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BACKGROUND

Avian influenza A(H5N1) is widespread in wild birds worldwide. It is causing outbreaks in poultry flocks and U.S. dairy cattle herds, with recent human cases in U.S. dairy, poultry, and wildlife workers with exposure to infected animals as well as sporadic cases in people without known exposure to infected animals. A multi-state outbreak of H5N1 influenza infection in dairy cows was first reported on March 25, 2024. H5N1 influenza infections in California dairy cows were first confirmed on August 30, 2024, and the first human cases of H5N1 influenza infection in California dairy workers were confirmed on October 3, 2024.

For information about other variant or novel influenza viruses, please see the California Department of Public Health (CDPH) <u>Variant Influenza Quickset</u>.

OVERVIEW OF HUMAN H5N1 INFLUENZA INFECTIONS

Human infections with avian influenza viruses are rare; H5N1 and H7N9 viruses have caused the majority of human avian influenza infections globally. Illnesses in humans from these infections have ranged in severity from no symptoms or mild illness (e.g., eye infection, upper respiratory symptoms) to severe disease (e.g., pneumonia) that sometimes resulted in death. To date, most U.S. human H5N1 influenza cases have been mild, although a severe case has been reported in Louisiana and Canada. No human-to-human transmission of H5N1 influenza virus has been detected in the United States.

Human infections with avian influenza viruses have occurred most often after close or lengthy unprotected contact (i.e., not wearing eye or respiratory protection or gloves) with infected birds or other animals, their saliva, mucous or feces. In the current outbreak, human infections with H5N1 influenza viruses have involved contact with infected poultry (generally while culling them) or infected dairy cows and their unpasteurized (raw) milk.

Human infections with avian influenza viruses can happen when virus gets into a person's eyes, nose or mouth, or is inhaled. This can happen when a person touches something that has virus on it and then touches their mouth, eyes or nose, or possibly when virus is in the air (in droplets or possibly dust) and a person breathes it in. The spread of avian influenza viruses from one infected person to a close contact is very rare, and when it has happened, it has not led to sustained spread among people. More information about avian influenza in humans is available at CDC's webpage on Avian Influenza Virus Infections in Humans.

CLINICAL AND EXPOSURE INFORMATION

Clinical Criteria:

Symptoms of H5N1 human influenza infection can include:

- Eye redness (conjunctivitis)
- Fever (temperature of >100°F/37.8°C or feeling feverish)*
- Cough
- Sore throat
- Runny or stuffy nose
- Muscle or body aches
- Headaches
- Fatigue
- Shortness of breath or difficulty breathing



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Less common signs and symptoms include diarrhea, nausea, vomiting, or seizures.

*Fever may not always be present.

Exposure Criteria (within the 10 days prior to symptom onset):

- Exposure to animals infected with H5N1 influenza virus (defined as follows):
 - Close contact (within six feet) with infected animals; such exposures can include, but are not limited to: handling, slaughtering, defeathering, butchering, culling, caring for, or milking; OR
 - Preparing or consuming raw animal products, or consuming uncooked or undercooked food or related uncooked food products, including unpasteurized milk, from infected animals; OR
 - Direct contact with surfaces contaminated with feces, unpasteurized milk or other unpasteurized dairy products, or animal parts (e.g., carcasses, internal organs) from infected animals; OR
- Exposure to an infected person: Close (within six feet), unprotected (without use of respiratory and eye protection) contact with a person who is a symptomatic confirmed, probable, or suspected H5N1 influenza case (e.g., in a household or healthcare facility); OR
- Laboratory exposure: Unprotected exposure to H5N1 influenza virus in a laboratory.

Human Infectious Period: Until further data are available, the infectious period should be considered to be from one day before symptom onset date (Day 0) until resolution of any eye infection, including redness (excluding subconjunctival hemorrhage) or drainage; any fever has been gone for 24 hours without the use of fever reducing medication; and other symptoms are mild and improving.

REPORTING

Clinicians should immediately notify their <u>local health department</u> (LHD) if they suspect avian influenza in a patient. LHDs should immediately notify CDPH of suspect cases by calling the Immunization Branch at (510) 620-3737. After hours, contact the CDPH Duty Officer at (916) 328-3605. Please enter all suspected, presumptive, and confirmed H5N1 influenza cases into CalREDIE using the "Influenza-Novel Strain" condition.

The CDC Human Infection with Novel Influenza A Virus Case Report Form should be completed for all presumptive and confirmed cases of H5N1 influenza infection as soon as possible. The CDC Human Infection with Novel Influenza A Virus Case Report Form can be obtained via the CalREDIE Document Repository or by emailing lnfluenzaSurveillance@cdph.ca.gov. Completed forms should be uploaded into the patient's record in CalREDIE or emailed to lnfluenzaSurveillance@cdph.ca.gov and AvianInfluenza@cdph.ca.gov.

TESTING

If a person who meets the exposure criteria above develops symptoms that could be consistent with H5N1 influenza infection within 10 days of exposure, they should be tested.

It is extremely helpful if suspect cases are referred to healthcare facilities that are prepared to accept such patients and that these facilities are notified ahead of time that a suspect H5N1 influenza case will be coming so appropriate precautions can be put in place.

Testing is not routinely recommended for <u>asymptomatic</u> exposed workers, but can be considered on a case-by-case basis, e.g., for those with discrete high-risk exposures such as an unprotected splash of raw milk from an infected cow into the eyes.



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Specimens should ideally be collected within 24–72 hours of symptom onset and no later than 10 days after symptom onset. If more than 10 days have elapsed after symptom onset, testing can be considered on a case-by-case basis and in discussion with CDPH.

Polymerase chain reaction (PCR) testing for H5N1 influenza is available at some local public health laboratories (PHL), the Viral and Rickettsial Disease Laboratory (VRDL) at CDPH, and CDC.

Laboratories should NOT attempt to perform viral culture on specimens from patients with suspected or laboratory-confirmed H5N1 influenza infection. Although some commercial laboratories now perform H5 subtyping, testing via a PHL is recommended for persons who meet the symptom and exposure criteria for H5N1 influenza in order to expedite public health response.

For additional testing guidance, please see the <u>VRDL Test Page - Novel/Avian Influenza Virus</u> (human) PCR (ca.gov).

Specimen collection and specimen types:

- Specimens should be collected using swabs with synthetic tips (e.g., polyester or Dacron®) and an aluminum or plastic shaft. Swabs with cotton tips and wooden shaft are NOT recommended.
- Specimens collected with swabs made of calcium alginate are NOT acceptable.
- Place swab(s) in specimen collection vial containing 2–3 mL of viral transport media (VTM) or universal transport media (UTM); tighten cap to avoid leakage.
- For all patients, collect the following respiratory specimens:
 - Separate anterior nares and oropharyngeal swabs, preferably in separate transport media vials, although they may be combined in a single transport media vial.
 - Nasopharyngeal swabs are acceptable, but to date have had a lower yield for positive test results in cases than oropharyngeal and anterior nares swabs.
- Patients with <u>conjunctivitis</u> should also have <u>conjunctival swab specimens</u> collected. Conjunctival swabs MUST be paired with oropharyngeal and anterior nares swab specimens or a nasopharyngeal swab specimen, even if the person does not have respiratory symptoms.
 - If conjunctivitis is present in both eyes, collect separate swabs from each eye and combine the swabs in a single transport media vial.
 - Conjunctival specimens from patients with conjunctivitis have been more sensitive for detection of H5 than other specimens to date in 2024.
- Patients who have ingested raw dairy products and have gastrointestinal symptoms, with or without respiratory symptoms, may also have a stool specimen collected and held for possible testing for enteric pathogens, as well as testing for influenza A if such testing becomes available.
- Patients with severe respiratory disease should also have lower respiratory tract specimens collected such as an endotracheal aspirate, bronchoalveolar lavage, or sputum.
- For severely ill persons, multiple respiratory tract specimens from different sites should be obtained to increase the potential for H5N1 influenza virus detection.

Specimen storage and handling:

- Freeze or refrigerate specimens after collection. Ship refrigerated specimens to VRDL on cold packs. Ship frozen specimens to VRDL on dry ice.
- Specimens submitted to local PHLs should follow specimen submission procedures for those laboratories.
- Specimens submitted to VRDL must be accompanied by a hard copy of the completed <u>VRDL</u>
 <u>General Purpose Specimen Submittal Form</u> (PDF) or a form generated in the <u>VRDL Lab Web</u>
 Portal.

Suspected case information to collect and submit:



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The following information should be obtained for suspected human cases and should be provided to the CDPH Immunization Branch and VRDL at the time the specimen is shipped to a PHL capable of performing H5 subtyping:

- Basic demographic information
 - Symptom onset date, date reported to public health, signs and symptoms, disease severity, and specimen collection date
- Animal and animal product contact history
 - Contact with livestock or poultry; if applicable, type of work (e.g., working in milking parlor, caring for ill animals)
 - o Contact with animal products, such as raw milk
 - Contact with wildlife and whether or not the wildlife appeared ill
- Workplace exposure information (CalConnect exposure ID or Farm ID)
- Contact with human H5N1 influenza case
- Antiviral treatment received
- Influenza A testing results (including subtyping results), if available
- Household member information
 - Number and ages and whether antiviral PEP received
- PPE use and if used, what PPE was used, particularly:
 - Type of eye protection (goggles or face shield); and
- Type of respiratory protection (medical/surgical mask vs. N95 or other type of respirator)
- Any healthcare received for illness

HOME ISOLATION FOR PERSONS WITH SUSPECTED, PRESUMPTIVE OR CONFIRMED H5N1 INFLUENZA INFECTION

To date, there have been no documented instances of human-to-human transmission of the H5N1 influenza virus (clade 2.3.4.4b) currently circulating in US poultry and dairy cows, but limited human-to-human transmission of other H5N1 influenza strains has occurred rarely in other countries. In addition, animal studies suggest this virus is not capable of spreading efficiently among people via respiratory aerosols compared to seasonal influenza viruses. Based on currently available information, the following recommendations apply to home isolation of non-hospitalized suspected cases until H5N1 influenza infection is ruled out and to non-hospitalized presumptive, probable or confirmed cases until release from isolation.

Isolation at home:

- Stay home unless it is necessary to see a healthcare provider or go to work if the LHD has not recommended work exclusion.
- If taking influenza antiviral medication, the ill person and their household contacts should continue to take it as prescribed unless instructed to stop.
- If living with other people (or pets), the ill person should:
 - Avoid contact with other household members and pets to the extent possible.
 - Wear a well-fitting mask for source control when indoor contact with other household members can't be avoided.
 - Cover any coughs or sneezes and clean hands with soap and water afterwards.
 - Try to take extra care to avoid contact with people at <u>increased risk</u> for complications from seasonal influenza virus infections.
 - Clean hands with soap and water frequently, particularly before contact with other household



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members.

- If soap and water are not available, use a 60% alcohol-based hand sanitizer to clean hands.
- Other household members should also clean their hands frequently.
- Avoid touching the eyes if conjunctivitis is present.
- Clean and disinfect frequently touched items and surfaces at least daily using household disinfectant or wipes.
- Avoid sharing bedding, towels and wash cloths with others, particularly if there has been contact with the eyes, and launder such items before use by others.
- Avoid sharing personal items with others, particularly items that have had contact with the eyes.

When to discontinue isolation:

- Isolation can be discontinued if H5N1 influenza has been ruled out by a documented negative test
 result for influenza A and, ideally for A(H5), for persons with previously documented H5N1
 influenza infection, by rRT-PCR testing at a PHL.
- If H5N1 influenza is confirmed, isolation should continue until:
 - Any eye infection, including redness (excluding subconjunctival hemorrhage) or drainage, is resolved;
 - Any fever (temperature of 100°F/37.8°C or higher) has been gone for at least 24 hours without the use of fever reducing medication; AND
 - Other symptoms are mild and improving.

Modified workplace isolation in non-healthcare settings:

- If individuals feel well enough to work, suspected, presumptive, probable, and confirmed cases may work if they and their coworkers:
 - Wear appropriate recommended PPE while working; and
 - Wash hands frequently with soap and water or if soap and water aren't available, a 60% alcohol-based hand sanitizer to clean hands; and
 - Wear well-fitting facemasks while together in breakrooms or other areas where PPE is typically not worn, including shared transportation to and from work.

General recommendations:

- Ill persons should monitor their symptoms and seek prompt medical attention if their illness worsens (e.g., difficulty breathing).
- If healthcare is needed, ill persons should inform healthcare providers that they have, or are being evaluated for, H5N1 influenza and wear a respirator or facemask when entering any healthcare facility.

HEALTHCARE FACILITY H5N1 INFLUENZA INFECTION PREVENTION AND CONTROL RECOMMENDATIONS

If a person with suspected or confirmed H5N1 influenza infection is referred to a healthcare facility, the healthcare facility should be alerted prior to patient arrival so appropriate infection control measures can be planned and immediately implemented. The ill person should be advised to wear a facemask on arrival.

If a patient with suspected or confirmed H5N1 influenza infection presents to a healthcare setting, healthcare providers should:

• Immediately mask the patient and place them in an airborne infection isolation room (AIIR) with



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the door closed. While in an AIIR the patient's mask may be removed.

- If an AIIR is not available, place the patient in a single-patient room with the door closed and have the patient remain masked.
- Use personal protective equipment that includes:
 - o Respiratory protection (fit-tested N95 respirator or higher level of protection)
 - Eye protection (goggles or face shield)
 - Gown and gloves
- Use diligent hand hygiene before and after contact with the patient.
- Limit room entry to essential personnel. Limit patient transport outside their room.
- If a non-AIIR room is used, after the patient leaves, the room should not be reused and unprotected individuals should not enter until sufficient time has elapsed for airborne-contaminant removal per <u>CDC guidance</u>.

For additional infection control guidance, such as management of exposed healthcare workers, visitor policies, environmental cleaning, and caution with aerosol-generating procedures, please refer to:

- CDC Interim Guidance for Infection Control Within Healthcare Settings When Caring for Confirmed Cases, Probable Cases, and Cases Under Investigation for Infection with Novel Influenza A Viruses Associated with Severe Disease
- Interim Guidance for Follow-up of Close Contacts of Persons Infected with Novel Influenza A Viruses Associated with Severe Human Disease or with Potential to Cause Severe Human Disease, and Use of Antiviral Medications for Post-exposure Prophylaxis

For applicable Cal/OSHA requirements in healthcare settings, please see <u>California's Aerosol Transmissible Diseases standard</u>.

RECOMMENDATIONS FOR INFLUENZA ANTIVIRAL TREATMENT

- Symptomatic persons with H5N1 influenza exposure: Persons with potential exposure to H5N1 influenza who develop compatible signs and symptoms should receive empiric influenza antiviral treatment with oseltamivir as soon as possible. Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of illness onset.
- Hospitalized patients who have confirmed, probable, presumptive, or suspected infection with H5N1 influenza infection, should receive antiviral treatment with oral or enterically administered oseltamivir as soon as possible regardless of time since illness onset. Antiviral treatment should not be delayed while waiting for laboratory testing results. Pending further data, longer courses of treatment (e.g., 10 days) should be considered for severely ill hospitalized patients with novel, including H5N1) influenza A virus infections.
- Additional recommendations from the <u>CDC-issued Emergency Use Instructions</u> (EUI) that differ from those for seasonal influenza oseltamivir treatment include initiation of treatment beyond 48 hours following symptom onset, and treatment and dosing regimens for term neonates under 2 weeks of age and preterm neonates and infants.
- For detailed guidance on dosing and treatment duration, please see Interim Guidance on the Use of Antiviral Medications for the Treatment of Human Infection with Novel Influenza A Viruses Associated with Severe Human Disease and the EUI for oseltamivir.

RECOMMENDATIONS FOR INFLUENZA ANTIVIRAL CHEMOPROPHYLAXIS

• Antiviral chemoprophylaxis is not routinely recommended for workers who used proper PPE and experienced no breaches in recommended PPE while handling sick or potentially infected animals as well as the raw products or contaminated environments (e.g., decontaminating infected



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environments, disposing of infected animal carcasses) but can be considered for persons meeting the exposure criteria on page 2, particularly those with unprotected discrete high-risk exposures such as a splash of raw milk from an infected cow into the eyes.

- Antiviral chemoprophylaxis is routinely recommended for household contacts of presumptive, probable and confirmed human cases.
- Antiviral chemoprophylaxis should be based on clinical and public health considerations, including type of exposure, duration of exposure, time since exposure, infection status of the animals the person was exposed to, and whether the exposed person is at increased risk for complications with seasonal influenza.
- If antiviral chemoprophylaxis is initiated, treatment dosing for the neuraminidase inhibitor oseltamivir (one dose twice daily) is recommended instead of the typical antiviral chemoprophylaxis regimen. For specific treatment dosage recommendations by age group, please see Influenza Antiviral Medications: Summary for Clinicians. Physicians should consult the manufacturer's package insert for dosing, limitations of populations studied, contraindications, and adverse effects.
- If exposure was time-limited and not ongoing, five days of medication (one dose twice daily) from the last known exposure is recommended.
- If the exposure is likely to be ongoing (e.g., household setting), a duration of 10 days is recommended because of the potential for prolonged infectiousness from the H5N1 influenza case-patient.
- Antiviral chemoprophylaxis of close contacts of a person with H5N1 influenza infection is
 also recommended with oseltamivir twice daily (treatment dosing) instead of the once daily preexposure prophylaxis dosing.
- Antiviral chemoprophylaxis is recommended for neonates and infants less than one year of age who are exposed to H5N1 influenza. See EUI for oseltamivir.
- For detailed guidance, please see <u>Interim Guidance on Follow-up of Close Contacts of Persons</u> Infected with Novel Influenza A Viruses, Use of Antiviral Medications for Chemoprophylaxis.

MONITORING EXPOSED PEOPLE IN NON-HEALTHCARE SETTINGS

Persons with exposure to infected humans or animals: All persons in close, unprotected contact with humans or animals infected with H5N1 influenza as well as the raw products or contaminated environments of infected animals, should be monitored for 10 days after last exposure. For dairy workers, monitoring can be discontinued as of the date when the quarantine of the affected farm is lifted.

Active monitoring is recommended when exposure occurs in a farm setting as appropriate PPE use is difficult to verify.

Fever and symptom monitoring: Exposed people should be monitored for the following symptoms: fever/feeling feverish; chills; cough; sore throat; runny/stuffy nose; eye tearing, eye redness, irritation or discharge; sneezing; difficulty breathing; shortness of breath; fatigue; muscle/body aches; headache; nausea; vomiting; diarrhea; seizure; rash.

- Active monitoring: Exposed people are assessed for the signs and symptoms described above
 at least once daily until 10 days after their last known exposure, or at a frequency or duration
 recommended by CDPH or the LHD. In a farm setting, monitoring should continue until the farm is
 released from quarantine. Monitoring can be performed in any of the following ways:
 - The LHD conducts daily health checks; or



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The farm conducts daily health checks, notifies the LHD immediately about symptomatic workers or workers who call in sick, and helps facilitate testing of ill workers.

- **USDA responders** should be actively monitored. It is acceptable to conduct monitoring on business days only for those who report wearing all appropriate PPE during their exposure.
- Passive monitoring: Each exposed person should be informed at the beginning of their
 monitoring period about the monitoring process, the symptoms and signs of concern, and when
 and how to contact the LHD symptoms develop, including after hours and on weekends. LHDs
 may recommend more frequent contact with exposed workers.
- Exposed people should be informed at the beginning of the monitoring period what to expect
 during the monitoring process, signs and symptoms of concern, and when and how to contact the
 LHD if symptoms develop, including after hours and on weekends.
- Close contacts of persons with presumptive, probable, or confirmed H5N1 influenza infection should be monitored daily through 10 days after their last known exposure to the case (prior to the case's release from isolation).

Employers with workers who have been exposed to animals with H5N1 influenza, their raw products, fecal material or environments must provide **medical services** for employees per the California Division of Occupational Safety and Health (Cal/OSHA) Aerosol Transmissible Diseases Standard. These services include medical surveillance (health checks) as recommended by CDC, CDPH, or the local health officer. These and other requirements can be found in the Cal/OSHA <u>Aerosol Transmissible Diseases-Zoonotic Standard</u>. For more detailed CDPH monitoring information, email AvianInfluenza@cdph.ca.gov.

CASE FINDING

Case finding activities should commence if preliminary PHL testing indicates a human infection with H5N1 influenza virus.

At a minimum:

- Identify close contacts (e.g., household contacts) of presumptive, probable, or confirmed cases. See "Clinical and Exposure Information" section above.
- Conduct daily active monitoring of close contacts of cases for symptoms associated with H5N1 influenza infection for 10 days from their last known exposure to a presumptive, probable, or confirmed case (until 10 days following release of case from isolation for household members).
- If a close contact develops symptoms or signs consistent with H5N1 influenza infection within 10 days of their last known exposure, promptly collect specimens for testing at a PHL.
- Please see testing section on pages 2-4 above for additional information.
- Consider alerting local healthcare providers to ask patients presenting with febrile respiratory illness and/or conjunctivitis about the possibility of recent exposure to infected animals or humans.
- Advise providers to collect specimens from patients meeting the above criteria for influenza testing at a PHL.

ADDITIONAL INFORMATION ON AVIAN INFLUENZA A(H5N1)

- VRDL Novel/Avian Influenza Virus (Human) PCR
- CDC general information on avian influenza
- CDC avian influenza information for health professionals and laboratorians
- HPAI in Livestock | Animal and Plant Health Inspection Service
- WHO Influenza (Avian and other zoonotic)
- OIE avian influenza



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- CDPH Bird Flu Website
- CDPH Raw Milk and Raw Dairy Products
- CDPH Avian Influenza A(H5N1) Information for Health Professionals
- CDPH CAHAN Health Alert: First cases of human Avian Influenza A (H5N1) in California & Preparation for CDPH Respiratory Virus Season (COVID-19, Influenza and RSV)
- CDPH Avian Influenza A(H5N1) Information for Local Health Departments