Good afternoon. I'm Nikki Grimsley, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Office of Emergency Risk Communication at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call: Update on Highly Pathogenic Avian Influenza A(H5N1) Virus for Clinicians and Healthcare Centers. All participants joining us today are in listen-only mode. Free continuing education is offered for this webinar and instructions on how to earn continuing education will be provided at the end of the call.

In compliance with continuing education requirements, all planners, presenters, and moderators must disclose all financial relationships in any amount with ineligible companies over the previous 24 months as well as any use of unlabeled product or products under investigational use. CDC, our planners, and presenters and moderators wish to disclose they have no financial relationships with ineligible companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients. Content will not include any discussion of the unlabeled use of a product or product under investigational use with the exception of Dr. Tim Uyeki who will discuss using oseltamivir at higher dosing for post-exposure prophylaxis than for controlling seasonal influenza. CDC did not accept financial or in-kind support from ineligible companies for this continuing education.

At the conclusion of today's session, participants will be able to accomplish the following. Discuss the epidemiology and clinical features of human cases of Highly Pathogenic Avian Influenza A(H5N1) virus infection. Describe risk of human infection with Highly Pathogenic Avian Influenza A(H5N1) viruses, identify higher risk populations, and what to assess in clinical settings. And describe testing, using antivirals, and infection prevention and control recommendations for patients with Highly Pathogenic Avian Influenza A(H5N1) virus infection.

After the presentations, there will be a Q&A session. You may submit questions at any time during today's presentation. To ask a question, click the Q&A button at the bottom of your screen. Then type your question in the Q&A box. Please note that we receive many more questions than we can answer during our webinars.

If you are a patient, please refer your question to your healthcare provider. If you are a member of the media, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov.

I would now like to welcome our presenters for today's COCA Call. We are pleased to have with us today Dr. Tim Uyeki, who is the chief medical officer in the Influenza Division in the National Center for Immunization and Respiratory Diseases at CDC; Dr. Ryan Fagan, who is a medical officer in the Prevention and Response Branch in the Division of Healthcare Quality Promotion in the National Center for Emerging and Zoonotic Infectious Diseases at CDC; and Alicia Budd, who is the team lead of the National Surveillance and Outbreak Response Team in the Epidemiology and Prevention Branch in the Influenza Division in the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention.

I'll now turn it over to Dr. Uyeki. Dr. Uyeki, please proceed.

Thanks very much. I'm going to talk about Highly Pathogenic Avian Influenza A(H5N1) virus. Next slide, please.

So to start with an overview, and I'll try to refer mostly to this virus as H5N1, but it is a Highly Pathogenic Avian Influenza A(H5N1) virus. This virus was actually first detected during a poultry outbreak in Scotland in 1959, but was not really recognized until the 1990s. And I'll talk about that in a little bit.

So these viruses infect the respiratory tract and the gastrointestinal tract of birds. And therefore, they can be found in the respiratory secretions. But more importantly, they're excreted in the feces of birds. And therefore, they can be in the environment, they can be present on the feathers of birds, and so forth.

Typically, when poultry and many wild birds are infected by H5N1 viruses, they experience rapid and very high mortality. And what's notable about these viruses as all influenza A viruses is that they continue to evolve. And they can evolve in two main ways. One is through exchange of gene segments in a process we refer to as genetic reassortment. They can also experience minor mutations in the genes of these viruses that can result in minor changes to the virus structure. And we refer to that as antigenic drift if it results in changes to the hemagglutinin protein, which is where the virus binds to receptors. But the bottom line is that these viruses are evolving. They're dynamic.

Now, we classify these viruses into groups that are called clades. And of note, there's a particular clade that we refer to as 2.3. 4. 4b. And these viruses emerged in 2020 in wild birds. And they have spread all around the world to many different regions and new countries. It's been unprecedented spread and it's predominantly spread through migratory waterfowl. And then local wild birds can be infected. There can be actual poultry outbreaks that are identified and spill over into many different terrestrial as well as marine mammals. This is also -- includes domesticated animals and livestock. In particular, over the last two years or so, there's been a huge range of different animal species that have been infected with many animals dying, including wildlife.

And this particular Clade 2. 3. 4. 4b of H5N1 viruses were first detected in wild birds in North America at the end of 2021. And what we saw in the United States is wild bird detections in early 2022 and poultry outbreaks that were first identified in February of 2022 and are ongoing.

And over the last few years, there have been nearly 100 million birds affected. That's commercial poultry and backyard bird flocks that have been affected in 48 states. There have been more than 9,500 wild birds detected in 50 states or territories. And in this year, we have seen the identification in livestock, including baby goats, but more prominently among dairy cattle. And I'll talk about that later. Next slide, please.

So in terms of human infections with H5N1 viruses, I mentioned that these viruses in birds infect the respiratory, but more importantly the gastrointestinal tract. In humans, these viruses bind preferentially to receptors that are most prevalent in the lower respiratory tract of people. These particular receptors are also found on human conjunctival issues. So in the human upper respiratory tract, there are not that many virus receptors for these particular viruses.

And so one of the concerns for risk of greater transmissibility to and among people would be if these viruses acquired the ability to bind very well to receptors that are present predominantly in the human upper respiratory tract. Now, the first time we heard about human infections with this virus was in 1997 in Hong Kong. And during that outbreak, there were 18 cases and six deaths. This was pretty alarming because this is the first time that an avian influenza A virus was found to go directly from poultry to infect people and actually result in death. And the main risk factor during that outbreak was visiting a live poultry market.

And as a result of that outbreak, Hong Kong enacted many different control measures. And one is that they depopulated all the poultry in the live poultry markets. And in some of the poultry farms, they stopped poultry importations. And they were able to clean up and control that outbreak. And we didn't really hear too much about human cases of H5N1 until 2003.

And then to date, since 1997, there have been more than 900 human cases reported. So the total right now is about 919 human cases reported from 24 countries and about a 51% case fatality proportion. Now, note that this total includes some cases that were just confirmed as Influenza A(H5) positive, but the neuraminidase, the N1 part, was not identified. And they are presumed H5N1 cases. Next slide.

So this is an epidemic curve of human H5N1 cases, which does include some just cases that were just A(H5) positive. Since 1997 reported by 24 countries. And what you see is in the middle of the epi curve. You see many different countries in different colors and you can see the periodicity of these epidemics in people. And since 2015 with that large epidemic of H5N1 cases in Egypt, you see a big drop off in cases.

And we've only had a relatively very small number of human cases, particularly since then. And you can see a slight uptick in cases really since 2022 and 2023, including this year. There have been over the last two years 36 cases to date reported by nine countries. The US has reported nine. Cambodia, 13.

Now, some of these cases were in fact a detection of virus in respiratory specimens of an asymptomatic poultry worker. And whether that actually includes actual true infection is a little bit unclear, but they met criteria for reporting to the World Health Organization under the International Health Regulations. So they were reported. Next slide, please.

So how do people acquire infection with these viruses? The predominant way is through unprotected exposures. And by unprotected, I mean without wearing recommended respiratory or eye protection. And it's unprotected exposures to poultry. By far and away since 1997, the vast majority of human H5N1 cases have had poultry exposures. And this includes direct or very close contact with sick or dead poultry, but it also could include visiting a live poultry market where you're not necessarily having direct contact or very, very close contact, but you're in a live poultry market where virus might be aerosolized and one might inhale virus.

There have been a small number of cases that had exposure to other infected animals. And this includes some clusters in people that had exposure to dead wild swans in Azerbaijan in 2006. And then in 2024 in the U. S. a small number of cases with exposure to infected dairy cows, sick

dairy cows. Now, there have also been a small number of cases that were thought to have occurred through limited, non-sustained human-to-human transmission from prolonged exposure to a symptomatic H5N1 patient. And so that has primarily occurred in households where you have one family member taking care of the symptomatic other family member. That has also occurred in healthcare facilities with a family member taking care of another sick family member.

And this just highlights the importance of protecting and isolating cases and protecting not only healthcare personnel, but also family members with recommended personal protective equipment. And so the diagrams on the right, the upper, and the lower, you can see that some of the modes of potential exposure and infection of people either through close or direct poultry exposure. And then more recently because of the dairy cattle outbreak in the U.S. that there have been workers exposed to dairy cattle. And that's how they acquired their infection. Next slide.

Just to say that there's not been a case of limited, non-sustained human-to-human transmission since 2007. We're always looking for it. We're very, very concerned about that. We want to prevent that, but it's not been reported since 2007. And none of these cases of human-to-human transmission, very limited non-sustained occurred in the U.S. These were all in other countries during 2004, 2005, 2006, 2007 during that time period. Next slide, please.

So U.S. cases. There had been nine human cases identified since 2022. Five of them were associated with poultry exposures and four were associated with dairy cattle exposures. So of the five associated with poultry exposures, two were confirmed with H5N1, three were just confirmed with H5, they're presumed H5N1 though, because they were exposed to H5N1 infected poultry.

First case was in April 2022. This was an individual who only reported fatigue. No other symptoms while depopulating poultry. We detected a very low level of viral RNA and an upper respiratory tract specimen. I don't personally believe that person was truly infected, but it met criteria for reporting to the World Health Organization. Now, this month there have been four cases identified in poultry workers who were symptomatic while they were performing poultry depopulation activities during a very large poultry outbreak in Colorado. All of these cases that I've mentioned were clinically mild. None of them have been hospitalized. There's been no evidence to date of any human-to-human transmission.

Now, there have been four cases associated with dairy cattle exposures. Three were confirmed with H5N1, one was confirmed, which is H5, but it's presumed H5N1. Just not enough virus to sequence to identify the neuraminidase subtype. These have all been identified during late March through this month. And all four cases have been in dairy farm workers in three states. All of them were clinically mild and they were not hospitalized. There were no cases of human-to-human transmission identified and all have recovered. And I'll talk a little bit more about these cases later. Next slide.

So, let me talk about some of the signs and symptoms of H5N1 virus infection in people. What we know historically, so there is a wide range, a wide clinical spectrum of symptomatic illness, many cases typically present with fever or feverishness and non-productive cough, muscle aches,

malaise, headaches, sore throat, and myalgia. Some patients may experience abdominal pain, vomiting, and diarrhea have been reported. And then a small number of cases historically have reported eye discomfort/redness/eye discharge, consistent with conjunctivitis is uncommon.

At least historically that conjunctivitis only can occur, but this has been reported in the U.S. in 2024. And you can see a photo in the upper right of the first patient with H5N1 virus infection associated with dairy cattle, and a dairy farm worker in Texas with bilateral conjunctivitis, can see subconjunctival hemorrhages.

Now in patients who progress to more severe disease. And that is typically progression to lower respiratory tract disease. This occurs around days 5 through 7 after symptom onset. And patients manifest signs and symptoms of lower respiratory tract disease with difficulty breathing, shortness of breath, chest pain, tachypnea. At hospital admission, typically, there are findings of hypoxia, signs of pneumonia. Classic laboratory, clinical laboratory findings are leukopenia, lymphopenia, and mild-to-moderate thrombocytopenia.

But notably, not all patients with severe H5N1 have these classic laboratory findings. There is a wide range. From a radiographic perspective, there is a wide range of signs of pneumonia, typically patchy, interstitial, lobar, but also diffuse-infiltrates and opacities, consolidation. It's typically bilateral disease. And you can see some from progression of some of the chest x-rays of patients on the right from Indonesia. Next slide.

So clinical complications. Pneumonia is the most common complication with progression of respiratory failure in acute respiratory distress syndrome. Notably, community-acquired bacterial co-infection is rare. However, patients who have respiratory failure and are intubated are at risk for ventilator associated pneumonia.

Some other complications include acute kidney injury as well as sepsis, shock, disseminated intravascular coagulation, multi-organ failure with respiratory and renal failure, cardiac failure, and a small number of cases with atypical complications, including encephalitis or meningoencephalitis, typically with pneumonia, concurrent pneumonia. One patient with Reye syndrome who was treated with salicylates, and spontaneous miscarriage in a pregnant woman has been reported. Next slide.

So, potential exposures, who might be exposed, are generally people with close, prolonged, or unprotected exposures to infected animals, which include livestock now, or to environments contaminated by infected animals are at greater risk of infection. And this includes people with occupational exposures such as dairy farm workers, slaughterhouse workers, potentially, although I'm not clear that there's ever been a case reported in a slaughterhouse worker, but it is potentially a group that might be exposed.

And because the virus has been found in raw cow milk, potentially, milk processing facility employees could be exposed. Certainly, poultry workers. If poultry are sick and die from H5N1 are exposed, and veterinarians and veterinary assistants who might be working on either poultry farms or dairy farms with infected animals. And so the most important question for a clinician to inquire about a patient who presents with conjunctivitis or acute respiratory illness symptoms is

to ask about recent animal exposures in the last 10 days. And if they -- also what should be asked is, you know, what the nature of those exposures were, particularly were they unprotected exposure.

So not wearing recommended eye or respiratory protection. And then as well has anyone been exposed to a symptomatic person either with suspected or confirmed H5N1 virus infection? Because of the rare possibility, but it's always a possibility of limited, non-sustained human-to-human transmission. Next slide, please.

So, let me move to influenza testing of outpatients. So in an outpatient, if H5N1 virus infection is suspected, not only should recommended personal protective equipment be followed and Dr. Fagan will cover this. So I'm not going to address this now. So patients who have acute respiratory symptoms. There are two kinds of respiratory specimens that should be collected from the upper respiratory tract. One is a nasal pharyngeal swab and the second is a combined nasal swab and a throat swab specimen.

So separate specimens, but those nasal swab and throat swabs should be placed together in one tube of viral transport media. So you'll have a combined nasal and throat swab specimen and a nasal pharyngeal swab specimen placed in separate tubes of viral transport media. If the patient has conjunctivitis only, then a conjunctival swab should be collected as well as a nasal pharyngeal swab, placed in separate tubes of viral transport media. If the patient has both acute respiratory symptoms and conjunctivitis, then you want to collect the conjunctival swab. And then the recommended specimens for those with acute respiratory symptoms.

Now note that influenza A virus testing and influenza A(H5) virus testing must be done at a public health laboratory. So the clinician needs to notify local public health or your state public health department, and you need to make plans for getting those specimens to a public health laboratory that can run the CDC real-time assay for influenza A testing, influenza A subtyping, and influenza A(H5) testing. So this is because influenza tests that are available in clinical settings, and there's a wide range of tests, both antigen detection and molecular detection, they cannot specifically identify H5N1 virus. They will only yield an influenza A positive result. You cannot differentiate H5N1 virus from seasonal influenza A(H3N2) or influenza A(H1N1)pm09 viruses.

You also can't differentiate from a different novel influenza A virus, either of swine origin or of avian origin. And so if in a clinical setting you get an influenza A positive result, you need to get those specimens subtyped for influenza A viruses, H1N2, and particularly H5 at a public health laboratory. Next slide, please.

For hospitalized patients, if the patient has lower respiratory tract disease, including, you know, recommended -- you should implement recommended personal protective equipment again. So collect the recommended upper respiratory tract specimens that I just covered, but also collect sputum for, again, influenza A and H5 testing at public health laboratories.

In patients with respiratory failure who are intubated, also collect an endotracheal aspirate specimen. Or if a bronchi alveolar lavage fluid specimen is available for testing of a wide range

of respiratory pathogens, which then that specimen should also be tested for influenza A and H5N1 or H5. And the reason is that there are patients in whom have cleared H5N1 from the upper respiratory tract, but have severe pneumonia and have ongoing viral replication in the lower respiratory tract. The diagnosis was not made by testing upper respiratory tract specimen, but was made by testing either an endotracheal aspirate or a bronchi alveolar lavage fluid specimen. So the bottom line is, if you strongly suspect H5N1 in a hospitalized patient on the basis of clinical findings and relevant exposure history, you should collect multiple respiratory specimens from different sites, upper and lower respiratory tract, on multiple days to maximize the potential for detecting H5N1 virus. Next slide, please.

So let me move to antiviral treatment and prophylaxis. So if H5N1 virus is suspected because of clinical findings and a relevant exposure history, clinicians are recommended to begin to start empiric antiviral treatment with oseltamivir as soon as possible while awaiting testing results. And so that's twice daily for five days for outpatients. And we do recommend home isolation for those with mild illness.

The local and state health public health department should be notified immediately, because they're going to have to both test the patient and then monitor and follow up the patient as soon as possible. If H5N1 virus infection is confirmed in that individual and they're have clinically mild illness, they should be on home isolation. And the question is how long? Well, some considerations are until there's clinical improvement or resolution of symptoms, as well as ideally repeat respiratory specimens are able to be collected and test negative for influenza. Now, in addition, if H5N1 virus infection is confirmed, we do recommend that household and other close contacts are recommended to receive oseltamivir at treatment dosing as soon as possible. So twice daily for five days.

And this can be extended for longer duration for ongoing exposures. And it is important that household contacts as well as the case need to be monitored for 10 days after the last exposure. So you want them to monitor the H5N1 patient for any potential progression to more severe disease. And you want to monitor the exposed household or other close contacts for any signs of illness -- signs or symptoms of illness for 10 days because you want to test them and isolate them. Next slide, please.

So, for clinical management of hospitalized patients. So, patients need to be isolated. Dr. Fagan will cover this as well. And then I'll just say, follow recommended infection prevention control measures, including the recommended PPE.

So oseltamivir treatment is recommended, certainly five days, twice daily. But for patients who are severely ill, patients may be treated for longer duration. And basically, clinical management is really supportive care of any complications, including advanced organ support and very good clinical care. Now, just to say a few words about immunomodulators. Please avoid moderate-to-high dose corticosteroids.

And the reason is, this is associated with prolonged viral shedding in some observational studies, and it may increase the risk for ventilator-associated pneumonia and mortality. There are no data for the use of other immunomodulators for H5N1 patients that have been used, say, for severe

COVID-19, such as the IL-6 receptor blockers or Janus kinase inhibitors. So we can't recommend or we can't comment on the use of these immunomodulators for severe H5N1. Next slide, please.

So let me move on to the current situation in dairy cattle. Next slide.

So since late March of 2024, the U. S. Department of Agriculture has confirmed H5N1 virus infections of dairy cattle herds in more than 155 dairy farms in 13 states. This is the Clade 2.3. 4. 4b virus. I think most people are probably aware that very, very high levels of virus have been identified in raw milk of acutely infected cattle. There are other animal species that have also been reported by USDA in association with infected dairy herds at these farms in the U.S. And that includes different species of wild birds as well as cats, raccoons, and opossums. Next slide, please.

And this is an ongoing outbreak evolving. Let me just talk about the four human H5 cases identified to date.

So, three of them have been identified as H5N1 and one of the cases it was just H5 was confirmed with low amount of virus to identify the neuraminidase subtype. First case was identified in the end of March, early April in Texas, two cases were identified in Michigan in May, and most recently, one case in Colorado. All were adult dairy farm workers in contact with cows. All had clinically mild illness. They were generally not wearing recommended respiratory or eye protection.

Three of the cases experienced conjunctivitis. Only one case had acute respiratory symptoms. All were offered oseltamivir and recovered without hospitalization. There is no evidence of secondary transmission human-to-human spread. Next slide, please.

So, I mentioned that H5N1 virus, particularly at very high levels, has been detected in raw cow milk of infected cows. However, the FDA has reassured us that in their studies, pasteurization kills H5N1 viruses and that pasteurized milk is safe to drink. But because virus has been identified in raw milk and particularly high levels, people should not drink raw milk or consume products made from raw milk. And CDC strongly recommends against consuming raw milk, contaminated with live H5N1 virus as a way to develop antibodies against H5N1 virus to protect against future disease. There is theoretical potential if one is consuming a raw milk to acquire H5N1 virus infection of the respiratory tract. So we do not recommend this. Next slide, please.

So, just a self-knowledge check, what are possible signs and symptoms of Highly Pathogenic Avian Influenza A(H5N1) virus infection of humans? A, non-productive cough, B, conjunctivitis, C, fever, D, signs of pneumonia, E, A and B only, that's non-productive cough, conjunctivitis, or F, all of the above. Next slide. The answer is all of the above.

Rationale is based on past clinical and hospital admission findings. These are all signs and symptoms observed in patients with H5N1 virus infection. Next slide, please. Thanks. And I'd like to turn it over to my colleague, Dr. Ryan Fagan. Next, Ryan.

Yes. Thank you and hello. I work on Healthcare Infection Prevention and Control Activities at CDC's Division of Healthcare Quality Promotion. I have a few brief slides to highlight some key points that I want to communicate. Next slide.

So for H5N1 Avian Influenza, CDC continues to point to the interim guidance for infection control and healthcare settings when caring for confirmed cases, probable cases, and cases under investigation for infection with novel avian influenza A viruses associated with severe disease. That interim guidance is linked on this slide and includes additional precautions beyond standard precautions in the current recommendations for seasonal respiratory viruses.

I do want to acknowledge that, you know, while fortunately most of the recent reports in the U.S. have not described severe illness, conditions supporting the continued use of the interim guidance include that the high human morbidity mortality associated with H5N1 influenza infections historically, which Dr. Uyeki described.

Currently is thought that there's extremely low to no human population immunity to the currently circulating H5N1 clades in the United States. We still are learning about the risk of human-to-human transmission. And ongoing transmission in animals provides opportunities for viral mutations and adaptations. And at present, there is not a widely available vaccine for H5N1, though given ongoing vaccine development efforts, that is an evolving situation. Next slide.

So here are some parts of the interim guidance I've selected to highlight based on inquiries we typically receive in situations involving emerging infections. The full recommendation should be reviewed when preparing your facility or caring for a patient with H5N1 avian influenza infection. First, upon identification, a patient with confirmed or suspected H5N1 should be placed in an airborne infection isolation room or AIIR. If an AIIR is not available, isolate the patient in a private room with the door closed.

Importantly, personal protective equipment or PPE for healthcare personnel who enter the room or care area of patients covered by this guidance includes gloves, an isolation gown, eye protection, and respiratory protection that is at least as protective as an N95 filtering face piece respirator. Source control is another important part of this guidance. Use of a face mask is recommended to contain respiratory secretions of symptomatic patients. Once in an AIIR, the patient's face mask can be removed, but should remain in place when not in an AIIR, including during transport and movement. Also use of face masks for source control can be considered for persons exposed to H5N1, but not yet symptomatic.

As a reminder, standard precautions should always be implemented for patient care activities in the context of H5N1 avian influenza. The interim guidance reminds us to use respiratory hygiene and cough etiquette to reduce transmission of respiratory infections, including the provision of tissues, face masks, hand hygiene supplies, and instructional signage at points of entry throughout the facility. You can continue to follow standard procedures for cleaning and disinfection for management of laundry and for management of food and service utensils. And lastly, continue to follow local medical waste regulations in accordance to your state or local authorities.

Per United States requirements for managing solid waste, Highly Pathogenic Avian Influenza viruses are not considered a category A infectious substance, except when cultured. Next slide.

That concludes my prepared remarks, and I'll remain available for Q&A. We do have a brief knowledge check here. So which of these is recommended for patients with suspected or confirmed H5N1 infection? A, patient placement in an airborne infection isolation room, B, PPE for healthcare personnel. That includes glove, gown, eye protection, and respiratory protection. Source control and following local medical waste regulations, or E, all of the above. Next slide.

And that is all of the above. All of these are recommended parts of the interim guidance for H5N1 in healthcare. That concludes my remarks. Next slide.

Hi, everyone. This is Alicia Budd. And I am going to be the final speaker this afternoon. Just talking briefly about some of the surveillance and monitoring work that is underway as part of the HPAI (H5N1) response. Next slide, please.

So, just sort of the bigger picture first. In terms of CDC's priorities, we continue to support the U.S. government response, and our work in particular is focused on the priority.

Alicia, I believe we have lost your audio. Can you hear us? Alicia, can you hear us? Dr. Uyeki, I'll defer to you.

Yes.

Should we maybe answer a few questions or would another presenter like to present information? We can come back to her.

Yeah. So what we could do is we could take a few questions. Give Alicia a chance to reconnect.

Hey, Tim. I just got back on. Can you hear me?

Okay. Yes.

Thank you. Sorry about that. Not sure what was happening. My computer has been working great through all the other presentations and decided to not work now. So apologies for that. And I guess I was here on the priorities page.

Lastly, just being that we are, of course, monitoring the virus itself, looking for any genetic changes that could indicate that the virus may be adapting in a way that would allow it to spread more readily, either to people or among people. Next slide, please.

So in terms of monitoring exposed people, this is actually work that we've been doing in various forms from many years now. We've been working closely with USDA and have developed joint monitoring guidance for how to -- you know, what should occur amongst exposed individuals.

And the guidance recommends that people exposed to infected birds, poultry, or other animals should be monitored for the development of symptoms, beginning with their first exposure and continuing through 10 days after their last exposure. And since the beginning of the H5N1 circulating in poultry in the U. S. in 2022, more than 9,500 exposed people have been monitored and about 350 of those developed symptoms and were subsequently tested for influenza A and for novel flu. And then in the current cattle outbreak, there have been at least 1,390 people who either have been or are currently being monitored by the states and there has been testing of more than 60 of those individuals. Next slide, please.

So, with the ongoing outbreak of H5N1 in dairy cows, in poultry, and in other animals, and alongside, you know, what happens every summer and fall, which is agricultural fair season, it becomes increasingly important that we're conducting surveillance for influenza viruses, both seasonal viruses, but also monitoring for novel flu A infections so that we can inform the appropriate public health actions. So, CDC in collaboration with our state and local and territorial public health partners have developed a multifaceted enhanced summer surveillance priorities that are aimed at identifying the spread of H5 either to people or among people in sort of a tiered approach, looking first at those individuals who are exposed to infected or potentially infected animals, but also extending that outward to keep an eye on what might be happening in the general population.

So part of this strategy includes asking providers, all of you who see patients in a clinical setting, to make sure that you're continuing to test for influenza and individuals who present with compatible illness. Tim has gone through that earlier, but, you know, things like respiratory illness and/or conjunctivitis. And that you do this throughout the summer, particularly focused on people who have recent relevant exposures, but also even for those that don't, you know, continuing to think of influenza throughout the summer and, you know, perform testing is important. Doing this really helps us maintain the flow of influenza positive specimens that are coming into our public health labs and that are being subtyped by our public health labs. And it also gives us the information that we need to investigate any increases that we might see in some of our other surveillance systems, for instance, syndromic or wastewater surveillance. Next slide, please.

So speaking of surveillance at CDC, we maintain a comprehensive layered influenza surveillance system. It's been in place for many years. It's a collaborative effort between CDC and many of our state and local partners and data are collected from a variety of sources. And they capture flu activity really whenever and wherever it's happening. We get data from public health labs, from clinical labs, vital statistics offices, healthcare providers, hospital clinics, and emergency departments. The data are analyzed and reviewed at least weekly, if not more frequently.

And we're monitoring these systems actively to look for H5 viruses in particular and also just to look for any increases in flu activity at this time of year when that wouldn't necessarily be expected. So as part of that routine surveillance work, public health labs have tested more than 34,000 specimens since March using a protocol that would have detected H5N1 or any other novel influenza virus if it were to be in that specimen. And through that work, no additional cases have been detected. And in addition to that, we're just not seeing any unusual indicators of

flu activity in people. Right now we are seeing the typical summer low levels of influenza activity nationally. Next slide, please.

So one thing I wanted to mention quickly because it's a bit newer, especially in the influenza realm is wastewater surveillance. So in May, CDC started sharing Influenza A Wastewater Surveillance Data from sites across the country. And you can see those here on the slide. And the sites are categorized based on the current level of influenza A virus that's detected in the wastewater at a particular site, compared to the levels that that site has seen during the prior influenza season.

So the data here in wastewater can be used to complement some of the other existing surveillance systems that I mentioned on the last slide. It's important to note that these data currently are only showing us that it's influenza A activity. It is not showing us influenza A subtypes in particular. So we can't determine from these data that are reported, whether this is talking about H5N1 in particular or more common seasonal influenza activity, or whether the source of the virus, regardless of subtype, whether that source is from animals or from people. So what we're doing with this information is when we see a site that is categorized as reporting a high level of influenza A activity, we work with our state and local health departments with USDA and with other partners to understand what might be impacting or causing that increased signal.

We look to see whether there is seasonal flu happening in that local area. We look to see whether there might be H5N1 circulating in animals in that area, or some other potential animal source of H5 in the area, or if we would also, of course, be looking to see whether it might indicate H5 activity amongst people. And we, of course, have not found that situation as of yet. Next slide, please.

So as I mentioned before, we have surveillance, but we also have particular investigations that are ongoing. CDC is working with health and agricultural partners at all levels, local, state, and federal levels, to try to answer some important public health questions that we have about this virus and in particular about this virus as it's presenting in cattle and the risk that that might pose to humans.

So the questions you see there on the slide, you know, we're trying to better understand, is there evidence of an infection with H5 unexposed populations? What's the spectrum of illness being experienced? And is asymptomatic infection part of the mix? What type of exposures to H5 viruses are occurring on these farms and in these dairies? We know as you heard earlier, you know, unpasteurized milk, there have been reports of high levels of virus there. We know from prior poultry outbreaks that there's high level of virus detected in poultry and poultry facilities when those animals are infected. And so we're also exploring what other types of exposures might be putting individuals at risk. And if there are particular behaviors and particular work that's happening in these situations that could either be putting people at risk of infection or alternatively might actually be protecting them from infection.

And so we've got epi investigations focusing on these questions as well as trying to assess the risk for symptomatic and asymptomatic infection. And this is happening through specimen

collection and different surveys to assess exposures. We've been working with the Michigan Department of Health and Human Services, providing some technical assistance to them as they conduct a serology study of folks who have been exposed to cows on a farm. And then also we are currently supporting the ongoing investigations in Colorado related to the human cases that you heard about earlier, associated with infection or, excuse me, exposure at a poultry facility. Next slide, please.

So with all the information put together that we have so far, we continue to believe that the overall risk to the general public remains low. However, we do know that for individuals who are working with or have other recreational exposures to H5 infected animals, those individuals may be at increased risk of infection and that they need to follow the recommended precautions. As well as following precautions, as I mentioned before, monitoring for symptoms in those individuals is important from their first day of exposure through 10 days past their last exposure. And then for those individuals who show or who develop any respiratory symptoms or conjunctivitis, testing for influenza needs to be facilitated as well.

And this again is where we need your help to continue testing these individuals who may present to you with compatible illness who have these exposures. Having you ask them about exposures in case it's something that may not be top of mind. And then performing testing as indicated as well. Next slide, please.

So just lastly, I wanted to put here together just some of the many resources that are available to you on the CDC website, including, you know, latest guidance documents and updates that are posted frequently on our website as well. Next slide, please.

So I will end here with your last knowledge check if this is true or false. All of these are important public health questions to consider during epidemiologic investigations. A, is there evidence of infection with H5 virus and exposed populations? B, if human infections with H5 virus are identified, what is the spectrum of illness? C, what are possible exposures to H5 virus and workers at farms and dairies? And D, what are potential behaviors associated with human infections with H5 virus or protection from infection? Next slide, please.

And the answer is true. All of those questions are important to consider during epidemiologic investigations, because we really want to understand the full scope of infection and to be able to provide recommendations to protect public health.

And with that, I will turn it over to the call organizers who can present some questions.

Presenters, thank you for providing this timely information to our audience. We will now go into our Q&A session. Please remember that to ask a question, click the Q&A button at the bottom of your screen. And then type your question.

Our first question, can you define what prolonged exposure means for human infections?

Yeah, hi. This is Tim Uyeki from CDC. So, in terms of the cases of limited, non-sustained human-to-human transmission when I mentioned prolonged exposure to a symptomatic

confirmed case, that has typically been many, many hours of caring for the person without use of any protective equipment. So very, very close within one meter for extensive periods of time. It's not five minutes or 15 minutes.

It's not walking by a person, but it's not a very short exposure. It's a very long, prolonged exposure. So we don't have a definitive time period for that, but it's not casual contact. It's not very short period, but very long periods of time. I hope that gives some context.

Over.

Thank you. Our next question, are there any reports of drug resistance in any H5N1 isolate or clade?

That's a great question. So, I'll start with available information from human cases. And so for the nine cases in the U.S. identified since 2022, for those in which we could look at all the -- both genetic sequences as well as take the virus and analyze that in antiviral inhibition assays for those viruses that have infected humans.

So either from poultry or from cows, none of those have been resistant to any of the recommended antiviral drugs that we recommend for seasonal influenza. That means the neuraminidase inhibitors, oseltamivir, zanamivir, and peramivir, as well as the cap-dependent endonuclease inhibitor, baloxavir. Now we only recommend oseltamivir. And the reason is, both for treatment as well as post-exposure prophylaxis. And again, at treatment dosing for post-exposure prophylaxis.

The reason is, historically, there are at least some data, observational data, on treatment of patients with H5N1 virus infection with oseltamivir. And those studies have shown that the earlier you initiate treatment. So ideally within the first two days, you can detect -- sorry, there is survival benefit compared to either no treatment or later initiation of oseltamivir. We really have no data for peramivir, zanamivir, and no data for baloxavir. And we do not recommend the use of baloxavir monotherapy because there's no human data and we don't know how to dose baloxavir for H5N1.

So, you know, basically, the human viruses to date have been susceptible to oseltamivir. We do recommend it, and not the others. If the situation changes and any of these viruses evolve to clearly be shown to have resistance, not just slightly reduced susceptibility, but resistance, high, high levels of resistance. And then we clearly change our antiviral recommendations, but there's no reason to change them for now. And so in terms of viruses that have infected animals or wild birds, for the most part, almost all of them are susceptible to oseltamivir as well as the other antiviral drugs.

And so overall, given all the data that's available, we do recommend oseltamivir treatment preferentially, as well as for post-exposure prophylaxis. Over.

Thank you, Dr. Uyeki. Our next question asks, and this is a two-part question, what data are available about potential viral transmission from ingesting raw milk? Is the mechanism of

transmission still some type of milk exposure to mucus membranes or can the virus be infectious via the GI tract?

That's a great question. And so this is an area of a lot of uncertainty unknowns. Now what we do know is receptors for this virus are these alpha-2, 3 sialic acid linked receptors, which are predominantly, most prevalent in the human lower respiratory tract. There are some alpha-2, 3 sialic acid linked receptors in the human upper airway, but they're primarily in the human lower airway. And so if one was to have their mouth full of raw milk with live H5N1 virus, there have been no cases first of all to date reported that are linked to consumption of raw cow milk.

But theoretically, one, if the virus is in your mouth, there could potentially be upper respiratory tract infection. And if one aspirated, there could be clearly infection of the lower respiratory tract. Now, if one swallows the milk because one will be swallowing the milk if -- and again, we CDC does not recommend consuming raw milk for any reason. The question is, can you establish H5N1 virus infection of a gastrointestinal tract? In general, it's very, very unlikely that that could happen. This virus infection -- this virus infects the respiratory tract.

And so it's very hard to believe. Now, there has been -- there was an autopsy study published in 2007 that did report detection of some viral particles in intestinal tissue in one area of the intestine. That does not prove infection and it does not prove that infection -- that the virus can then go to the respiratory tract. So we don't know. In general, we think it's very unlikely.

In contrast, what I can say is that there have been severely ill H5N1 patients who have had diarrhea and virus has been detected and in fact isolated from a diarrheal specimen. So the other way, if you have virus infection of the respiratory tract and you can potentially have dissemination of that virus, you could have virus that's swallowed and still viable in the gastrointestinal tract, but in terms of consuming milk, raw milk with virus, we don't know exactly, but we don't think that gastrointestinal tract infection would get established and would be the way a person is infected, but it's an unknown theoretical area because humans don't have many of these virus receptors. For the virus in the gastrointestinal tract, there are some. So again, there are theoretical possibilities of how one could get infected, but we don't know, but it would be a very bad mistake to intentionally consume virus -- intentionally consume raw milk with infectious H5N1 virus. Thanks. Over.

Thank you, Dr. Uyeki. We have time for one more question. What is the recommendation for testing in a hospitalized patient with lower respiratory symptoms if the patient is not able to supply sputum?

Yeah. That's a very good question. I think that's clinical judgment. I think there could be considerations to inducing sputum, but you definitely want to test upper respiratory tract specimens, which would be a nasopharyngeal swab and then combine nasal and throat swabs. In contrast to SARS-CoV-2, saliva is not really a clinical specimen that we would recommend testing.

And so I think that there could be some consideration to maybe collecting induced sputum and testing that, but otherwise one would just have to test upper respiratory tract specimens. And

probably should be -- might want to consider repeated specimen collection and testing if H5N1 virus infection was strongly suspected on the basis of history of exposure to infected animals. Over.

Thank you very much, and thank you to all of our presenters for sharing your expertise with us today.

This year, CDC is moving from the Training and Continuing Education Online, TCEO system, that provides access to CDC educational activities for continuing education to CDC TRAIN. If you do not already have a TRAIN account, please create one at https//www.train.org/cdctrain.

All new activities that offer continuing education from CDC will only be listed in CDC TRAIN. CDC TRAIN is a gateway into the TRAIN Learning Network, the most comprehensive catalog of shared public health training opportunities. This transition will allow you to access non-credit and for-credit educational activities and track your learning, including CE in one place. Many CDC accredited activities are already listed in CDC TRAIN and the move to one system improves efficiency and makes it easier for learners, CDC staff, and partners to offer and earn CE in one place. You can continue to use TCEO for existing activities that have CE set to expire in 2024, since these courses will not move to CDC TRAIN.

You may also use TCEO for existing activities with CE set to expire in 2025 before the courses transition to CDC TRAIN sometime next year. If you begin one of these courses in TCEO, we will let you know when the course will move to CDC TRAIN. You can access and download CE transcripts and certificates in TCEO through the end of 2025. Instructions will be available on both platforms and a learner support team will also be available to answer your questions. All continuing education for COCA Calls are issued online through CDC TRAIN.

Those who participate in today's live COCA Call and wish to receive continuing education, please complete the online evaluation and post-test before August 19, 2024, with the course code WC4520R-071624. The registration code is COCA071624. Those who participate in the on-demand activity and wish to receive continuing education should complete the online evaluation and post-test between August 20, 2024 and August 20, 2026, and use course code WD4520R-071624.

Today's COCA Call will be available to view on-demand a few hours after the live COCA Call at emergency.cdc.gov/coca. A transcript and closed caption video will also be available on-demand on the COCA Call's webpage about a week after today's live session. You can visit emergency.cdc.gov/coca for more details about this COCA Call and other upcoming calls.

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Again, thank you for joining us for today's COCA Call, and have a great day.