

Concerns on H5N1 avian influenza given the outbreak in U.S. dairy cattle



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The recent outbreak of H5N1 avian influenza in dairy cattle across several United States (US) states has raised significant concern nationally and globally. This Highly Pathogenic Avian Influenza (HPAI) outbreak has been confirmed in various states, including Texas, Kansas, Michigan, Idaho, South Dakota, New Mexico, Ohio and North Carolina (Fig. 1). It primarily affects older cows, leading to symptoms such as reduced appetite, fever, and decreased milk production.¹ It was recently announced that milk sold commercially in 10 states contained fragments of the H5N1 Influenza, although this does not directly represent a risk.² Surveillance and early detection of H5N1 avian influenza are paramount to effective prevention and control efforts.³ The virus, while not yet detected in the commercial milk supply, remains under close monitoring due to its potential impact on animal and human health. Ten goats have died in Minnesota, ranging from 5 to 9 days old. Brain and tissue samples from five goat kids were positive for H5N1. The risk to the public is currently deemed low, with one identified human case attributed to direct exposure to infected animals (Table 1).¹

Genomic sequencing of viral RNA from clinical specimens is crucial in assessing genetic reassortment and detecting mutations that may affect transmissibility or antiviral resistance.^{4,5} Early detection of H5N1 infection in humans is essential for preventing further spread and reducing the risk of severe disease and mortality. We highlight the importance of implementing biosafety measures, such as conducting real-time reverse transcription polymerase chain reaction (RT-PCR) under appropriate biosafety conditions and enhancing surveillance efforts to monitor the evolution of H5N1 virus strains.^{3,5,6} Additionally, in consultation with relevant stakeholders, poultry vaccination may be a complementary tool in disease control strategies.⁷ Prevention is essential as, with this evolving situation, there are many potential threats of H5N1 for humans and animals, including outbreaks, in which still, the pathogenic effect of the circulating strains for humans is not clear, but could lead to infection, severe disease and even death in the worst scenario. If such a situation progresses, it may require a coordinated global response involving governments, healthcare organisations, researchers, and international agencies to mitigate its impact and prevent further spread.

Furthermore, genetic sequencing findings from infected cattle with H5N1 provide valuable insights into transmission dynamics and potential public health risks associated with the virus.⁸ Continued strict surveillance and research are imperative to monitor and mitigate the spread of H5N1 in both animal and human populations,

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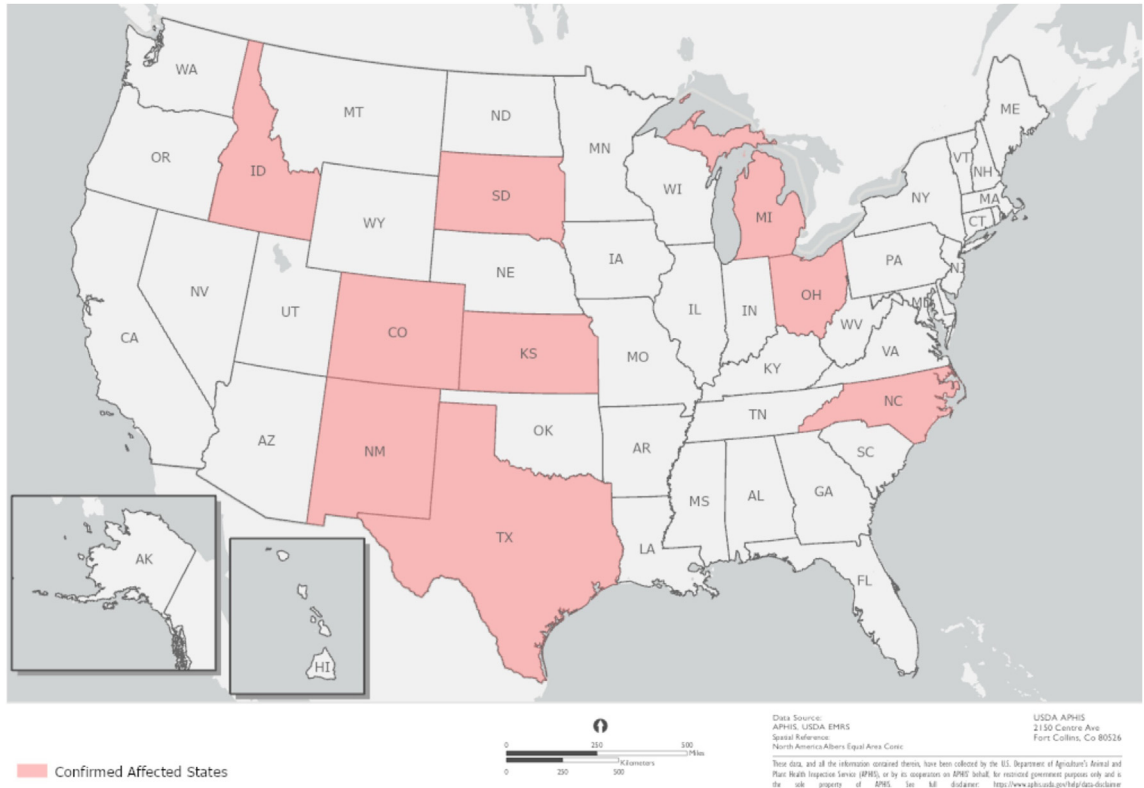


Fig. 1: Confirmed cases of HPAI in domestic livestock in the USA, May 16, 2024, according to the animal and plant health inspection service (APHIS) of the U.S. Department of agriculture (USDA). Reproduced from <https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock>.

to detect and act upon any human risks as soon as possible. Proactive surveillance, early detection, and collaboration among local, state, and federal health agencies, as well as cattle farmers and dairy distributors, are essential to effectively manage and contain the current outbreak of H5N1 avian influenza in U.S. dairy cattle. Before crossing state lines, dairy cattle must

undergo testing for the Influenza A virus at a designated National Animal Health Laboratory Network (NAHLN) facility and receive a negative result. In the event of a positive test among dairy cattle intended for interstate travel, herd owners will need to furnish epidemiological details, such as tracing the movement of animals. Compliance with conditions outlined by the Animal and

Case summary	Description
Human case	01
Age	18 Year
Date of report	March 25, 2024
Location	United States, Texas
Virus strain	Highly Pathogenic Avian Influenza (HPAI) A (H5N1)
Symptoms	Eye redness (consistent with conjunctivitis)
Genetic clade	Clade 2.3.4.4b
Detection method	Throat swab, Unpasteurized milk samples
Detection in dairy cattle	Texas, Kansas, Michigan, Idaho, South Dakota, New Mexico, Ohio, North Carolina and Colorado.
Treatment	Isolation, Antiviral medication
Vaccine availability	Candidate vaccine viruses (CVVs) available for manufacturing if necessary
Prevention	Avoidance of unprotected exposures to infected animals, raw milk products, use of personal protective equipment (PPE)
Public health assessment	Low for the general public, Increased risk for those with close or prolonged, unprotected exposures to infected birds or animals

Table 1: Analysis of HPAI avian influenza A (H5N1) human case and outbreak dynamics.^{3,4}

Plant Health Inspection Service (APHIS) is mandatory for dairy cattle destined for interstate transport. Immediate implementation of these measures applies to lactating dairy cattle. In contrast, considerations for other categories of dairy cattle will be contingent upon scientific evaluations of the virus and its evolving risk factors, as explained in forthcoming guidance. By implementing robust prevention and control strategies, we can mitigate the spread of the virus and protect both animal and human health. H5N1 Influenza spillover from cattle to humans poses a risk, potentially associated with epidemics. Vigilant surveillance, stringent biosecurity measures, and prompt response are critical to prevent transmission. Understanding and addressing this threat through interdisciplinary collaboration is paramount to safeguarding public health and averting catastrophic consequences, committing to a One Health approach to protect lives and the environment.

Contributors

RS and AJRM conceived the idea of the Comment and drafted the first versions; the rest of the authors contributed to subsequent revised versions. All authors approved the final version.

Declaration of interests

None.

References

- 1 Global Center for Health Security. Bird flu spreads to dairy cows. <https://www.unmc.edu/healthsecurity/transmission/2024/03/26/bird-flu-spreads-to-dairy-cows/>. Accessed April 10, 2024.
- 2 Cohen J. The U.S. government is taking action to stop 'cow flu.' Is it too little, too late? *Science*. 2024. <https://doi.org/10.1126/science.z2o5wt8>.
- 3 Fu X, Wang Q, Ma B, et al. Advances in detection techniques for the H5N1 avian influenza virus. *Int J Mol Sci*. 2023;24(24):17157.
- 4 CDC. Highly pathogenic avian influenza A (H5N1) virus infection reported in a person in the U.S. <https://www.cdc.gov/media/releases/2024/p0401-avian-flu.html>. Accessed April 11, 2024.
- 5 Avian influenza A(H5N1) - United States of America. <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON512>. Accessed April 11, 2024.
- 6 Welkers MRA, Pawestri HA, Fonville JM, et al. Genetic diversity and host adaptation of avian H5N1 influenza viruses during human infection. *Emerg Microb Infect*. 2019;8(1):262–271.
- 7 Verhagen JH, Fouchier RAM, Lewis N. Highly pathogenic avian influenza viruses at the wild–domestic bird interface in Europe: future directions for research and surveillance. *Viruses*. 2021;13(2):212.
- 8 Haider N, Kock R, Zumla A, Lee SS. Consequences and global risks of highly pathogenic avian influenza outbreaks in poultry in the United Kingdom. *Int J Infect Dis*. 2023;129:162–164.