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Guests: Dr. Tulip Jhaveri from the division of Infectious Diseases at the University of Mississippi Medical Center and Dr. Esther Babady from the Department of Pathology and Laboratory Medicine and the Department of Medicine's Infectious Disease Service at Memorial Sloan Kettering Cancer Center.

Randye Kaye: Hello, and welcome to this edition of *JALM* Talk, from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye.

Respiratory viral infections are among the most frequent infections experienced worldwide, and they're a common reason for health care visits. The symptoms overlap for most respiratory viruses, and they may be indistinguishable from bacterial infections. The ability to identify the causative pathogen by laboratory or point-of-care testing can allow for actionable therapeutic decision-making and can also have prognostic implications. However, currently available tests for respiratory infections vary widely and selection and interpretation of these tests requires thoughtful consideration.

The May 2024 issue of *JALM* features the "ADLM Guidance Document on Laboratory Diagnosis of Respiratory Viruses," written with the support of ADLM's Academy. This guidance document addresses key questions related to best practices for the laboratory diagnosis of respiratory viral infections, including who to test, when to test, and what tests to use. The document also provides an algorithm to help laboratories decide on the most appropriate tests to use. Today, we are joined by two of the articles' authors, Dr. Tulip Jhaveri and Dr. Esther Babady.

Dr. Jhaveri is an Assistant Professor of Medicine in the Division of Infectious Diseases at the University of Mississippi Medical Center. He is a board-certified Infectious Disease physician and Clinical Microbiologist. Dr. Babady is the Chief of Clinical Microbiology Service, an Attending Microbiologist, and a Professor in the Department of Pathology and Laboratory Medicine and the Department of Medicine's Infectious Disease Service at Memorial Sloan Kettering Cancer Center. Dr. Babady chaired the guidance document writing group. Welcome, Doctors Jhaveri and Babady. First, why did you decide to write this guidance document on laboratory diagnosis of respiratory viruses?

Esther Babady: Well, thank you first for the invitation to join the podcast. This is really cool. The really simple answer to why did we decide to do this is just, we were invited by the Academy to write this particular guidance. However, both TJ and I are clinical microbiologists and TJ is also an infectious disease clinician. So, as clinical microbiologist ID people, of course, respiratory virus testing is beyond close to our hearts and I big proponent of testing for viruses. So, anything that gives me an opportunity to discuss and talk about viral testing, I'm game. But more importantly, I also participated in a similar guidance with ASM, I want to say about five years ago. This was pre-COVID. And prior to that, prior to COVID, most of the testing for respiratory virus was really under the purview of clinical microbiologists and infectious disease physician, I would say.

As we all know, COVID really changed the game, and now we can do the respiratory testing pretty much everywhere, right, even at home, and I think this is something we discussed in the guidance. So, I thought this was really a great opportunity for us, as clinical microbiologists and infectious disease docs, to really use that expertise to provide some guidance in terms of respiratory testing for those who may not have been as familiar prior to COVID with this. The number of tests that's now available and where they can be performed, again has changed it so that now, this is ADLM, so a lot of other laboratory medicine folks are able to do this testing. So we thought that this was actually a really great opportunity to contribute some of our knowledge and expertise, beyond just clinical microbiologists and ID physician. So that was really the motivation for doing this.

Randye Kaye: Okay, wonderful, and being invited is always nice as well. Thank you.

Esther Babady: Right?

Randye Kaye: Can you summarize some of the main take-home messages from the guidance document?

Tulip Jhaveri: Yes. Our guidance document describes different tests used for the diagnosis of respiratory viral infections. It helps us understand who to test, why to test, what tests are available, and how to interpret the results. With regards to who to test, we can break it down to children and adults. Testing of pediatric patients should be limited to hospitalized children or those with underlying conditions. Among adults, aging and immunocompromised patients should be tested. Immunocompetent adult patients may be tested only if results will impact management, primarily for flu and COVID.

As far as why to test, here are some of the reasons for performing respiratory viral testing. Number one, diagnostic testing. For example, initiation of appropriate antivirals or discontinuation of unnecessary antibiotics. Number two, infection control guidance. For example, implementation of appropriate isolation measures, cohorting of patients, and surveillance during outbreak situations. Or number three, for evaluation of local seroprevalence.

In terms of what test can be used, the preferred method is nucleic acid amplification tests, or NAAT. When a NAAT is not readily available, antigen tests could provide an alternative, however, they have lower sensitivity compared to NAAT. Direct fluorescent antibody tests, serologies, and viral cultures are not recommended for routine diagnosis. The preferred specimen type for an upper respiratory tract infection is a nasopharyngeal swab. For infections in the lower respiratory tract, bronchoalveolar lavage can be used. Test results should be interpreted considering clinical symptoms. Positive molecular or antigen test results in patients without symptoms may reflect asymptomatic carriage, presymptomatic infection, or shedding following resolved infections.

Similarly, negative test results in symptomatic patients may be false negative results and repeat testing is recommended. Correlates of viral loads, for example cycle threshold, provided by some molecular tests should be interpreted with caution given lack of standardization.

Randye Kaye: All right, thank you. That's a lot of take-home messages. Can you talk a bit about the role of diagnostic stewardship in testing for respiratory viruses?

Tulip Jhaveri: Sure. We all know that emerging diagnostics for respiratory viruses are providing clinicians with information more rapidly than ever before. However, with this cutting-edge technology, there are significant associated costs. This makes diagnostic stewardship valuable. Diagnostic stewardship selects the right test for the right patient, generating accurate results at the right time, to guide appropriate clinical behavior while conserving health care resources. Key stakeholders should make decisions regarding which new diagnostics are needed, how they will be used, whether their costs are justified for the value it brings, and the overall impact they would have on clinical outcomes.

Here are some examples of diagnostics stewardship; having built-in EMR algorithms to guide appropriate test selection or utilizing targeted NAAT first, instead of broad multiplex respiratory panels in low impact situations. If patients do not

meet appropriate use criteria, approval from infectious disease providers or clinical lab directors may be indicated.

Randye Kaye: All right. Thank you. Well, let me ask both of you, one at a time, of course, who is the intended audience for the guidance document and how should the guidance be used?

Esther Babady: I can start. This is a guidance document that's aimed at really all of laboratory medicine clinicians and laboratory directors. This is really reflected by the wide range of type of testing that is now available, right? So, TJ mentioned viral culture, which we don't recommend anymore, but this is something that most clinical microbiologists and clinical virologists will be really familiar with. However, now we have those rapid PCR tests or the NAAT tests that you can do in the emergency room, which means that this guidance will be very useful to ED doc and primary care physician that may have access to these tests. Additionally, some of these tests, while they may not be CLIA waived point-of-care type of tests, they might be simple enough to be run even in clinical chemistry.

We had this discussion many years back as where do we do molecular testing for infectious disease now? You know, with the simplicity of some of these tests, they can be done anywhere. So, a clinical chemist, a clinical hematologist, any lab medicine person, can actually have many of these tests in the laboratory. So, as a guidance document, I think this has a wide appeal and would be really of use and utility to the broader lab medicine audience, and some of our ED and primary care physicians.

Tulip Jhaveri: Thanks, Esther, and I can talk about the second part of the question, how this guidance should be used. As we talked about, this guidance addresses best practices for lab diagnosis of respiratory viral infections, it summarizes different tests use to detect respiratory viruses based on the viral pathogens, regulatory status of the test, the turnaround time of the test results, and the analytical and clinical performance. With the help of tables, figures, and algorithms, it provides a framework for appropriate utilization of viral diagnostic tests. During clinical decision making, this document should not serve as a sole piece of information used. It should rather be used as a supplement or an adjunct to clinical judgment and other considerations. The recommendations that have been made here are based on authors' expert opinion after a thorough review of most updated evidence.

The authors in our guidance comprise experts from both infectious diseases as well as clinical microbiology, thus representing both clinical and the lab side, and also from different types of institutions serving a wide variety of patients from community hospitals to specialized tertiary care

centers. As novel viruses and consequently newer tests emerge in the market, we hope to periodically update this guidance document for our readers, which Esther will talk about in a bit.

Randye Kaye: All right, thank you. So, let's get to that. Finally, there are emerging technologies for respiratory virus testing. How do you anticipate that this guidance might change?

Esther Babady: Yes, as I mentioned earlier in the introduction, I couldn't have imagined 5, 10 years ago that I would be on a podcast for ADLM talking about respiratory viruses, but the way the technology has improved and developed, again has opened it up so that it can really be performed anywhere. I'm anticipating the same thing will continue to happen, but not just about emerging diagnostic technology, but also treatment. A lot of the information in the guidance document relates to why you're testing and who you're testing. Part of it is because for certain viruses and certain patient population, there are treatment options. But that's not the case for all the viruses that we discussed in the guidance.

I'm anticipating that, hopefully, as things improve, we'll have more treatment option, which then will make us have to update the guidance because now there is a utility in testing maybe a broader range of patient using some of the existing tests, or we're going to have like a novel amazing test that gives us even more information about the biology of the viruses, and the impact this may have on treatments and decision that clinicians can make for management of patients. So, I am really excited about what the future holds and I think that as the technology emerge, we definitely will have to continue staying on top of it, and then just updating the guidance to reflect on what's really available, both in terms of tests and treatment, and how to best help both our lab medicine colleagues and clinicians to best take care of our patients. The more things change, I think the more we'll have to update the guidance.

Randye Kaye: Of course, well, doctors, thank you so much for joining us today.

Esther Babady: Absolutely. Thank you again for the invitation.

Tulip Jhaveri: Thank you for having us.

Randye Kaye: That was Dr. Tulip Jhaveri and Dr. Esther Babady describing the "ADLM Guidance Document on Laboratory Diagnosis of Respiratory Viruses." Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.