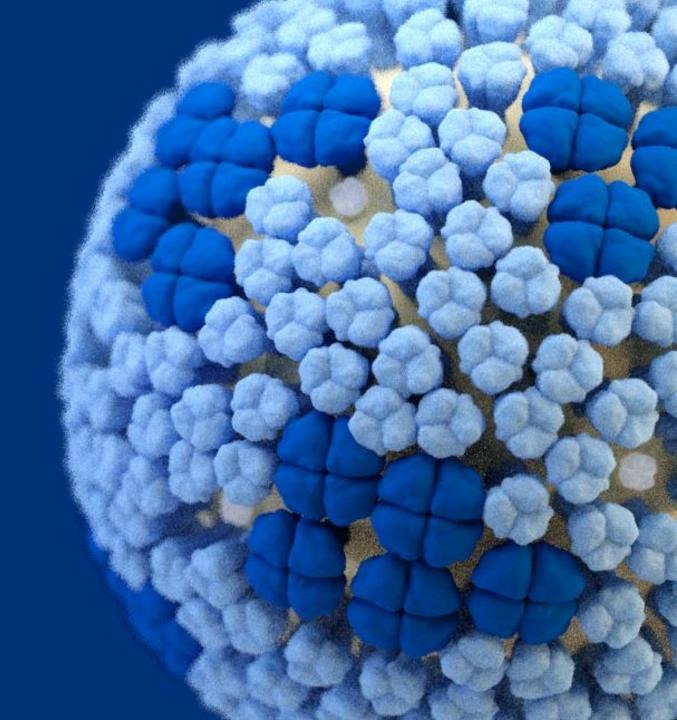
Highly Pathogenic Avian Influenza A (H5N1)

Tom Shimabukuro, MD, MPH, MBA

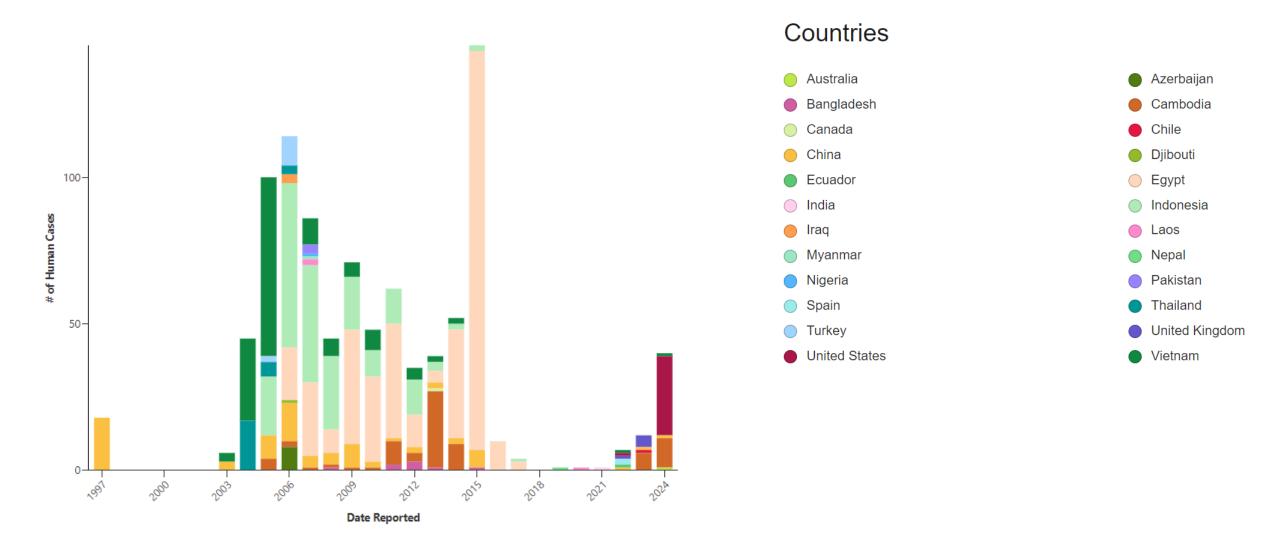
Influenza Division

National Center for Immunization and Respiratory Diseases (NCIRD)

Centers for Disease Control and Prevention (CDC) December 5, 2024

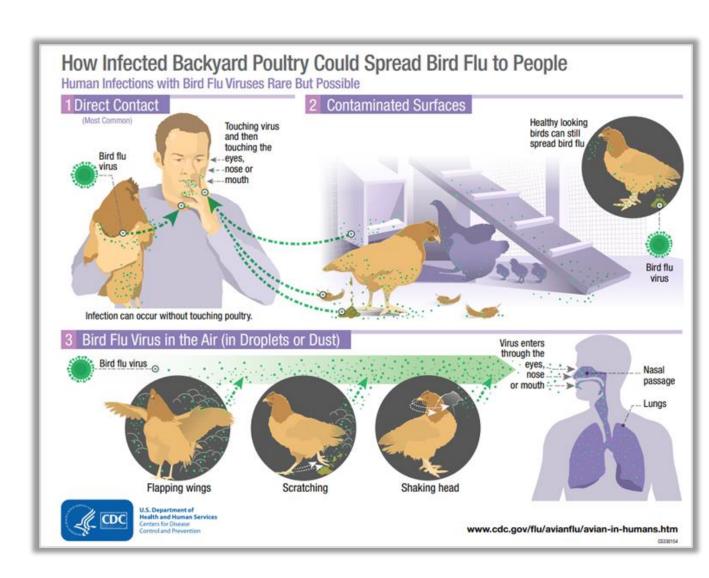


HPAI A(H5N1)/HPAI A(H5) Human Cases Since 1997



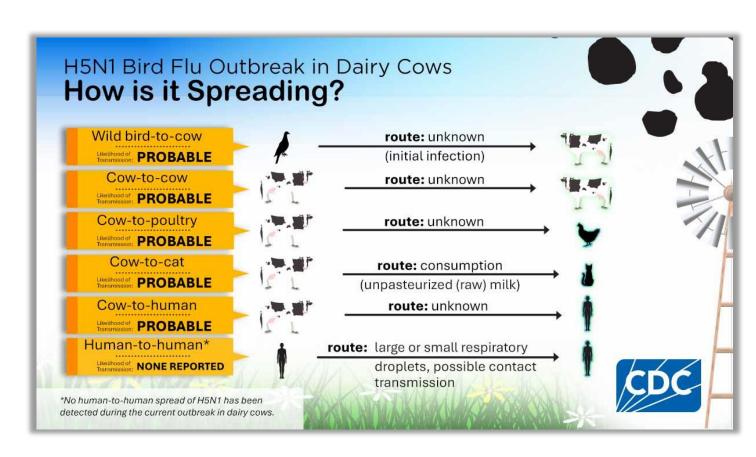
Historical Human Exposures to HPAI A(H5N1) Viruses

- Historically, human infections have been the result of:
 - Poultry exposures
 - Direct/close contact with sick or dead poultry
 - Visiting a live poultry market
 - Exposure to other infected animals
 - Direct contact or close exposure (swans, dairy cows)
 - Limited, non-sustained human-tohuman transmission has occurred globally in the past (not in the United States)



CDC's Priorities

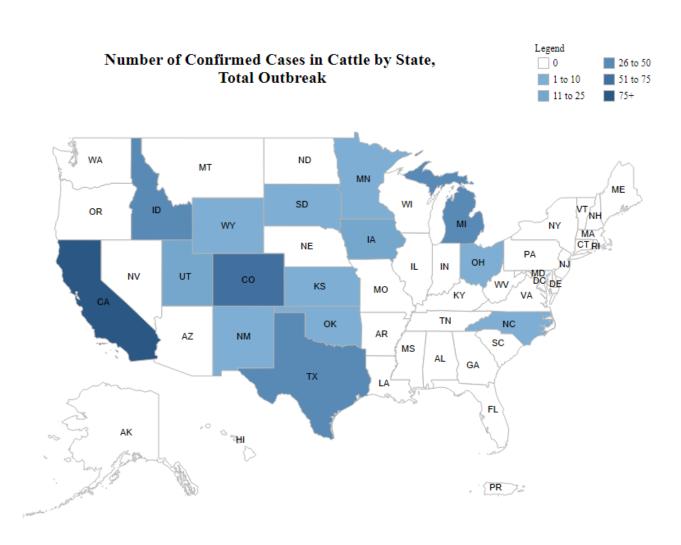
- Supporting and engaging public health and agricultural partners
- Protecting human health and safety
- Understanding risk to people from HPAI A(H5N1) viruses
- Assessing HPAI A(H5N1) viruses for genetic changes



Avian Influenza Social Media Toolkit | Bird Flu | CDC

HPAI A(H5N1) Situation Update – Dairy Herds

- As of December 2, 2024, USDA has confirmed HPAI A(H5N1) in U.S. dairy herds in 689 farms across 15 states
 - Dairy cow illness was observed in early 2024
 - Significant decrease in milk production and quality
 - March 25, 2024: USDA first reported HPAI A(H5N1) confirmed in cows from Texas and Kansas



HPAI A(H5) Human Cases, United States, During 2024

57 Confirmed Total Reported Human Cases in the United States

Confirmed human case summary during the 2024 outbreak, by state and exposure source

Exposure Source

State	Cattle	Poultry	Unknown	State Total
California	30	0	1	31
Colorado	1	9	0	10
Michigan	2	0	0	2
Missouri	0	0	1	1
Oregon	0	1	0	1
Texas	1	0	0	1
Washington	0	11	0	11
Source Total	34	21	2	57

NOTE: One additional case was previously detected in a poultry worker in Colorado in 2022.

- Cases with dairy cattle and poultry exposures have been clinically mild
 - Mainly eye symptoms (conjunctivitis, eye d/c)
 - Some cases reported mild respiratory and systemic symptoms (e.g., subjective fever)
- 2 cases with unknown exposures detected by regular influenza surveillance
 - Adult patient in Missouri (August 2024)
 - Patient with multiple underlying health conditions and was hospitalized symptoms not typical of a respiratory illness
 - Illness was not severe, patient treated with oseltamivir and recovered
 - Child patient in California (November 2024)
 - Patient had mild symptoms, treated with oseltamivir and recovered
 - Low levels of HPAI A(H5) viral material detected
 - Patient positive for other common respiratory viruses

HPAI A(H5N1) case in British Columbia, Canada

- In November 2024, a teenager from British Columbia was hospitalized and subsequently diagnosed with influenza A(H5) virus infection; during hospitalization, the patient became critically ill
- The case was identified through routine influenza surveillance conducted at the hospital
- The Public Health Agency of Canada has confirmed that the virus from the case is closely related to viruses detected in wild birds in the region and to avian influenza H5N1 viruses from ongoing outbreaks in poultry in British Columbia (Influenza A (H5N1), clade 2.3.4.4b, genotype D1.1).
- Changes have been observed in the virus sequenced from the patient that may indicate an increased ability to bind human receptors
- Changes observed in the virus were identified as mixtures of mutations and may have been generated by replication of this virus in the patient with advanced disease rather than transmitted at the time of infection
- Although concerning, and a reminder that this virus can develop changes during a human infection, these changes would be more concerning if identified in animal hosts or in an early human upper respiratory tract infection when these mutations MIGHT facilitate transmission
- Extensive contact tracing indicate no evidence of human-to-human transmission

Influenza A(H5) Human Cases–Virus Sequences to Date

- Sequences maintain primarily avian genetic characteristics and lack changes that would make the virus better adapted to infect or spread among humans
- **Diagnostics**: No impact to the current CDC influenza diagnostic assay's ability to detect A(H5N1) viruses
- **Treatments**: Genetic markers associated with minor reductions in susceptibility to FDA approved antiviral drugs for influenza have been identified in four viruses sequenced from human cases and do not represent viruses that are spreading among animals
- Candidate Vaccine Viruses (CVVs)
 - Hemagglutinins of human influenza viruses remain antigenically related to three available CVVs
- CDC continues to monitor influenza A(H5N1) viruses for these and other concerning changes, including changes that would signal an increased ability to infect humans to be transmitted from person-to-person, or changes that would indicate that currently available diagnostics, antiviral treatments, or CVVs would be less effective; so far, no such changes have been identified

Symptom Monitoring Recommendations

- All people with direct or close exposure to animals infected with influenza A(H5N1) should be monitored for illness during exposure and for 10 days after their last exposure
- Signs/symptoms may include:
 - feeling feverish, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue, eye redness (or conjunctivitis), shortness of breath or difficulty breathing
 - less commonly, diarrhea, nausea, vomiting, or seizures
- If signs/symptoms develop, seek medical evaluation for possible influenza testing and antiviral treatment
- Symptomatic persons should isolate away from others during this evaluation
- State and local health departments are monitoring workers on impacted farms and can facilitate testing and treatment



Ongoing Human Monitoring

 CDC is continuing to support state and local health departments monitoring exposed people during and for 10 days after last exposure Total people monitored

Total people tested

Human cases

390+
after exposure to infected animals

55
cases detected through targeted
H5 surveillance

Targeted H5 surveillance (since March 24, 2024)

Current HPAI Outbreak (2024)

CDC and state and local health departments monitor people exposed to infected birds, poultry, dairy cows and other animals for 10 days after exposure. Between March 24, 2024, and now, there have been

- At least 8,700 people monitored
 - At least 5,620 with exposures to dairy cows
 - At least 3,100 with exposures to birds and other animals including poultry (non-dairy cow source)
- At least 400 persons tested for novel influenza A
 - At least 146 with exposures to dairy cows
 - At least 260 with exposures to birds and other animals including poultry (non-dairy cow source)

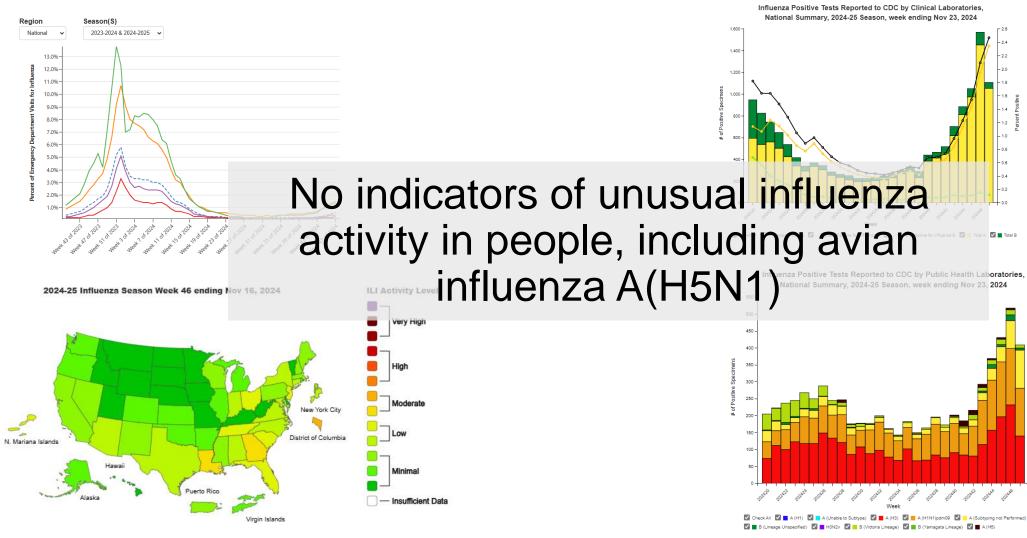
H5 Bird Flu: Current Situation | Bird Flu | CDC

How CDC is monitoring influenza data among people to better understand the current avian influenza A (H5N1) situation | Bird Flu | CDC

(Through December 2-3, 2024)

Surveillance, Human Monitoring, and Testing

Since Feb 2024, public health laboratory monitoring includes testing of over **61,000 specimens** using a protocol that would have detected influenza A(H5) or other novel influenza viruses, **2 people have** tested positive (MO and CA cases)



Findings from a Michigan and Colorado Seroprevalence Study

- Health officials in Michigan and Colorado conducted surveys and serologic testing to identify HPAI A(H5) infections among workers on impacted dairies
- Surveys and blood samples were collected a median of 49 days after exposure from 115 workers across the two states
- 8 of 115 workers showed evidence of previous HPAI A(H5) infections (7% prevalence); among those with prior infections:
 - All spoke Spanish, all cleaned milking parlors or milked cows, none wore respiratory protection, and a minority wore eye protection
 - Few reported direct work with the sick cows
- Supports the need for active outreach in languages that workers speak to educate about infection risks and preventive practices
- Need for active monitoring and testing in real-time by state and local public health partners

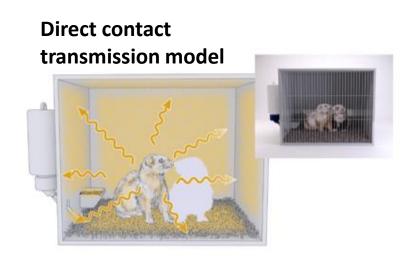


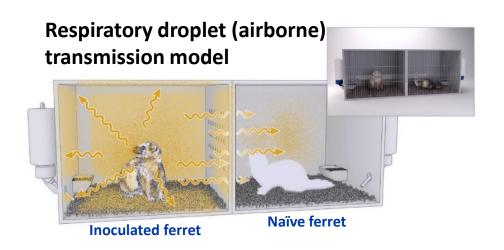
Ferret Studies

- Ferret model permits study of influenza disease severity and transmissibility at the same time
- Ferrets present with many clinical signs of infection shared by humans
 - But not conjunctivitis
- Limitations of ferret model
 - Ferrets in sustained contact 24/7
 - Inoculation doses used in these studies may not be representative of natural exposure in humans
 - Ferrets used in most studies have no preexisting antibodies to influenza, unlike most humans who have had disease or vaccinations
 - General limitations of animal models

Pathogenesis and Transmission of Human Influenza A(H5N1) Viruses in Ferrets

Influenza A(H5N1) Virus	Mean Max Weight Loss (inoculated ferrets)	Lethality (inoculated ferrets)	Direct Contact Transmission (ferrets co-housed)	Resp Droplet Transmission (refer to image)
A/Texas/37/2024(H5N1) (1 st human case in 2024)*	13%	9/9 (100%)	3/3 (100%)	4/6 (66%)
A/Michigan/90/2024(H5N1) (2 nd human case in 2024) [†]	9.1%	0/6 (0%)	3/3 (100%)	2/3 (66%)





Ferret Studies Summary

Severity

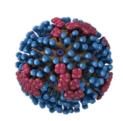
- The Michigan human A(H5N1) virus caused <u>less severe disease</u> in ferrets than the Texas human A(H5N1) virus
- Less mean maximum weight loss, 9.1% vs. 13%
- Lower lethality, 0/6 (0%) vs. 9/9 (100%)

Transmission

- The Michigan human A(H5N1) virus still transmits with some capacity by the respiratory droplet route, similar to what was observed with Texas human A(H5N1) virus
- These findings are important because the Michigan human A(H5N1) virus better represents currently circulating viruses compared to the Texas human A(H5N1) virus

CDC Influenza Risk Assessment Tool (IRAT)

- Evaluative tool for prioritizing resources for pandemic preparedness
- Viruses scored using 10 risk elements by U.S. government subject matter experts for emergence and public health impact
- **Emergence** is the risk of a novel influenza virus acquiring the ability to spread easily and efficiently in people
- **Public health impact** is the potential severity of human disease caused by the virus, the burden on society if a novel influenza virus were to begin spreading efficiently and sustainably among people



- **Genomic variation**
- Receptor binding
- **Transmission in Laboratory animals**
- **Antivirals and Treatment Options**



Virus

- **Existing Population Immunity**
- **Disease Severity and Pathogenesis**

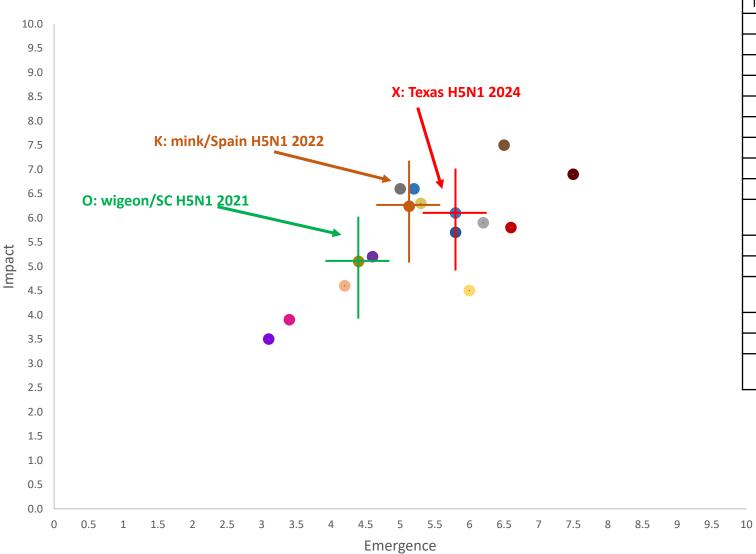
Global Geographic Distribution

Antigenic Relationship to Vaccine Candidates Population 7.



- **Ecology**
- Infection in Animals, Human Risk of Infection
- 10. Human Infections and Transmission

IRAT Virus Emergence and Impact – Comparison of Risk Scores



Data label	Influenza Virus	Emergence Score	Impact Score
Α	A(H1N1) [A/swine/Shandong/1207/2016]	7.5	6.9
В	A(H3N2) variant [A/Ohio/13/2017]	6.6	5.8
С	A(H7N9) [A/Hong Kong/125/2017]	6.5	7.5
Е	A(H9N2) Y280 lineage [A/Anhui-Lujiang/13/2018]	6.2	5.9
F	A(H3N2) variant [A/Indiana/08/2011]	6.0	4.5
X	A(H5N1) clade 2.3.4.4b [A/Texas/37/2024A]	5.8	6.1
G	A(H1N2) variant [A/California/62/2018]	5.8	5.7
1	A(H5N6) clade 2.3.4.4b [A/Sichuan/06681/2021]	5.3	6.3
J	A(H5N1) Clade 1 [A/Vietnam/1203/2004]	5.2	6.6
K	A(H5N1) Clade 2.3.4.4b [A/mink/Spain/3691- 8_22VIR10586-10/2022]	5.1	6.2
L	A(H5N6) [A/Yunnan/14564/2015] – like	5.0	6.6
N	A(H5N8) clade 2.3.4.4b [A/Astrakhan/3212/2020]	4.6	5.2
0	A(H5N1) clade 2.3.4.4b [A/American wigeon/South Carolina/AH0195145/2021]	4.4	5.1
Q	A(H5N8) [A/gyrfalcon/Washington/41088/2014]	4.2	4.6
U	A(H7N8) [A/turkey/Indiana/1573-2/2016]	3.4	3.9
V	A(H7N9) [A/chicken/Tennessee/17-007431- 3/2017]	3.1	3.5

- X: H5N1 clade 2.3.4.4b [A/Texas/37/2024^a] (X)
 Emergence = 5.8, Impact = 6.1
- A: Highest emergence score Eurasian Avian/swine H1N1 in China Emergence = 7.5, Impact = 6.9
- C: Highest Impact score avian H7N9 in China Emergence = 6.5, Impact = 7.5

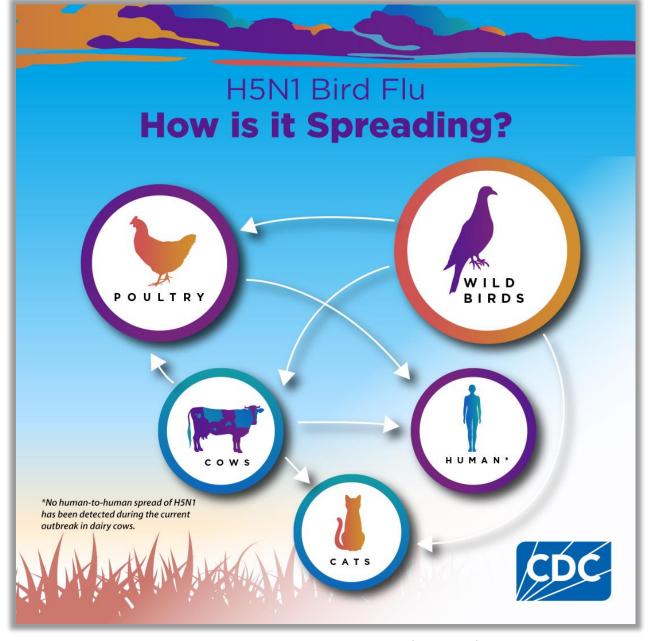
IRAT Summary

- The IRAT is an evaluative tool used by public health partners for prioritizing resources for influenza pandemic preparedness
- It is NOT intended to predict a pandemic and is NOT to be used to assess the overall population risk nor individual risk
- Using A(H5N1) clade 2.3.4.4b [A/Texas/37/2024(H5N1)] as the prototype virus, the score remains in the "moderate" potential pandemic influenza risk category
- The mean-high and mean-low acceptable score ranges for all the clade 2.3.4.4b viruses overlap, indicating that these viruses remain similar, and their overall risk scores remain "moderate"
- Based on available data, CDC's current assessment is that the risk to the general public from avian influenza A(H5N1) virus remains low
- IRATs can be updated if the situation warrants reassessment

Public Health Risk

- Overall risk to the public for HPAI A(H5N1) remains low
- Greater risk for people with close, prolonged, or unprotected exposures to infected animals, or to environments contaminated by infected animals
- Exposed individuals should monitor for symptoms after first exposure and for 10 days after last exposure

Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations | Avian Influenza (Flu) (cdc.gov)



Avian Influenza Social Media Toolkit | Bird Flu | CDC

Protéjase del virus H5N1 si trabaja con animales de granja

El H5N1 es un virus de la influenza aviar que podría enfermarlo. Use el equipo de protección personal (EPP) recomendado cuando trabaje directamente o de cerca con animales enfermos o muertos, heces, camas (*litter*) y leche cruda de animales u otros materiales que podrían tener el virus.



Lávese las manos con agua y jabón y luego póngase el EPP en este orden:

- 1. Overoles resistentes a líquidos.
- 2. Delantal a prueba de agua, si es necesario para las tareas del trabajo.
- Respirador aprobado por NIOSH (NIOSH Approved® Respirator; p. ej., respirador con pieza facial filtrante N95® o respirador con media máscara elastomérica).
- Gafas protectoras o protector facial que no tengan canales de ventilación o que tengan ventilación indirecta y se ajusten de manera adecuada.
- 5. Cubierta para la cabeza o el cabello.
- 6. Guantes.
- 7. Botas.

Avian Influenza Social Media Toolkit | Bird Flu | CDC

<u>Avian Influenza Social Media Toolkit | Bird Flu | CDC</u>

Protect Yourself From H5N1 When Working With Farm Animals

H5N1 is a bird flu virus that could make you sick. Wear recommended personal protective equipment (PPE) when working directly or closely with sick or dead animals, animal feces, litter, raw milk, and other materials that might have the virus.



Wash hands with soap and water, then put on PPE in this order:

- 1. Fluid-resistant coveralls
- 2. Waterproof apron, if needed for job task
- 3. NIOSH Approved® Respirator (e.g., N95® filtering facepiece respirator or elastomeric half mask respirator)
- 4. Properly-fitted unvented *or* indirectly vented safety goggles or face shield
- 5. Head cover or hair cover
- 6. Gloves
- 7. Boots



Resources from CDC

Situation Updates

CDC A(H5N1) Bird Flu Response Update | Avian Influenza (Flu)

Surveillance Updates

How CDC is monitoring influenza data among people to better understand the current avian influenza A (H5N1) situation | Avian Influenza (Flu)

Technical Report

Technical Report: Highly Pathogenic Avian Influenza A(H5N1) Viruses | Avian Influenza (Flu) (cdc.gov)

Updated Recommendations

Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations

Recommendations for Worker Protection and Use of Personal Protective Equipment (PPE) to Reduce Exposure to Novel Influenza A Viruses Associated with Severe Disease in Humans



Q SEARCH

JULY 19, 2024 ESPAÑOL

CDC A(H5N1) Bird Flu Response Update, July 19, 2024

AT A GLANCE

CDC provides an update on its response activities related to the multistate outbreak of avian influenza A(H5N1) virus, or "H5N1 bird flu," in dairy cows and other animals in the United States.

What to Know

In this week's Spotlight, we include the key findings from the recent Michigan-led study that tested the blood of farmworkers from two dairy farms that experienced an outbreak of highly pathogenic avian influenza A(H5N1) virus among cattle. The study looked for antibodies that would indicate infection with the virus. None of the blood samples collected from people who had been exposed to infected dairy cows showed avian influenza A(H5N1) neutralizing antibodies. This is an important finding because it suggests that asymptomatic infections in people are not occurring and provides support to the current testing approach – i.e., collecting samples from symptomatic people who have been exposed to sick animals.

Today's edition also includes details about CDC's analysis of the genetic sequence (RNA) from one of the infected Colorado poutry farm workers diagnosed with avian influenza A(H5N1) virus infection. The findings are reassuring, showing it is closely related to the first human case discovered in Michigan and that it does not have changes associated with antiviral resistance. The full sequence was uploaded to a public database so that researchers in the U.S. and around the world can analyze it.

Finally, we confirm in today's Spotlight two additional cases of avian influenza in Colorado pouttry farm workers. There was a recent pouttry outbreak on the farm with human cases that were exposed to the virus related to a culting of birds, and we have confirmed avian influenza A(H5N1) virus infection in six poultry workers from that event. The infected workers have all experienced mild symptoms, and workers exposed to the virus have been offered antiviral medication.

CDC Update

July 19, 2024 - CDC continues to respond to the public health challenge posed by a multistate outbreak of avian influenza A(H5N1) virus, or "H5N1 bird flu," in dairy cows, poultry 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), Administration for Strategic Preparedness and Response (ASPR), state public health and animal health officials, and other partners using a One Health approach. Since April 2024. 10 human cases of avian influenza A(H5) infection have been reported in the United States Four of these cases were associated with exposure to sick dairy cows and six were associated with exposure to avian influenza A(H5N1)-infected poultry.* [A1(B) This include: two additional cases in Colorado that were confirmed by CDC this week and not previously reported. The two new cases were in poultry workers with exposure to infected poultry during depopulation and disposal activities. Similar to previous cases, illness was mild. Based on the information available at this time, CDC's current H5N1 bird flu human health risk assessment for the U.S. general public remains low. On the animal health side, USDA is reporting that 157 dairy cow herds in 13 U.S. states have confirmed cases of avian influenza A(H5N1) virus infections in dairy cows as the number of infected herds continues to grow. USDA reports that since April 2024, there have been A(H5) detections in 34 commercial flocks and 16 backyard flocks, for a total of 18.32 million birds affected.

ON THIS PAGE

What to Know

CDC Update

Publication Highlights

CDC Recommendations

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News & Spotligh

CDC A(H5N1) Bird Flu Response Update August 2, 2024

CDC A(H5N1) Bird Flu Respons Update July 26, 2024

CDC A(H5N1) Bird Flu Respon

Acknowledgments

CDC Influenza Division

- Virology, Surveillance, and Diagnosis Branch
- Epidemiology and Prevention Branch
- Immunology and Pathogenesis Branch
- Global Influenza Branch
- Office of the Director

CDC 2024 Influenza A(H5N1) Response

Thank you

