techniques can guarantee the production of safe products.*

Advice for people working on farms

Those at risk of exposure to exposed to potentially infected animals should:

- be provided with and trained in proper use of appropriate personal protective equipment (which are exclusively dedicated to this activity)
- wear appropriate personal protective equipment, including gloves, coverall, face, eye and foot protection, and particulate respirator
- regularly perform hand hygiene (with alcohol-based hand rub or preferably hand washing with soap and clean water if visibly soiled) in addition to the frequent environmental cleaning and disinfection
- if symptoms of illness develop, receive early and appropriate clinical management and sampling according to appropriate case definitions and investigations

Advice for the public

Given the observed extent and frequency of avian influenza in poultry, wild birds and some wild and domestic mammals, the public should:

- avoid contact with animals that are sick or dead from unknown causes, including wild animals
- report dead birds and mammals or request their removal by contacting local wildlife or veterinary authorities
- follow good food safety and hygiene practices (especially hand washing)
- properly handle and cook eggs, poultry meat and other animal products
- avoid slaughtering and preparing sick animals for consumption
- avoid consuming raw milk
- seek health care if feeling unwell and inform health care provider of possible exposure

https://iris.who.int/bitstream/handle/10665/372248/9789240076884-eng.pdf?sequence=1

What is WHO doing?

- Genetic and antigenic characterization of influenza viruses with WHO Collaborating Centres and reference labs
  - Markers of mammalian adaptation
  - Genetic and antigenic similarity to candidate vaccine viruses (CVVs)
  - Antiviral susceptibility (genetic and phenotypic)
  - Validation of diagnostic assays
  - Human population immunity
  - Risk assessments and updates to candidate vaccine viruses
- Routine surveillance and monitoring for influenza
- Communications
- Ongoing preparedness activities
  - Vaccine access through Pandemic Influenza Preparedness Framework
  - Clinical management
  - Pandemic surveillance guidance
- Food safety
- International Health Regulations (2005)
- Coordinating with animal health partners (FAO, WOAH, OFFLU) and external partners

Ongoing risk assessment

- Situation in animals globally
  - Countries should maintain surveillance in birds, monitor and investigate cases in non-avian species, including livestock, report cases of high pathogenicity avian influenza in all animal species to WOAH and other international organizations
- Transmission studies in different animal models, including the role of asymptomatic animals in transmission
- Serology studies in humans and cows
- Validation of diagnostics for animals and humans
- Testing of food products
- Maintain surveillance in human populations
- Encourage sequencing and sharing of genetic sequence data from animal and human viruses
- Evaluate pipelines for vaccine development and deployment should it be needed
- Update risk assessments and guidance

Thank you

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