APHL All Member Call:
Highly Pathogenic Avian Influenza A(H5N1)
April 10, 2024

Call Summary

Contact for Questions or Suggestions
APHL Influenza Contact: fluquestions@aphl.org

Slides presented during this call are available here.

Welcome (*Scott Becker, APHL*)
Last week, the Texas Department of State Health Services and CDC reported the first human case of Noval Avian influenza in a farm worker in Texas This is related to ongoing cases of highly pathogenic avian influenza (HPAI) detected in dairy cows. As of April 9th, there have been confirmed cases found in livestock in 6 states.

The Texas Experience (*Cynthia Reinoso Webb, Ph.D., Texas Tech University Bioterrorism Response Laboratory*)
Veterinarians had a large role in the state and regional zoonosis control in detecting this human case. Veterinarians were the first to reach out to zoonosis, and through them to public health, which initiated a response by the regional public health department.

On the day of testing, the clinical specimen was collected about 2 PM. The laboratory received the sample at 5 PM and had the presumptive positive result at about 9 PM. The samples were shipped the following day for a Saturday arrival at CDC and were confirmed the same evening.

During this entire process, there was constant communication with the regional health department, the state associate commissioner for public health, and the CDC Influenza Division. The laboratory contacted CDC the day before testing clinical samples.

As an LRN lab, they have communicated with sentinel labs, covering 67 counties in West Texas. They have provided guidance documents on submission of samples and reporting, emphasizing the submission of paired conjunctival swabs and nasopharyngeal (NP) swab. They have also issued guidance and biosafety considerations with routine testing for respiratory and conjunctival samples as they come in for routine testing of all kinds.

The laboratory plans to perform a validation using the paired NP and conjunctival samples and is preparing for high throughput testing if needed.

Public health faces unique complexities when serving the dairy worker. This population is made up of mostly migrants, some possibly undocumented individuals who may not have, who may not trust the government or government entities and may not have insurance transportation or stable place to live. Public health should reach out to target populations where they are in order to best serve them.

Situational Update and Overview of CDC Response (*Sonja Olsen, Ph.D., CDC)*
USDA has now confirmed HPAI in dairy herds in 20 farms across 6 states and one human case. Those farms are in Texas (9), Kansas (3), New Mexico (4), Michigan (2), Ohio (1), and Idaho (1).

CDC has recently posted updated Interim Recommendations for Prevention, Monitoring, and Public Health Investigations. Last Friday, CDC also published to the health alert network (HAN) to inform clinicians, state health departments, and the public about updated information on the human case and also to emphasize the key information in the current guidance. All of the CDC material is available in both Spanish and English, and CDC is working closely with public health partners to determine if other language or other access barriers exist.

CDC is working with state health partners to expand human monitoring. The recommendations include monitoring people who are exposed to infected animals, such as livestock, in addition to wild birds and poultry. If an exposed individual is ill, they should be tested and receive treatment; this includes both symptoms of respiratory illness and conjunctivitis. CDC continues to be ready to provide confirmatory testing of any human specimens that are submitted by PHLs.

CDC has deposited influenza viral genetic sequences from the human case in public repositories both in (GISAID and GenBank) and shared Summary Analysis of Genetic Sequences of Highly Pathogenic Avian Influenza A(H5N1) Viruses in Texas.

Review of Human Testing Recommendations (*John Barnes, Ph.D., CDC)*
The recommended testing algorithm begins with either the Influenza A/B typing kit or the Flu SC2 Multiplex. Positive specimens then move on to the appropriate subtyping or lineage typing kit. However, if you are in an area screening people that have come into contact with a positive poultry or cow you can shift to use the H5 subtyping kit first. If those results are negative for the H5 markers, then you could proceed with the typical algorithm for influenza.

Specimen collection recommendations are dependent upon symptoms, but ideally two specimens are requested:

- Individuals with **respiratory symptoms**:
    1. NP swab
    2. Combined nasal swab (NS) oropharyngeal swab (OS) (e.g. two swabs combined into one viral transport media vial)
- Individuals with **conjunctivitis** (with or without respiratory symptoms):
    1. Conjunctival swab
    2. NP swab

CDC does not yet have conjunctival swabs as an approved specimen type on their diagnostic assay, but is discussing with FDA how to add that specimen type. In the meantime CDC is working with their CLIA director and will be standing up a laboratory developed test (LDT) with conjunctival swabs in order to support CLIA results.

Reagent Availability Update (*John Barnes, Ph.D., CDC)*
CDC has cleared diagnostic influenza in-vitro diagnostic (IVD) kits available for PHLs through the International Reagent Resource (IRR) at no cost. There are certain limits to kits, but if your PHLs needs additional kits, describe the situation in your IRR submission form comments.

- Influenza A/B typing kit: 1st line influenza virus diagnosis
- Flu SC2 Multiplex: 1st line influenza virus or SARS-CoV-2 diagnosis
- Influenza A-Subtyping kit: Determines if typical human epidemic/endemic (“seasonal”) influenza virus

- Influenza B-lineage typing kit: Determines if typical human epidemic/endemic ("seasonal") influenza virus
- Influenza A/H5 Subtyping kit: Determines if it is H5 avian influenza virus
    - Should not be performed unless the patient meets clinical and epidemiological criteria for testing suspect specimens (see Case Definition for Investigation of Human Infection with Avian Influenza A Viruses in the United States)
    - Test results with both H5a and H5b markers positive are considered presumptive positive and the sample should be sent to CDC as a diagnostic specimen for confirmation (i.e. Category B shipping).
    - Test results with either H5a or H5b markers positive should also be sent to CDC for additional testing.

Currently IRR has 750 of the Influenza A/H5 Subtyping kits ready for distribution. CDC recently inspected the inventory and made a double lot of the H5 kit to ensure they have plenty of kits available. This is enough for up to 750,000 tests.

Select Agent Questions and Concerns (*John Barnes, Ph.D., CDC)*
When PHLs are testing for H5 and have a positive result, remember that it is considered a presumptive positive and not considered a select agent. These can be shipped as Category B. Presumptive positives **must be confirmed at CDC** and then the agency will begin the appropriate select agent paperwork and related considerations. PHLs are to notify CDC immediately (flusupport@cdc.gov) of any H5 presumptive positive or any influenza A positive with inconclusive results using the influenza A subtyping kits.

Brief Reminders Regarding Reporting/PHLIP (*Alicia Budd, CDC)*
After first reaching out to CDC Influenza Division laboratory via flusupport@cdc.gov and notifying your epidemiologists, test results should be reported as a part of PHLs' regular PHLIP transmissions to CDC. Most PHLs already have their H5 testing mapped to their PHLIP message, but a few do not. Please reach out if you do not have this set up or are unsure, either to APHL (laura.carlton@aphl.org) or to CDC and we can determine the best route for your laboratory.

Questions and Answers (Q&A)

Q: If we get at suspect case would there be a need to run the H7 subtyping kit as well?
A: Not at this time.

Q: Is there an anticipated timeline for the LDT development?
A: CDC expected to have the LDT validation complete in the next several days and anticipates a little additional time will be needed to finalize the paperwork with FDA. CDC will share updates with APHL as this progresses.

Q: What kind of shipping (i.e. standard, rapid) should be used for sending specimens to CDC?
A: Overnight Category B shipping should be sufficient, with as early in the day delivery as possible.

Q: Does CDC know the sensitivity of some of the non-CDC diagnostic tests?
A: No, with the information CDC currently has, the CDC assay appears to be the only assay that is currently in production and is able to give an H5 diagnosis. FDA anticipates other influenza assays to detect the virus and give a diagnosis of influenza A positive.

Q: How should PHLs report results to epi for the conjunctival swabs?
A. For the time being, the results are not reported to the patient but can be given to epi in a public health emergency. CDC is hopeful to have it validated as a specimen type soon.

Q: Should suspect H5 specimens be processed in BSL-3 facilities until extracted or inactivated?
A: Technically diagnostics can be run at BSL-2, but with potential select agent considerations PHLs may choose to use BSL-3 until inactivated. This is at the discretion of your PHL.

Q: What role is CDC playing to support local hospitals or is this the role designated to PHL/agencies?
A: CDC is deferring to state public health laboratories and regional public health laboratories in the area. The IVD kits available in IRR are here to support the state/local effort.

Q: Does CDC have inactivation data for the various extraction buffers?
A: Yes, CDC reviewed quantity and concentration in the past and will share that data through APHL.

Q: What is the test result interpretation if one swab is presumptive positive and the other swab is not detected?
A: The swabs are interpreted separately. If either one is positive, it is a presumptive positive, but the conjunctival swab result could not be reported out as of yet.

Q: Is raw milk a matrix that CDC or USDA is planning to use for monitoring of dairy herds?
A: FDA is responsible for milk testing.

Q: Are other high throughput platforms (such as King Fisher Flex) being considered for the H5 assay?
A: CDC is currently working with FDA on the mechanism to add additional platforms. King Fisher Flex would not be one considered, however, because it is not IVD labeled.

Q: Is the use of CDC test kits reagents being made available to local public health labs that are not part of the of the regional laboratory network?
A: The H5 assay is available to all laboratories approved to run the CDC influenza diagnostic panels and actively ordering from IRR.

Q: Are any sanitizing agents that are food safe considered effective against the spread of HPAI?
A: FDA is doing to testing to ensure the food supply is safe, including testing to show pasteurization of milk products kills the virus. APHL is in touch with FDA and hopes to have a representative present on a future call.

Q: Has HPAI been detected only in dairy cows or also in beef cattle?
A: Only in dairy cattle.