Call Date
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Call Agenda
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Jasmine Chaitram, CDC Division of Laboratory Systems

Opening Remarks

Reynolds M. Salerno, CDC Acting Associate Director for Laboratory Science and Safety

Announcements

Jasmine Chaitram, CDC Division of Laboratory Systems

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John Barnes, CDC Influenza Division

Update on Testing for Measles

Stephen Crooke and Paul Rota, CDC Division of Viral Diseases

Call Transcript
Jasmine Chaitram: Hello, everyone. Thank you for joining the Laboratory Outreach Communication System Call. I want to start off by saying happy Medical Laboratory Professionals Week. We are glad you could be with us during this week of important laboratory recognition.

I'm Jasmine Chaitram. I am with the Division of Laboratory Systems at CDC. Sean Courtney is on a break and will be back with you next month. Before I go into any announcements or talk about today's agenda, which I'm going to show briefly, I'm going to introduce Dr. Reynolds Salerno. He is the Acting Director of the Office of Laboratory Science and Safety. I had to stutter a little bit there because he has many acting roles. And I wasn't really sure which one I should say. But either way, I'm going to turn it over to Ren for a message about Laboratory Week.

Reynolds Salerno: Thank you, Jasmine. Can you hear me OK?

Jasmine Chaitram: Yes, you're good.

Reynolds Salerno: OK, so I really appreciate the invitation to participate in today's call. I'm grateful that I have the privilege of joining all of you at the start of the 49th annual Medical Laboratory Professionals Week.

Everyone on this call understands the vital role that laboratory scientists and professionals play in protecting the nation's health. And know we all too well that these contributions often go unrecognized or underappreciated. CDC Director Dr. Mandy Cohen has repeatedly and publicly said that clinical, environmental, and public health laboratories are core public health infrastructure. Your work is extremely important and highly valued, both to CDC and to the American people.

Each year, CDC celebrates Lab Week to honor the nation's laboratory scientists and professionals, and to acknowledge your role in safeguarding the well-being of the American people. Our theme for Lab Week 2024, *The Future is Lab*, affirms the resilience, innovation, and agility of a workforce that continually adapts to meet new and evolving challenges.

To the laboratory scientists and professionals on the line as well as your colleagues who are not here, please know that you have my sincerest admiration. It would be difficult to overstate how important you are to patients, to healthcare providers, and to public health officials. We at CDC are committed to supporting you and your work in any way we can.

CDC will continue to provide resources, guidance, and collaboration opportunities to empower you and support you as you fulfill your day-to-day responsibilities and to help you prepare to respond to the next public health emergency. On behalf of CDC, thank you for the critical work you do every single day.
I encourage everyone to join CDC as we celebrate Lab Week 2024 and share your appreciation for laboratory scientists and professionals. We believe that CDC has created some fantastic material to help you in this process. These include downloadable Zooms and Team backgrounds, printable *The Future is Lab* stickers, our Lab Week graphic coloring page, and a CDC word search puzzle.

I'm sure that links are being provided right now as I speak in the chat to help you find all that information on our website. You can also use the digital toolkit to share social media messages and digital graphics with your networks. Again, thank you for the opportunity to speak with you today. And I will give the floor back to Jasmine.

Jasmine Chaitram: Thank you so much, Dr. Salerno, for your remarks and for joining us today. Really appreciate that. All right, I'm going to cover a couple of announcements really quickly before we go into our agenda items. The first is that the OneLab Summit begins this week. And you have an opportunity to register for a free three-day virtual event that connects laboratory professionals on topics of laboratory education and training needs.

Attendance is open to anyone that is interested or involved in the laboratory profession. This year's theme is *Thrive: People, Planning, Preparedness*. The event is designed for laboratory professionals to increase their knowledge of laboratory training development tools and practices, gain insight from the clinical and public health laboratory community's success and resilience, network and collaborate with peers, partners, and CDC experts in laboratory education and training, learn more about OneLab and its communities of practice, and earn P.A.C.E. credits. So you can register now through the QR code on the slide or on the link in the chat that Nette is going to put in there for us.

Another important topic that I wanted to give you an announcement about is that DLS is launching the ECHO Biosafety Program which was launched-- well, it was launched in 2023 to develop and engage a biosafety community of practice to address biosafety challenges and clinical and public health laboratories. The program fosters solutions for biosafety challenges.

The important part is that we are going to have our next session on April 30. And that's a Tuesday. And that session will focus on Planning: Developing and Achieving Biorisk Management Objectives. And you can access the Zoom link or detailed information about upcoming sessions and resources from past sessions through the ECHO Biosafety website link provided on the slide and in the chat.

OK, other things that we usually say is that we love your feedback on training and workforce development needs. So please contact us with any thoughts on feedback on that, labtrainingneeds@cdc.gov. Just a reminder that the LOCS Calls are archived on the DLS website.

So if you miss it or have to drop early, you can always go to the website to get the transcripts, the slides, the recording all from previous calls. And then we also have LOCS emails. If you're receiving those, those can also be found on this website.

So as we go through today's call, if you have a question, we do ask that you put that down in the question and answer section of the Zoom webinar system. And you can do that by clicking on the Q&A button at the bottom of your Zoom tool there. Sometimes, folks put the questions in the chat. But we'd rather you don't do that because we won't be able to track those questions later.

And sometimes, we're not able to answer all of the questions because we don't have the subject matter experts. Or we need to do some additional follow-up. So we really appreciate if you put those questions in the Q&A. And if you're not opposed to it, make sure you leave your email so we can follow up with you if we need to.

And what we always say on these calls is that the calls are really targeted for laboratory professionals. And if this is anyone from the media has decided to join, we'd rather that you actually contact CDC Media Relations for information. And if you happen to be a patient that has joined, please contact your healthcare provider.

All right, and then just a reminder, if you do go to that archive, because today's speakers are actually both from CDC, but if you go back to the LOCS archive to look at decks from previous presentations, just a reminder that they may not contain material from panelists who are affiliated from CDC. And so it's not necessarily CDC's official position on that topic.

All right, with that, I think the topic many of you have joined to hear about is going to be presented by Dr. John Barnes. And this is an update on the situation here with reporting and testing guidance for influenza A/H5. And John, I will turn it to you.

John Barnes: Thank you very much, Jasmine. Hello, everybody. Thank you for joining. And hopefully I can give you a little bit of a situation report as we know it right now, and then some guidance that we're really trying to get out to the community on how to test for this influenza A/H5 outbreak that we have right now in cattle. Next slide, please.

So the situation report is this. During the week of March 25, USDA confirmed detections of highly pathogenic avian influenza in dairy cows. And as of this morning, there were-- this has been confirmed in 26 farms in eight states. And you can see the breakdown here. We have Texas with the most, New Mexico, Kansas, Michigan, Ohio, Idaho, North Carolina, and South Carolina-- South Dakota, excuse me.

Genetic sequencing of the viruses that were found in these infected cattle indicated that these were H5 HA clade 2.3.4.4b. Now, this is a clade that we've been dealing with in the U.S. that has been having outbreaks in wild birds for the last couple of years. And when we looked at these sequences, there were no known markers of resistance to approved antiviral drugs that came up.

And we really think that an existing H5 candidate vaccine viruses are expected to provide good protection against the H5N1 viruses detected in cattle. So we also noticed that none of these sequence seem to impact our current CDC influenza diagnostic assays at the U.S. or global health public laboratories' ability to detect these H5N1 viruses. Next slide, please.

On April 1, the state of Texas announced that a person had tested positive for highly pathogenic avian influenza, H5N1 virus. This infection occurred in a person who had direct exposure to cattle, presumed to be infected with this highly pathogenic avian influenza. The main symptom that the patient reported was eye redness and conjunctivitis.

And this set, we took-- there were two samples collected, NP swab and a conjunctival swab. And they were both tested at Texas Tech University Bioterrorism Response Laboratory. And the real-time PCR results indicated that both specimens were presumptive positive for influenza H5 virus by the CDC diagnostic assay.

These specimens were then sent to CDC for further testing. They were received and tested in our laboratories here and confirmed as highly pathogenic avian influenza by our labs. We have conducted genetic sequencing on the virus from the patient in Texas. From the clinical specimens, we were only able to actually-- to get the sequence from the conjunctival swab.

There was quite a bit of virus in that specimen. And there were no known markers for antiviral resistance. The virus was very closely related to the cattle sequences that we've been seeing and the vaccine candidate-- vaccine virus sequences we have as well for this H5N1 clade. They were also identified as clade 2.3.4.4b as well, with very minor changes from the viral sequences in cattle.

Of note, the sequence was only successfully generated from the patient's conjunctival specimen. This was consistent with the patient reporting only conjunctivitis with no respiratory or other symptoms. And it was suggestive of a lack of respiratory infection in the patient. Next slide.

So CDC has been doing a lot in response to this case. We've been supporting confirmatory testing for presumptive positives and conducting in-depth sequencing analysis. We can do that and help our

laboratories should they run across this issue. We're also undertaking an effort to clear conjunctival swabs, but reaching out both to FDA and setting up an LDT for CLIA.

We've instituted and issued a number of guidance documents that have been-- a lot of which have been posted into the chat, for prevention monitoring and public health investigations on our website to include exposures to mammals infected with H5N1. We have recommendations for those who come in contact with poultry and livestock, including farmers and farm workers, including PPE guidance for those people, guidance for clinicians on monitoring, testing, and antiviral treatment of patients with exposure to avian influenza virus infections.

And then on Friday, April 5, CDC published a HAN to inform clinicians, state health departments, and the public of the updated information on the human case and emphasize information in CDC's updated interim guidance. All of CDC's current avian influenza A H5N1 virus materials are made available in Spanish and English. And we're working closely with public health partners to determine and address if other language access barriers exist. Next slide.

So the risk to the public, CDC continues to assess the risk as low for the general public. However, for those with close or prolonged unprotected exposures to infected birds or animals or to environments contaminated by infected birds or other animals with HPAI, those are of greater risk. And we do have guidance about PPE in those situations. Next slide.

One of the things that we would like to emphasize, again, is CDC does have a number of CDC-- of influenza IVD kits that we support. These are influenza kits that are 510K approved, as I mentioned, IVD kits from-- these are for first-line typing kits for influenza virus or SARS-2 diagnosis, our AB typing kit or the Flu-SC2 multiplex kit.

We also have subtyping kits for B lineage typing and subtyping kits for A that detect if it's the human epidemic or seasonal strains of the influenza virus. And then the one that I'll talk most about today, which is the IVD, A/H5 subtyping kit, which determines that if it is this H5, highly pathogenic avian influenza virus. Next slide.

This is a complex algorithm. And I won't go through all of it here. But essentially, through this test, you can test for influenza-suspected patients and type and subtype those patients. And if neither one of those subtypes of human were to work, then you can go into based on exposure, testing in for some of the avian subtypes. And we have H5 testing subtypes that can be done.

In those cases, we ask that CDC be contacted immediately when we have suspected cases. So that we can really talk through the process. And we do have guidance on that. So please reach out. Next slide. There's another option for those people, if you are monitoring people that have been on a farm with confirmed H5 and you're monitoring those people, this influenza A subtyping H5 PCR can be run as its own. It has both our pan influenza A marker, which determines if it is influenza A positive, as well as our both H5 markers and H5 A and H5 B marker that we require for full positivity of that kit.

That can be run as a standalone test in these cases where you're really just asking the question have these people been exposed and are currently positive with this particular virus. So this is an option. And then you can reflex back into the rest of the assay as you would see on the slide. Next slide.

One of the things that we've been looking at and going through right now is with H5 is the specimen collection. And really, we're encouraging people to take two swabs for both types of symptoms that they may encounter. For respiratory-based symptoms, we would like if you could take an NP swab and a combined NS/OP swab if you can.

That's essentially taking two swab sticks, one for the throat swab and one for the nasal swab, and putting them in the same VTM material for that combined then, and then a classic NP swab for that.
For conjunctivitis, we're currently working with-- as I said, working with FDA and our own CLIA director here at CDC to get these approved. And we hope to do that very shortly. But one of the things that we are trying to do right now is collect both of these swabs. So that we can see-- have a paired swab with a respiratory standard when we take this conjunctival swab.

So for this particular test, we would like it if you could take a conjunctival swab, as well as an NP swab at the same time. Ship those as to particular tubes in that shipment for that patient. So that we can have that pairing as we go forward. Next slide.

So H5 specimens with a presumptive positive or inconclusive results, the specimen per our test is only presumptively positive if influenza A(H5) if both tests, InfA and both H5 tests are positive, H5 targets are positive. A result is inconclusive if the test is positive for A(H5) targets and negative for the InfA.
But we still would like to see either one of those sent to the CDC immediately for further evaluation.
Reminder, any H5 positive correspondence to us should be labeled as presumptive positive. It is in the IFU that this is a presumptive positive until it can be confirmed at CDC. This is also because we want to make sure that all of our partners are in compliance with current understanding of the select agent guidelines associated with this virus.

Highly pathogenic avian influenza is a select agent. And we want to make sure that labs are operating as this is only a presumptive diagnosis, and not necessarily a full diagnosis of this virus. Next slide.

Specimen notification and shipping to us, please notify us immediately through flusupport@cdc.gov. And please send the following clinical specimens to us immediately. If we have what we call unsubtypeable, if in our assay, if it means that you have influenza A Ct that is less than 35, and we do not get a human pandemic H1 hit or H3 hit to us, or any of these presumptive positive viruses, H5, to us immediately as you can. And I'm the contact that you need.

And there's my information right here that you can give me. This flusupport@cdc.gov mailbox comes to a lot of different people here at CDC. It is a good way of getting in touch with my team, multiple people on my team monitor this mailbox. And we'll get back to you as soon as possible. Next slide.

For diagnostic specimen submission, we have new guidance. So there is-- please make sure that you submit the 50.34 or CSTOR which is required for all diagnostic submissions when report-- or when you want a report back to the patient or healthcare provider. And send those completed forms and tracking information electronically to flusupport@cdc.gov. We will work with our accessioning group here at CDC to get these prioritized.

And if you send that information to us, we can get your results back to you as quickly as possible. Ship these, again, to me at John Barnes at CDC. And there's my-- there's my information. Next slide, please. And that is it. So thank you very much, Jasmine.

Jasmine Chaitram: Yeah, thank you very much, John, for joining us and for giving us all that great information. There are a number of questions for you. I wanted to start off with a question about just some clarification about the kits that you mentioned. Which laboratories have access to those kits?

John Barnes: So the public health laboratories have access to those kits in their free kits through the IRR. We are granting right now license, royalty-free access to our H5 kit if any person would like that to utilize as part of their own network. And if you want that to explore that possibility, then please contact me. And we can get you in touch with tech transfer and start that process.

Jasmine Chaitram: Oh, that's great. So to follow up on that, what is the recommendation for clinical laboratories that test for influenza A but are not able to do any further subtyping?

John Barnes: For those cases, if one of the things that you ought to do is reach out to the local public health laboratories, all of these kits per this algorithm are in their inventory. And they can be used through the public health lab based system. So if you work with your public health lab in the state, then you can work out a deal where you can actually get those submitted in if that is the desire.

Jasmine Chaitram: Awesome, so regarding specimen collection where you showed collecting two swabs, when do you think the CDC website and guidance will be updated to reflect that recommendation to collect two swabs, as well as that conjunctival specimen?

John Barnes: So we have asked the CDC websites, they should actually have an update to some of that guidance right now. And then we are working with-- we have our data is through collection. And we actually have it into quality review right now before we submit both to FDA and our own CLIA director. So we're waiting for that to check before we actually go forward. So I'm hoping that will be very soon.

Jasmine Chaitram: OK, thank you. And I think the next question is about UTM. It seems like CDC is not able to collect two test specimens that are submitted in UTM? And that can be challenging. So are there any plans to do validation of UTM?

John Barnes: We haven't planned on that right as of yet. But if that continues to be a problem, we can certainly work with our CLIA director to see that was-- we can alleviate that issue. Or if it's a further issue, then maybe we can actually address it with FDA as well.

Jasmine Chaitram: OK, speaking of FDA, they have cleared influenza tests-- how do commercial FDA cleared influenza tests perform for detection of H5N1? I'm not sure that they have. Do they have cleared tests?

John Barnes: Yes, they do. There's multiple cleared commercial tests. They do not perform for the detection of H5N1. Currently, there is only one. And I'm not sure if that assay is actually being manufactured. It's an antigen test. But the other tests that do give an influenza A detection that are-- we have talked to our colleagues at FDA, and they've been doing in-silico analyses on those and have come to the conclusion that a lot of those seem to be-- there should be no problem with them actually giving an influenza A diagnosis for anybody infected with this virus.

Jasmine Chaitram: OK, and then what was the reasoning for testing that person, that individual with the conjunctivitis? Was there a reason? Or is it mostly because of the cattle exposure?

John Barnes: So conjunctivitis has been known to be a symptom of high path avian influenza in the past. And so that was one symptom that I think people were on the lookout for. It is a kind of an unusual symptom. But it isn't that uncommon. And so it was a bit uncommon the way that this presented itself, of course, because the cattle-to-human transmission has not really been documented before. And so it was kind of new to us in that way. But it was-- there was a close contact and then conjunctivitis between the two. That's why the testing was done.

Jasmine Chaitram: All right, I think I've got like two more for you. The specimen samples for avian influenza testing have been designated as BSL-2. Is this likely to remain as BSL-2?

John Barnes: So if this virus is BSL-2, this-- high path avian influenza is not a BSL-2 virus. Diagnosis of any of these viruses can be run in BSL-2. But the high path avian influenza is a select agent virus and is BSL-3 once confirmed. So I just wanted to make that information clear.

Jasmine Chaitram: That's great. The next question is about wastewater testing. I'm not sure you can answer that. Do you want me to ask you anyway?

John Barnes: So we've been looking into that. We have no idea how the high path avian influenza virus assay works in wastewater. A lot of the areas we have, this would be a challenge because they're on septic. And also conjunctivitis, we don't get a lot of shedding of influenza in wastewater anyway. And with conjunctivitis as the main symptom, that is going to be potentially even less virus in there.

My concern with doing this type of testing is that it is going to be really, really hard to identify what is coming from infected cattle and birds and what is coming from people. So I don't think that is-- we have a good answer for how to tease that apart right now.

Jasmine Chaitram: Great points and great presentation. Thank you so much for joining us today and answering all these questions. We really appreciate your time. I'm going to move us over to the next speaker. But thank you again, John.

All right, so our next topic for today is an update on testing for measles. And this will be from Stephen Crooke and Paul Rota from CDC. I'm going to turn it over I guess to Paul first. I see you on camera.

Paul Rota: All right, yeah, thanks, Jasmine. Yeah, I'm going to start off and then hand over to Steve-- Stephen for a little while. And then I'll finish up. We had given an update on measles testing in, I think, last September on this LOCS Call. But since we're seeing increased frequency of detection of measles in the U.S., we thought it would be a good idea to do an update, at least a brief update. So can I have the next slide, please?

I just want to draw everybody's attention to an MMWR that was published last Thursday, which covers the measles in the United States from January 1, 2020 to March 28, 2024. So it's a pretty up-to-date summary of measles activity in the U.S. And if you-- on the bottom part of the slide is the epi curve that was included in that MMWR.

And you can look-- if you look to the right, you can see that the frequency of importations into the U.S. has increased substantially in the beginning part in the first three months, at least, of 2024. And this is due to the global resurgence of measles. So measles cases are increasing in all of the WHO regions, and especially the European region. And therefore, we get an increased frequency of importations into the United States. Next slide, please.

So this is just the data summary for measles cases and outbreaks as of April 11. So the website that you see on the top line there at cdc.gov will be updated by noon every Friday. So if you want a current case count, you can check in. So you can see we have already exceeded the number of cases that we had in all of 2023. And we're only in March. We are up to 121 total cases.

Majority of these are younger individuals under 5. And most of our cases are in unvaccinated individuals with unknown vaccine history. As you can see on the right-hand side, 56% of the cases required hospitalization. And you can look at the age group of the hospitalized. Next slide, please.
So we're going to have a quick review of the diagnostics. I'm going to turn it over to my colleague, Stephen Crooke, for the next couple of slides.

Stephen Crooke: Thanks, Paul. So what you're seeing on this slide here is a visual representation of the detection of analytes or biomarkers for measles infection with a time course respective to disease onset.

So walking through this really quickly, the red trace shows the frequency at which virus can be detected by PCR with respect to disease and rash onset.

And so that's most sensitive in the first one to three days of rash onset. And after that, the orange trace shows the frequency at which serum can be detected by serology. And so there's a slight delay in IGM detection, around three to five days is peak detection of serum IgM for measles. But you'll note that curve trails off a bit with time. And so you can still reliably detect IgM in a fair number of specimens several weeks out from rash onset.

And then the blue trace just illustrates the kinetics of serum IgG rising after exposure to the virus, which is a few days behind IgM. It peaks around 9 to 10 days and persists for months to years after. Next slide, please.

So the preferred test for measles starts with molecular testing. And so RT-PCR is the test preferred to detect viral RNA. And you can use a number of specimen types for this, throat swabs, NP/OP swabs, and urine. This test is available through our labs at CDC laboratories, at the Vaccine Preventable Disease Reference Centers, which are supported through APHL, as well as many state public health labs.

And many of these labs, the VPD Reference Centers, for sure, and many state labs, use the CDC assay. So it's the same PCR assay being used for detection. More recently, commercial laboratories have entered the molecular testing space for measles. And I think Paul will touch on this a bit later. So it's available commercially as well.

There are some more advanced methods that are used for supporting case investigations for measles. With molecular testing, the MeVa assay, as we colloquially call it, stands for Measles Vaccine Detection. It's a specialized RT-PCR assay that specifically detects measles vaccine strains and can be used to confirm vaccine reactions.

This is particularly important when outbreaks are concurrently occurring with vaccination. So if you have a mass immunization going on with concurrent circulating measles, it can be hard to distinguish if someone was-- if someone was also exposed and they were recently vaccinated, this test can help differentiate an actual measles infection from recent vaccination. This is available at CDC, the VPD Reference Centers, and we're working with other state public health laboratories for onboarding of this test to make it more widely available.

Measles genotyping is more advanced in terms of helping to work through transmission pathways and monitor disease spread and epidemiology. It's basically Sanger sequencing of the N450 region is a standard WHO protocol. This is available also through CDC, the VPD Reference Centers, and some state public health labs.

And this data is reported through a WHO database which is-- which compiles sequences from laboratories around the world and can be used to help genotype these specimens. But when there's only

two known genotypes circulating over the last several years, and so that precludes sometimes the need to do more in-depth sequencing to look at transmission pathways. And so whole genome sequencing can be performed at many of these laboratories. And that provides increased resolution for tracking transmission pathways of measles. Next slide.

Serologic testing is also available for measles diagnosis. ELISA to detect measles specific IgM in serum specimens is the frontline for diagnostics in the serologic space. Many state public health labs and commercial laboratories are equipped for serology testing. And CDC offers serologic testing as well. Of note, we use what's known as a capture assay, which has high sensitivity and specificity relative to most commercially available IgM tests.

ELISAs to detect IgG in serum are also widely available at state public health labs and at CDC. Commercial laboratories offer this testing as well. And it's often conducted in conjunction with IgM testing as part of some of their test orders. Importantly to note, IgG is not routinely used for case confirmation. It can be useful for case classification.

In the instances where it is used for case confirmation, this requires testing between appropriately timed acute and convalescent serum specimens from the same individual. And then further specialized serologic testing for case classification can be the detection of measles or the measurement of measles specific IgE avidity. This is a lab-developed test that we offer through CDC and can be used primarily to help classify confirmed measles cases. Next slide, please.

Some special notes to take into account for IgM testing, both for measles and in general, is that there are some advantages. But there are also some disadvantages that should be considered. So IgM testing is readily available at many laboratories. It can be semi-automated in most cases by several clinical laboratories and their platforms.

And the turnaround time is relatively quick. If you recall a couple of slides ago, the time course for detection, there's a longer window for detection after rash onset. So IgM is most sensitive from day three onwards after rash onset and can be detected for up to six to eight weeks after acute measles. Some disadvantages with IgM testing, low positive predictive value and low incidence settings, which is what we have in the United States since measles has been eliminated since 2000.

Testing with a low positive predictive value runs the risk of false positives. So we stress that cases tested for measles serology should meet the clinical case definition. Or there should be reasonable suspicion of disease based on contact or international travel. And also the risk of a false negative can occur if a specimen is collected prior to three days after rash onset.

So if you collect a serum specimen very early in the course of disease, it may result negative, even if it really is a measles case. And there's also the risk of false positivity occurring due to cross-reactivity with other febrile rash illnesses. So diseases that may clinically present similar to measles, such as parvovirus

B19 or human herpes viruses can also cross-react on serologic tests for measles. Next slide. So now, I'll turn it back over to Paul to finish out the rest of the presentation.

Paul Rota: OK, thanks, Stephen. So the next three slides or slides that we presented in our seminar last September. But I think it's important to repeat this information since we're seeing a big increase in requests for measles testing. We're aware that many commercial labs are now offering testing for measles, both serologic testing and molecular testing that Stephen just described.

And certainly, the availability of these tests at commercial labs has many advantages. It certainly expands the availability of testing, allowing potentially faster turnaround times. Providers are familiar with commercial labs. And this is part of their normal specimen flow to be sending specimens to the commercial labs. And the results are usually linked to provider electronic medical records systems. So there's a good flow of information. Next slide, please.

However, there are some potential challenges for testing in commercial or clinical laboratories. And these are listed on the slide here. Oftentimes, we don't know the limit of detection or the sensitivity and specificity of RT-PCR assays. There may be a lack of detail about the performance of IgM assay formats. And as Stephen mentioned, the capture format seems to give better specificity and sensitivity. So we prefer that format.

Need to make sure that these assays are capable of detecting all the variants, the different variants of the virus. It's also important that the test results, that the testing is done in collaboration with state and county department of public health for interpretation of the results because measles is a reportable disease. And it's important that the clinicians work with their state and county health departments to make sure that results are reported in a timely manner.

The acceptable specimen types varies among laboratories. And depending on the specimen types, it may be difficult. If a clinical lab is accepting a broader range of specimen types than, for example, CDC, it may be difficult to do additional testing. One of the issues for measles is that as Stephen mentioned, we get sequence information from measles strains to use-- and use that information to track transmission pathway. And measles-positive samples are not routinely genotyped in commercial labs.

And sometimes, these specimens are unavailable for additional testing. The measles vaccine-specific assay, the MeVa, is not available in commercial labs. So this results in a loss of response time and the risk for vaccine reactions to be considered as measles cases. It's really important to rapidly confirm a measles vaccine reaction because this means that those-- that case, those individuals would not have to be quarantined.

So the public health response is not required for a vaccine reaction. So if the MeVa is not available or not available quickly, the sample would have to go for sequencing. If it's just listed as measles-positive, one would have to assume it's a wild type. And that would have to be treated as a wild-type case.

And the MeVa is particularly important in outbreak settings where you have a large number of cases. And outbreak response vaccination activities may be occurring. So then you would have individuals who are potentially exposed and vaccinated. And then when they develop rash, it would be difficult to determine whether that rash was caused by exposure to wild-type virus or a vaccine-associated rash without additional testing.

There's also questions about specimen storage and stability because we need to make sure that if samples are tested at a commercial lab, that they're stored in the proper condition. So that if they we need to retest them, they meet our specimen storage criteria. And the next slide, please.

So these are some of the considerations that we would like people to think about. I mean, turnaround time and reporting are critical. So especially for suspect measles cases, it's really important that the results get returned as soon as possible because there are important public health actions that need to be taken in a positive-- if the case is positive.

We would like-- it would be great if the serum samples were available for follow-up testing. We would-- at the CDC, we would retest them with our IgM capture assay. And as Stephen mentioned, we can also get some additional information for case classification by performing IgG avidity testing. And these are tests that we would run at CDC.

Sometimes, reflex testing is negative for measles negative samples. For example, rubella, if that was the case, sometimes it's needed. And sometimes it's not. It would be important to have these samples, PCR positive samples available for routine genotyping by CDC or the APHL Vaccine Preventable Disease Reference Centers.

As we said, sequence data are needed to maintain an accurate sequence database and are needed to track transmission pathways. And we're finding the sequence data very helpful, particularly this year, now that we're having a lot of cases. Because sometimes, that sequence data can quickly tell us whether cases are on the same transmission pathway or on different pathways. And it's important to collect, ship, and store samples in a manner that's consistent with the CDC test directory, which is available online. So I'll stop here. And myself and Stephen would be happy to take any questions. Thanks.

Jasmine Chaitram: All right, thank you very much for that presentation. We did have a couple of questions in the chat. The first one I'm going to ask you is, can cases of measles give false positive results on rubella IgM ELISA.

Stephen Crooke: I can take that one. Sorry, I had trouble finding my mute button. So the performance characteristics of IgM tests are going to vary based on the test. So I'd encourage anyone to either check if you're using an FDA-approved kit or to assess that based on the specific assay. But speaking from experience, routinely, we do not see cross-reactivity with rubella that often, if at all.

Jasmine Chaitram: Thank you. And Stephen, the graph you showed, the curve for the PCR detection, was that just for NP? Or was that for urine as well?

Stephen Crooke: That should reflect PCR detection for all specimen types. But I will defer to Paul or maybe Bettina who are more well versed in molecular testing.

Paul Rota: That was an attempt to look at all specimen types. And then, of course, the detection by PCR can be variable. So we've had specimens out sometimes even 15 days that are positive. That graph was trying to reflect the optimum time period for collection of specimens. We don't like-- we believe those specimens should be collected as soon as possible after a case is considered a suspect measles case. And one of the issues we've had in the past is sometimes, they would collect a serum sample at first contact with the patient. And then when the IgM's positive, go back and try to get a throat swab, or a urine sample for RT-PCR. And by that point, the detection frequency drops quite a bit.

Jasmine Chaitram: OK, and folks really like that graph and asked if they could get a copy of it. And if it's OK with Stephen and Paul, then when we go to post the slides from this talk, we'll put it on our archive website that I had mentioned earlier at the beginning of the call. And it will be available there. But just got to make sure that our CDC colleagues are OK with posting that information publicly. And we can follow up with you on that.

The next question is do we know what is causing the uptick in measles cases? And do vaccinated people have cause for concern at this point?

Paul Rota: Vaccinated people don't have cause for concern at this point. And so CDC is encouraging people to review their vaccination status. Certainly, anyone who is considering travel outside the United States should look at the CDC recommendations for vaccination for international travel to make sure you're updated on your MMR.

I think the reason for the uptick, I think this is an aftermath of the COVID-19 pandemic. As you know, COVID-19 was massively disruptive for global-- for public health everywhere in the world. And the result was that many of the vaccination campaigns for measles were either delayed or canceled.

And so global vaccination campaigns have recovered for many antigens. But they've been much slower to recover for the measles and rubella, which leaves us with an increasing amount of susceptibility in many countries. And I think with the-- now with we've seen a return of international travel to at least pre-COVID levels, with the increased susceptibility from the delays in vaccination, we're seeing an uptick in measles cases globally.

Jasmine Chaitram: Thank you. And is there-- where can folks find a list of the VPDs if they wanted to, if they needed to locate one?

Paul Rota: I think the website was on our slides. I believe it's-- the link is on there. So there's a link to the-- you could always just look for the website for APHL. And they-- and look for infectious disease. And that will have a link to the Reference Centers.

Jasmine Chaitram: Alright, great. And last question, can measles be sequenced by next generation sequencing?

Paul Rota: Yeah, absolutely. Our routine genotyping is the N450, as Stephen mentioned, because that's what all of the labs in the World Health Organization network are doing. So this gives us at least a minimum amount of sequence information that we can compare. As you know, many of the global laboratories are still-- many of them are in resource limited settings. So may not-- next generation sequencing methods may not be available to them.

So we're continuing with the Sanger. Though the WHO network is rapidly moving toward using next-generation methods. But yeah, there's plenty of methods available that work very well and give high-quality sequence information. Don't want to get into too many details here. But if you have questions, you're welcome to send us an email.

Jasmine Chaitram: All right, thank you so much, Paul and Stephen for joining us today. We don't have any other questions for you. We appreciate your time and may have come back on another call.

Paul Rota: All right, thanks, everybody.

Jasmine Chaitram: All right, all right, I'm going to wrap us up real quickly. Just a reminder that our next call is scheduled for May 20. It's the third Monday of every month from 3:00 to 4:00. And for those of you that ask for copies of the slides, as I mentioned, that they are archived on our LOCS website. Just a note of caution that it does take us a couple of weeks to get everything transcribed, and nice and neat into the format that you can access it.

So don't expect it tomorrow, but it's coming. We have some social media websites. And once again, happy Lab Week. And thank you all for joining us. And we appreciate you being here. And we appreciate everything you do. And thank you for your service. So hopefully wherever you are, you're being recognized for the important work that you do. Have a good day.