



#WIGWednesdays

May 20, 2020

“Update on the COVID-19 Outbreak: Understanding the Impact of Diagnostic Testing Modalities”

Featuring:

Lucy Gettman, Executive Director, Women In Government

Indiana State Representative Lisa Beck

Dr. Jamie Phillips, Senior Scientific Affairs Manager Medical and Scientific Affairs Roche Diagnostics Corporation

Lucy Gettman: Welcome to #WIGWednesday, our weekly virtual series delivering timely information to women state legislators and other policy leaders. I’m Lucy Gettman, Executive Director of Women In Government, a non-profit, non-partisan organization by and for women state legislators across the country.

WIG’s Board of Directors are sitting women state legislators who guide our programming and initiatives throughout the year.

To make this an interactive experience, we’d like to get the conversation started by asking an anonymous response question: “What testing have YOU experienced personally?” Please select all of the options that apply to you.

Before I introduce our moderator for today, I’d like to invite you all personally to [register for WIG’s exciting virtual Summer Summit starting June 17th](#)! Please be sure to check our social media accounts – [Facebook](#), [Twitter](#), [Instagram](#), and [LinkedIn](#) - and our [website](#) regularly for agenda updates as we continue to confirm speakers!

Today, we are honored to welcome WIG State Director Indiana State Representative Lisa Beck as moderator for this session: “Update on the COVID-19 Outbreak: Understanding the Impact of Diagnostic Testing Modalities.”

As a State Director, Representative Beck is part of a national network of legislative leaders helping WIG to provide expert forums and networking opportunities. Representative Beck represents Crown Point, Hobart, Winfield, and a small portion of Porter County. She is the ranking Minority Member of the Labor/Pensions Committee, and a Member of the Small Business & Economic Development Committee and Courts & Criminal Codes Committee. She is an attorney in Northwest Indiana, having previously been a Lake County Prosecutor. She is married to Vernon Beck, the USW Local 12775 president, and they raised two daughters – Natalie who is a Licensed Clinical Social Worker in Chicago, and Katie who is a new graduate of the Kent Law School in Chicago. She lives with her husband in Crown Point, Indiana. Representative Beck, the floor is now yours!

Representative Lisa Beck: Thank you, Lucy, for inviting me today. I am honored to be an Indiana State Director for Women In Government, and I’m also honored to moderate today’s webinar which features an expert speaker from Roche Diagnostics, which is also in Indiana. Before I introduce today’s speaker, I’d like attendees to be aware of how #WIGWednesdays are managed. All attendees are muted through the system. If you have questions or comments during the presentation, please be sure to identify



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yourself by name and then write them in the Chat Box that can be found in the Zoom Meeting Toolbar and please make sure you have selected “To: Everyone” from the drop-down menu. Finally, [all #WIGWednesday presentations](#) will be available on the Women In Government website a few days post-event.

Now, please join me in welcoming Dr. Jamie Phillips who will speak about the role of diagnostic testing modalities in helping combat the spread of COVID-19.

Dr. Jamie Phillips obtained her Masters and PhD in Infectious Diseases from the University of Georgia. During her graduate studies, she focused on Coronavirus viral genome annotation and identification of genes associated with pathogens. In between her Masters and PhD program, she spent time in Ghana aiding the Ministry of Health with developing a vaccine program for women and children. Following her graduate studies, she held a two-year postdoctoral position serving as the primary molecular virologist in a small diagnostic lab.

After her postdoctoral position, Jamie held a research associate position at the University of California-Davis where she aided in validating diagnostic tests and looking at the role co-infections play with influenza viruses. In 2014, Jamie joined Aalto Scientific, where she served as the Director of Research. This position enabled her to obtain a broad knowledge of clinical chemistry lab analyzers and point of care tests.

In 2017, Jamie joined Roche Diagnostics in their Medical and Scientific Affairs Division in Fishers, Indiana supporting their molecular POC (point of care) devices. In this current role she serves as a subject matter expert for respiratory pathogens and antimicrobial stewardship initiatives. Starting in early January, Jamie joined Roche's Emergency Response team and has been playing an integral role on the launch of Roche's SARS-CoV-2 diagnostics assays.

Dr. Phillips, welcome to #WIGWednesday and I turn the mic over to you.

Dr. Jamie Phillips: Thank you so much for that wonderful introduction, Representative Beck.

As mentioned today, I'm going to be discussing the SARS Coronavirus 2 outbreak, responding to a public health emergency with an emphasis on the diagnostic modalities that are available and their clinical utility.

As Representative Beck mentioned, I obtained my PhD from the University of Georgia in Infectious Diseases, specifically studying coronavirus genome annotation, identifying the genes that are associated with pathogenicity or attenuation of the virus.

For the purposes of today's talk, I'm going to go over the background on coronaviruses. I'm going to hit on the epidemiology of the SARS Coronavirus 2 to date, and then I'm going to talk about the different diagnostic modalities that are available for this novel virus.



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The World Health Organization was informed of cases of pneumonia of unknown origin in late December of 2019. This virus was then isolated and sequenced on January 7, and it was named, due to sequence identity, SARS-CoV-2. The disease that this virus creates is known as Coronavirus Disease 2019 or COVID-19.

Coronaviruses are the largest of all RNA viruses. They're actually thought to have proofreading capabilities, and they get their name because they have a large outer glycoprotein known as a spike protein. When viewed under an electron microscope, they give this crown appearance, thus the name coronaviruses. They are ubiquitous, meaning they're found all over and in many animal species. The occurrence of a zoonotic transmission event, meaning a virus that typically circulates in an animal population crossing over into the human population, has occurred previously. There are two notable zoonotic transmission events: the severe acute respiratory syndrome virus (SARS-CoV-1) occurring in China, and a more recent Middle Eastern respiratory syndrome virus (MERS-CoV) isolated out of Saudi Arabia in 2012.

When we look at these two previous zoonotic events, we know that the intermediate host has been defined. For SARS-CoV-1, the palm civet cat was the intermediate host, whereas for MERS-CoV, camels had been identified as the intermediate host.

But as we look at SARS-CoV-2, the intermediate host has not been definitively defined. We know that there are multiple reports that a wet market in Wuhan with many different animal species is where the virus originated, but the exact intermediate host based on sequence identity has not been identified, although the virus does have 96% sequence identity to viruses that circulate in the bat population.

The signs and symptoms of those that have this viral infection, if symptomatic, are fever, respiratory symptoms, abdominal pain, diarrhea, vomiting, headache, and myalgia. We also know that there are asymptomatic infections. This means an individual may be infected—the virus replicates and they are potentially shedding this virus to others—but is not showing the aforementioned clinical signs. The route of transmission has been identified as respiratory secretions, and the incubation period for this virus is 2 to 14 days with a median of 5 days. The incubation period is defined as that initial exposure of that respiratory secretion to the onset of clinical illness. We also know that this virus can progress and in certain individuals cause severe respiratory disease and lead to mortality.

When looking at clinical stages of COVID-19, we can break it down into three stages. Stage one or early infection is typically indicative of one having a mild fever, a dry cough, diarrhea, and a headache. Stage two would be your pulmonary phase—your shortness of breath and your hypoxia. Stage three is the cytokine storm or things such as cardiac failure. There are potential therapies that are being investigated for all of these stages, but for the purposes of today's talk, we will not be discussing them.

Looking back at early January – and this is data taken from John Hopkins University – we see that China had reported a total of 2,800 cases, resulting in 81 deaths. We flash forward two months to March 26,



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and we see that this virus had spread to the rest of the world. At this point, the confirmed cases were roughly half a million and had resulted in 24,000 deaths. Just two weeks later, we see a jump to 1.3 million total confirmed cases and roughly 78,000 deaths. This jump could be attributed to the addition of diagnostic tests being available.

We know that in early May we are at roughly 3.5 million confirmed cases and 250,000 deaths. Looking at this data this morning, we know that the mortality has gone up to 300,000 globally, so there is a definitive need to test for this virus.

When we start talking about the available modalities, there are a lot of questions on what their clinical utility is. What does the result mean to you? Today, I'm going to focus on molecular testing and serology testing.

Molecular testing or nucleic acid testing is identifying the pathogen. We see here the priorities from CDC for this type of testing. Inclusive of these priorities is also antigen testing, which is identifying the protein on the virus. CDC recommends that health care providers place a high priority of testing on hospitalized patients with symptoms as well as healthcare facility workers, workers in congregate living settings, and first responders - all with symptoms. They also include high priority for testing for residents in long term care facilities or other congregate living settings, including prisons and shelters - again with symptoms.

It's important that they've updated this as of May 6th, and they place not a priority (not a high priority) on testing persons with symptoms that are not hospitalized as well as persons without symptoms who are prioritized by health departments. To me, this is important because if we think of using long term care facilities, as an example, we know that in Washington there was an outbreak in a long-term care facility. The percent positivity within that setting was 34%. Of that 34% who were positive, 57% of those were asymptomatic, so placing a priority on testing additional individuals that are not symptomatic is important.

Let's discuss the stages of transient viral infections in order to really understand when these different tests should be utilized. A person is first infected via respiratory droplets, and typically this virus is at a low viral load. This virus then infects the host's cell, hijacks it, and manufactures more virus, increasing the amount of virus that is present in this individual. In these first two stages, the nucleic acid amplification tests are optimal in identifying the pathogen due to the sensitivity of these tests.

As the infection progresses, individuals will mount an immune response. There are low affinity immunoglobulins that are circulating early during infection. These can be immunoglobulin M which are pentamers. As the infection progresses, our bodies make a specific antibody to this disease that in many cases is typically neutralizing, so it prohibits the virus from replicating. These would be your high affinity IgG immunoglobulins.

When we are testing, what are we trying to find out? If you are looking at pathogen testing—your nucleic acid amplification test or your antigen-based test—you are going to find out if a person is



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currently infected with SARS-CoV-2. If you're looking at serology, where the test is detecting an immunoglobulin, you're asking: has a person previously been infected with SARS-CoV-2?

These tests are different. They have different specimen types. Typically nucleic acid amplification tests are done using a nasopharyngeal (nose) swab, oropharyngeal (cheek) swab, a lavage, or other bodily fluids. On the other hand, antibody detection tests use your blood serum or your blood plasma. They have different value and use cases per each setting. It is really important to understand what these are detecting so that when you are making decisions within your state, you are recommending the optimal testing modality for each setting to get the answers you need.

Roche launched a Polymerase Chain Reaction (PCR assay) on February 14. It's important to note that this was research use only. This was our fastest way to get something to the market for those labs who could run a Research Use Only (RUO) assay. It included two steps – first, using a MagNa pure 96 system for the actual extraction, and then second, the amplification and analysis occurred in the z480 analyzer system. This platform here could do about 96 samples per run, and each run took about two and a half hours.

Since then, Roche has received two Emergency Use Authorizations (EUA). EUA approvals are given by the FDA when there are no other available alternatives. This was the case with this novel virus when it started circulating in the human population. There were no diagnostics that were specific to this pathogen. The FDA does provide guidance, and Roche follows all guidance and requirements provided.

In the timeline on the slide, on top of the months we can see Roche, and on the bottom we can see the rest of world. In late December we see those unknown pneumonia cases, and in late January, the World Health Organization declared a public emergency. March 13 was when Roche received their EUA for a high-throughput molecular— that's the nucleic acid amplification tests that we've been talking about— on the Roche 6800 and the 8800 systems.

You can see that platform on the slide here. It's fully automated, it's high-throughput, and it's a closed system. This is great to understand because by using a closed system, you're protecting the health care provider workers who are running these types of tests.

This platform was approved for use for qualitative detection, so you would get a positive or negative result. The specimen type could be a clinician-instructed, self-collected nasal swab or a clinician-collected nasal nasopharyngeal and/or oropharyngeal (cheek) swab. This is important to recognize when you're trying to determine which testing modalities are optimal for all of the different settings that you have in your various states.

It is important to understand the specimen type. Is it approved that a patient can self-collect that specimen type? This is important if you're trying to reduce the risk that a healthcare provider has when obtaining that patient sample. This isn't optimal for all settings, but it's something to consider.



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Here on the slide you can see the two platforms that this test can operate on. When you look at the 6800, there are about 384 results per eight-hour shifts, and when you look at the 8800, you can see that it's roughly 1,800 per eight-hour shift.

Going back to the timeline, we see that Roche received their second Emergency Use Authorization (EUA) in March for an anti SARS-Cov-2 assay. This is an immunoglobulin assay that indicates whether an individual has been infected. And this assay, the way Roche has designed it, is a double-antigen sandwich. This is making sure that only high affinity antibodies are being detected, which enables us to have a high degree of confidence that these antibodies are representing SARS-CoV-2 infections, as opposed to any other coronaviruses that are circulating. It's important to note that there are four different strains of human coronaviruses that circulate annually, representing about 10 to 15 percent of upper and respiratory tract infections.

Even though we have the serology tests available and they are detecting those high affinity immunoglobulins, there's still a lot that we don't know yet, because this is such a novel pathogen. Is immunological response protective? Does the presence of antibodies indicate immunity? If so, how long does that immunity last? When we think back to SARS-CoV-1, we know that immunity only lasted two to three years in certain individuals. Another question is, how long will it take to reach herd immunity?

These are all really important factors to be thinking about because a lot of us are discussing the frequency of testing healthcare workers or workers that want to get back to work in any setting. We don't know how many times an individual will need to be tested in order to show - if we have the information that they are neutralizing—that they still have that reduced risk of infection. There are many laboratories that are currently working on these questions, and we hope to have answers soon, which I think will dictate many of the institutions' testing algorithms.

With that, I'd like to let you know that Roche is working in alignment with the government and has allocation measures in place that offer testing to all 50 states and Puerto Rico across a combination of hospitals and large reference laboratories. This is specific for the 6800 and 8800 PCR that we have available. If there are additional questions, healthcare providers can contact us at the number listed, and we have general information and updates regarding COVID-19.

With that, I'd like to stop here and entertain everyone's questions. Thank you so much.

Representative Lisa Beck: Thank you, Dr. Phillips! We really appreciate this very important information! This is especially timely as many of us are considering how to move forward in re-opening our communities.

We do have time right now to answer a few questions from the audience, and we do have several questions that have been submitted. So, I'm going to go ahead and start with the first questions.



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From Representative Wendy Thomas of New Hampshire - she's asking the speaker to comment on reports of the viruses mutating and that the East Coast virus is acting a little differently than the West Coast virus.

Dr. Jamie Phillips: Absolutely. Thank you for that wonderful question. When we look at phylogenetic relatedness, we know that there are different clades forming of this virus. Coronaviruses, as mentioned, are the largest of all RNA viruses, so they are thought to actually exist in what is known as a quasi-species theory. There are many different variants of the same virus, per se, within one respiratory secretion. The fittest virus in each individual is then selected for and transmitted to the next individual.

Seeing that divergence on the coasts, especially with the isolation measures that we put into place, are somewhat predictable for this virus. I have not read anything that indicates, though, that these viruses are antigenically different, meaning that their outer structural proteins are different. Basically, the divergence is occurring at the nucleotide level. The majority of nucleic acid amplification tests actually use more than one primer set. Roche's use multiple primer sets that target different regions of the genome. So as this virus evolves - which we know it will because it's an RNA virus - we don't expect it to evolve where the testing primers are no longer able to detect it, and that's due to the primer design of the test.

Representative Lisa Beck: I'm going to ask a question of my own that I get a lot. Is a person able to get the virus twice? And since there is a different version, can you get each of the versions?

Dr. Jamie Phillips: The short answer is we don't know the answer to that. We don't know if the antibodies that we are detecting are neutralizing. If they are neutralizing, then that would indicate that no, it is not likely a reinfection would occur.

If the virus changes antigenically, which happens with influenza, those antibodies that we were talking about that could confer protection would no longer protect against that. Then, that would enable the virus to infect the individual again.

What I will say, though, is if an individual has been infected and they are re-infected, it is likely that their initial clinical symptoms will be consistent with the second infection. This means that if a person was asymptomatic with initial infection and there are no significant changes in that individual's immune status, then typically we would expect to their second infection to mimic the first one. But fantastic question, and we just don't have all the answers for you yet.

Representative Lisa Beck: I'm going to read the second question. There are reports that the virus is being shed in stools (although it may not be live). How does this impact treatment or care?

Dr. Jamie Phillips: I've read those publications, and there are reports of shedding in the stool. I think that to this individual's point, it hasn't been assessed on whether it's residual nucleic acid or it's actually viable virus. I do think that we could potentially use stool samples, if needed, but I don't know how that



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would impact care. I think the optimal collection for pathogen testing is the nasal nasopharyngeal or oropharyngeal swab.

Representative Lisa Beck: Third question: if someone believes they have been exposed, should they self-quarantine for five days and then get tested for the virus or just self-quarantine for 14 days?

Dr. Jamie Phillips: I think this really depends on the geographic location and the health status of the individual. There is no way to have a blanket answer to that. We know that the data indicates those with co-morbidities such as diabetes are likely to have a more severe infection. I think it would depend on the prevalence of the pathogen within your geographic location and your immune status. I would need that information in order to aid you with whether or not you should be tested immediately or not.

Representative Lisa Beck: The fourth question comes from Washington State Representative Cindy Ryu. Her question is: How expensive are the machines shown on the slides in the presentation, and how much is the cost per test?

Dr. Jamie Phillips: I do not know the answer to that, but I can have one of my commercial partners contact you. We keep a firewall in between medical and scientific affairs and our commercial colleagues, but I will get that information back to you.

Representative Lisa Beck: Representative Ryu has another question. Zicam and other zinc products seem to reduce/shorten colds. Do you think they might be helpful for COVID?

Dr. Jamie Phillips: I personally have not seen any data that supports that, so I can't comment.

Representative Lisa Beck: One of the questions that I get asked a lot has to do with being put on a respirator. I've heard people say that once you're put on a respirator, your chances are so small. I'm just wondering whether there's anything else they could do besides the respirator.

Dr. Jamie Phillips: I think it goes back to the different stages and that person's immune response. I've seen success stories when individuals are incubated in those certain settings. I can't really comment too much. Are you asking if that is absolutely necessary?

Representative Lisa Beck: Maybe that is the question because it seems like they wouldn't use a respirator unless they needed it. A lot of what I hear from people is that they're really concerned that if they get put on a respirator, that's the end. I just wondered if you had any comment on that.

Dr. Jamie Phillips: I think that our health care providers are doing the best they can and only using those when needed.

Representative Lisa Beck: In several of your slides, you had a depiction of the world, and in the US and Europe, it was almost solid red. Is that because we're testing more in Europe and the US?



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Dr. Jamie Phillips: Yes, quite likely in comparison to other regions of the world that are reporting a lower level of confirmed cases. It's extremely likely.

Representative Lisa Beck: There's one more question from Raul Phillips: Can a test tell if you have been infected before you start showing signs of being ill?

Dr. Jamie Phillips: The nucleic acid amplification test is a very sensitive test. If you are an asymptomatic carrier but are shedding the virus and the viruses are actively replicating, then in those instances, it could detect the infection.

Representative Lisa Beck: Dr. Phillips, do you have anything else that you would like to say in closing remarks?

Dr. Jamie Phillips: No, thank you so much for having me today.

Representative Lisa Beck: Thank you again, Dr. Phillips, and thank you to everyone for joining us for today's WIG Wednesday. Representative Ryu also commented that it was an excellent presentation and that as a former microbiology and immunology student, she really enjoyed it.

Please join us for upcoming #WIGWednesdays!

The May 27 session will be “Mental Health Resources for You and Your Constituents in the Time of COVID-19” with Colorado State Senate President Pro Tempore Nancy Todd as moderator and featured speaker Paul Gionfriddo, CEO of Mental Health America.

The June 3 session will be “Amazon's Response to COVID-19: Supporting Employees, Customers, and Communities.”

[Registration](#) and [resources for all WIG Wednesday events](#) can be found at www-dot-women-in-government-dot-org, and don't forget to register for the upcoming WIG Summer Summit series!

Thank you again for joining us and stay safe!



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