Weekly Influenza A(H5N1) Key Points

May 10, 2024

Summary

- CDC continues to respond to the public health challenge posed by a multistate outbreak of avian influenza A(H5N1) virus, or "A(H5N1) virus," in dairy cows and other animals in the United States.
- CDC is working in collaboration with the U.S. Department of Agriculture (USDA), the Food and Drug Administration (FDA), state public health and animal health officials, and other partners using a One Health approach.
- USDA is now reporting that 42 dairy cattle herds in nine U.S. states have confirmed cases of A(H5N1) virus infections in cattle.
- There have been no additional human cases detected since the one recent case from Texas was reported on April 1, 2024, despite the fact that more than 260 people have been monitored as a result of their exposure to infected or potentially infected animals and at least 33 who have developed flu-like symptoms have been tested.
- This is a rapidly changing situation, and CDC is committed to providing frequent and timely updates.

In this document

What CDC is Doing

- CDC's response to this outbreak of influenza A(H5N1) virus in dairy cattle and other animals most recently includes:
    - Continuing to support states that are monitoring people with exposure to cows, birds, or other domestic or wild animals infected, or potentially infected, with avian influenza A(H5N1) viruses. Testing of symptomatic people who have exposures is being done by state or local officials, and CDC is conducting confirmatory testing when needed.
    - Continuing discussions with multiple states about state-led field investigations to explore key scientific and public health questions related to the ongoing outbreak. CDC is playing a coordinating role with regard to investigation protocols so that data collection can be standardized across states and results can be pooled. CDC's multilingual and multidisciplinary epidemiological field teams are standing by, ready to deploy to support on-site studies if requested.
    - Working to make personal protective equipment (PPE) available for affected farmworkers by asking that jurisdictions use their existing stockpiles for workers on dairy farms, poultry farms, and in slaughterhouses, prioritizing distribution of PPE to affected farms. If needed, HHS/ASPR has indicated it can provide PPE from the strategic national stockpile.
    - Continuing work to better characterize the virus from the human case in Texas.
    - This week, CDC researchers inoculated (infected) ferrets with the virus from the one human infection for its laboratory studies. Ferrets are used as a model for people

because they get sick and spread influenza viruses in a manner similar to people. The goals of these animal studies, include:

- Assessing the severity of illness and transmissibility of the virus under different contact scenarios by infecting ferrets and assessing the outcome, including:
  - via direct or close contact, with healthy and infected ferrets in the same space; and
  - via respiratory droplets, with healthy and infected ferrets in side-by-side spaces separated by a wall with holes in it.
- Results from the animal studies will be available in approximately three weeks. Experimental infection of cell lines is forthcoming.

- Continuing to engage with manufacturers of commercial diagnostic tests and clinical partners to make progress toward the goal of having an A(H5N1) test that is widely available if needed.
- Continuing the process so that all states can conduct A(H5) testing on eye specimens using CDC's H5 test. CDC submitted the official request package for this to FDA at the end of last week.
  - Use of eye swabs with the CDC H5 test when the testing is performed by CDC was approved by the CDC Clinical Laboratory Improvement Amendment (CLIA) director on April 27th, which means results of testing of eye swabs at CDC can be reported back for patient care. Some state public health laboratories have also taken the step to have eye swabs approved as a sample type for testing under their internal CLIA authorization. Originally, the test was designed for use with respiratory specimens.
  - Once FDA authorizes the use of that specimen type with the test, all states will be able to do the testing themselves.

- Continuing to engage One Health partner organizations from public health, agriculture, wildlife, milk regulatory officials, and others to share information and ensure preparedness to prevent and respond to this emerging infectious disease threat and for any potential human infections.
- Continuing to monitor flu surveillance data, especially in areas where A(H5N1) viruses have been detected in dairy cattle or other animals, for any unusual trends in flu-like illness, flu, or conjunctivitis.
  - Overall, for the most recent week of data, CDC flu surveillance systems show no indicators of unusual flu activity in people, including avian influenza A(H5N1) viruses.

CDC Recommendations

- CDC has interim recommendations for prevention, monitoring, and public health investigations of A(H5N1) virus infections in people. CDC also has updated recommendations for worker protection and use of personal protective equipment (PPE).
- Following these recommendations is central to reducing a person's risk and containing the overall public health risk.

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- Additionally, as a reminder, while CDC believes the current risk of A(H5N1) infection to the general public remains low, high levels of A(H5N1) virus have been found in unpasteurized ("raw") milk.
- CDC and FDA recommend against the consumption of raw milk or raw milk products.
- The risk of human infection from drinking raw milk containing live A(H5N1) virus specifically is unknown.
- To date, A(H5N1) viruses have not acquired the ability to bind to virus receptors that are most prevalent in the upper respiratory tract of people.
- If a person consumed raw milk with live A(H5N1) virus, the person could become infected, theoretically, by the virus binding to a limited amount of virus receptors in the upper respiratory tract or by aspiration of virus into the lower respiratory tract where receptors that A(H5N1) viruses can bind to are more widely distributed.

Ongoing Surveillance Needed

- Genetic analysis of the human A(H5N1) virus and hundreds of cattle viruses indicate these viruses are still mainly avian in nature and do not currently have the ability to easily infect or spread among people.
- However, because of the potential for influenza viruses to constantly change, continual surveillance and preparedness efforts are critical, and CDC is taking measures to be ready in case the current risk assessment for the general public changes.
- The immediate goal is to prevent further spread of this virus between animals and people. CDC will continue to monitor these viruses and update and adjust guidance as needed.

H5N1 Seroprevalence Among Poultry Workers

Background:

- Serology is the scientific study of blood to look at the response of the immune system to vaccines or infections with pathogens, influenza viruses.
- A seroprevalence study or sero-survey is an investigation that tests blood for the presence of antibodies to a pathogen of interest, such as highly pathogenic avian influenza A(H5N1) virus.
- In an H5N1 seroprevalence study, people who test positive for antibodies to H5N1 virus are referred to as seropositive. Usually, detecting antibodies to H5N1 virus is evidence of infection with the virus in the past. The percentage of people in a study population who have antibodies to a particular virus is called "seroprevalence."

Data Summary:

- A 2020 systematic review and meta-analysis of more than 60 peer reviewed articles (from January 1, 1997-September 1, 2020) looked at highly pathogenic avian influenza A (H5N1) virus antibody seroprevalence among people who had poultry exposures as well as people without specific exposures to poultry.

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- Seroprevalence of A(H5N1) virus antibodies was low overall but was higher among people with poultry exposures, compared with people who did not have exposure to poultry.
    - People with poultry exposures in areas with widespread H5N1 outbreaks in poultry also had higher seroprevalence than people who also had poultry exposure but were not in areas with H5N1 outbreaks in poultry.
    - People who were exposed due to their work in live poultry markets had higher frequencies of virus-specific antibodies than poultry farmers or veterinarians likely because they were typically involved in higher risk activities, like butchering and processing poultry.
- The review also found that, despite this, relatively few people among the groups of people studied who were at increased risk for exposure to A(H5N1) virus had been previously infected with A(H5N1) virus.
- Among the studies that used WHO's recommended seropositive antibody titer threshold (the level of antibodies in your blood that shows you've been infected with H5N1), seroprevalence ranged from 0 to 7% (with a median of 0%).
    - Among these studies, the mean seroprevalence among people with specific poultry exposures including poultry workers, poultry cullers, and people with mixed poultry and human exposures (exposure to people infected with H5N1) was 0.2%, 0.6%, and 1.8%, respectively.
    - The World Health Organization (WHO) has issued guidance to define a seropositive result. This is important because studies that do not use the WHO seropositive criteria can over-estimate seroprevalence.
    - A(H5N1) virus antibody seroprevalence was reported as 0% in more than half of the studies that used the WHO or a modified WHO seropositive definition.
- Importantly, human seropositivity has been lower with more recent clades of A(H5N1) virus circulating in wild birds and causing poultry outbreaks than it was with earlier H5 viruses.
- Most of these studies were conducted internationally in countries with outbreaks of avian influenza in poultry with studies primarily in Asia, Africa, and the Middle East, and several studies in Europe, Canada, and the United States.
- These studies looked at a range of exposures, including different occupational and behavioral exposures (e.g., poultry workers, poultry cullers, poultry-exposed residences, household contacts of H5N1 human cases, social contacts, health care workers, mixed poultry and human exposures, and the general public).
- The findings of this systematic review suggest that A(H5N1) viruses have not been well adapted to spread to and among people.
- However, the study reaffirmed that risk does increase with exposure, and people who have close, prolonged contact with infected animals, their byproducts, or environments may be at increased risk of infection.
- The meta-analysis reviewed seroprevalence studies of persons exposed to A(H5N1) viruses that circulated among wild birds and caused poultry outbreaks in the past. Given the recent wide geographic spread of highly pathogenic avian influenza A (H5N1) virus, clade 2.3.4.4b since 2022, among wild birds worldwide, with poultry outbreaks and spillover to infect many kinds of

mammals, including dairy cows in the United States, new seroprevalence studies are needed to inform better understanding of the public health risk of these viruses.

Risk of Influenza A(H5N1) Virus Infection from Consuming Live Virus

- The risk of human infection from drinking raw milk containing live HPAI A(H5N1) virus is unknown.
- There are unpublished anecdotal reports of raw duck blood consumption as a potential source of HPAI A(H5N1) virus infection in a small number of human cases in the past.
- HPAI A(H5N1) viruses rarely cause infection of the respiratory tract of people and preferentially bind to virus receptors that are most prevalent in the lower respiratory tract.
- To date, HPAI A(H5N1) viruses have not acquired the ability to bind to virus receptors that are most prevalent in the upper respiratory tract of people.
- Recently, HPAI A(H5N1) virus was also shown to also infect conjunctival tissues of a dairy worker in Texas.
- If a person consumed unpasteurized milk with live HPAI A(H5N1) virus, the person could become infected, theoretically, by the virus binding to a limited amount of virus receptors in the upper respiratory tract or by aspiration of virus into the lower respiratory tract where receptors that HPAI A(H5N1) viruses can bind to are more widely distributed.