Infectious Questions EP 27: Serology and COVID-19 (2019-nCoV, Pt 12)

Shivoan: Welcome to Infectious Questions, a public health podcast produced by the National Collaborating Centre for Infectious Diseases. I'm Shivoan Balakumar. Our series on COVID-19 continues, covering topics and questions of interest among public health practitioners in Canada. If you have any questions to submit, please send them to nccid@umanitoba.ca or find us on our website at nccid.ca. This is the twelfth episode of our series, and today we'll be taking a more in-depth look into the state of serology testing in Canada. You'll learn about the strengths and limitations of serology testing and the different ways that serology testing can support Canada's COVID-19 response. NCCID's Dr. Alexandra Wierzbowski spoke with Dr. Graham Tipples, the Medical Scientific Director of Alberta's Provincial Public Health Laboratory. Here's Alexandra with Dr. Tipples.

Dr. Wierzbowski: What is it that public health professionals need to know about serology testing for the novel 2019 coronavirus?

Dr. Tipples: So, a couple of things. A serology test is typically what we refer to as a test looking for a marker in blood or serum. Commonly, it's antibodies that we're looking for. The detection of the antibodies in the sera can be done through a method which is called an enzyme linked immunosorbent assay or an ELISA. So, antibodies are an important part of the immune system and, for viral infections, antibodies can be explicitly formed towards the virus proteins, which are also called the antigens, virus antigens. So, if you can detect a specific COVID antibody, that can indicate that a person has previously been infected with COVID virus. So, you can detect antibody in sera, which can indicate that someone has already been exposed to COVID. What's still being worked out right now is how early on you can use that serology test to say someone has got an active or acute infection. So, right now, it's more appropriately used as just an indicator that someone has previously been exposed to that virus.

It's not appropriately used as a diagnostic test for early acute infections and that's because there's a window of time between onset of symptoms and how many days after the antibodies start to develop and are detectable through the ELISA. So, there's a window of time where someone may test negative but be infected. So, there's a risk of having a false negative result if using serology for a diagnostic test. The main thing to understand, there's no one perfect test, and whatever test is used you need to know how it's appropriately applied. So, for serology testing, the most appropriate use is for looking at past infections or prior exposure to COVID as opposed to a diagnostic tool, so for molecular testing, which would be looking for early acute active infections.

Dr. Wierzbowski: You touched on this a little bit already, but could you please tell us what are some of the important limitations of serology testing for COVID-19?

Dr. Tipples: With any new tests or any new virus or any pathogen, there's a period where we need to understand better the immune response and the appropriateness of using different markers for diagnostic or surveillance purposes. So, in this regard, serology, as I mentioned earlier, to detect an acute infection, a recent acute infection, IgM antibodies are indicative of an acute infection. However, for COVID, what we don't know is how quickly the IgM antibodies are developed. So, what we do know, we have some early data to show that the IgM antibodies do not get developed for five to seven to 10 days post-onset of symptoms. So, the use of an IgM test as a diagnostic tool is not particularly a good idea. However, with IgG antibodies, which are indicative of past infection and typically present for an extended time, the detection of an IgG antibody is a good indication of prior exposure to that particular pathogen, COVID in this instance.

We need to clearly understand, for COVID, because it's a coronavirus, and because there are many coronaviruses out there, several of which cause the common cold — we need to be sure that the tests that are being developed for serology for COVID-19 are actually specific for COVID-19 and not inadvertently picking up antibodies directed at other coronaviruses.

Dr. Wierzbowski: Can you talk about immunity to COVID-19? What is known, and at what point would a serology test result imply lifelong or long-term immunity to COVID-19?

Dr. Tipples: So, the issue of immunity is interesting. We don't know yet. That's the straightforward answer right now. If you look at other viruses, take measles for example. There's an excellent vaccine that's been around since the 60s, immunization elicits an immune response and then people typically have lifelong immunity for measles. If someone detects positive for IgG antibodies for measles, it's going to be a rare situation that someone gets re-infected. Is it impossible? No. Is it rare? Absolutely.

Let's take a different virus. Mumps virus. There's a vaccine for it. The vaccine isn't as good as for measles, so you can get people that have had two doses of mumps vaccine, but still can get re-infected. That's why you get these mumps outbreaks percolating even though you've got a vaccine, right? So, for COVID now, we just don't know the answers to those yet. The antibodies that are detected using these Health Canada licence tests, they're just detecting an IgG antibody. What we don't know is whether those antibodies are neutralizing antibodies. Do those antibodies buy into the virus and prevent infection of that virus into the cell?. That would be a neutralizing antibody. And until further work is done and research is done, we won't know about protective antibodies

that confer immunity versus someone who has previously been exposed and has antibodies, which may not be protective.

Dr. Wierzbowski: As serology tests are being approved in Canada, what is it that public health professionals need to know about these tests?

Dr. Tipples: Right now, there are two Health Canada licence serology tests approved. In the coming weeks, I'm sure there will be more. The main thing to know is that any test that is implemented in a diagnostic lab has to be very, very thoroughly validated. Is it fit for use? Does it do what it's supposed to do? Plus, the Health Canada approval is required for sale for diagnostic purposes in Canada. So, there's going to be more tests that are coming along, and the diagnostic labs in the public health labs will need to evaluate and validate those tests thoroughly. Like all clinical testing, the tests are ordered by an appropriate healthcare provider and, right now, in terms of who can get the test or who should get these tests, those details are still actually being worked out as to what's the appropriateness of serology testing in Canada.

There's a national immunity task force that's working on serology-related issues starting to answering questions like what does protective immunity mean? How should serosurveys be set up? And what are the appropriate uses for serology in Canada? So, those are the things that are currently being worked out and work is underway within the different provinces, and collaboratively across Canada, to answer how best to implement serology in Canada. There are various scenarios that serology, with the Health Canada approved test, could be used.

So, a particular scenario could be to do a serosurvey - trying to get an understanding at a specific point in time for a particular population, how many people have previously been exposed to COVID-19? The idea would be to design your serosurvey as such that you could do it in a particular geographic area and repeat it periodically over time to monitor the spread of the virus for the specific population. Importantly, too, is also to design it so the different jurisdictions can have comparable results, and you can compare what's going on in BC to Ontario, for example, or Alberta to the Maritimes. You want a standardized way to do these serosurveys.

There's other applications, for example, there might be a specific outbreak investigation where, you know, if you're looking for active cases, you would collect swabs and do PCR testing, the usual way we've been doing the testing. But if it's been a couple of weeks since that outbreak and you're trying to do a little bit more, well, who may have been exposed in that particular outbreak situation? In that sense, serology might be an appropriate tool to look at contacts or others who may have been exposed a couple of weeks prior.

Another final way that serology might be used is in a specific case. Suppose the diagnostics are not entirely clear if it's a low viral load and is it positive or is it negative. If after two weeks or so you're still unclear if that person has COVID, because the molecular tests weren't being definitive, you could use your serology to do it. It's another tool to go back and look at that particular case to help sort out whether that patient was infected or not. So, there are various ways that serology can be used, and these commercial assays can be used. That's what needs to be understood. It's all about the appropriate use of that test. That's key.

Dr. Wierzbowski: Can you comment on when public health labs across Canada will have access to these tests?

Dr. Tipples: It's a two-part question. So, one becomes available once the commercial tests are Health Canada approved. There are some that are Health Canada approved. Now, are the different jurisdictions ready to say, "Hey, we're going to start using them now"? I don't believe so. Certainly, in Alberta, we're not there yet. We're working with other provincial partners to determine, as I've been talking about, how best to apply serology, in particular the design of the serosurvey. So, I would expect in the coming weeks a little bit more definition around how these serosurveys should be designed and some of the first ones will get the ball rolling. Perhaps by mid-June, some of the jurisdictions will be starting to do some of their serosurvey work. It's not an imminent tool, but I think we're getting closer to have serology as another tool in our toolbox to use.

Dr. Wierzbowski: Once the provinces will have these tests, who should be the priority for testing?

Dr. Tipples: I think you have to determine what question you're trying to answer when you're doing the serology test. So, if it's a serosurvey, any serosurvey will be set up to look at a specific population. For example, if there's a geographic area that's been a little bit harder hit by COVID so far, how that serosurvey is designed might be slightly different from a geographic area that has had fewer cases. Similarly, you might want to be looking at healthcare workers or long-term care facility staff. It depends on what the intent of the serosurvey is. With that all said, I think a key population that requires close attention is the long-term care facilities; whatever we need to do to keep the virus out of those institutions is critical. That's in terms of the key population that needs to be protected. Then you use your different lab tools and your public health investigation tools accordingly to answer the specific questions that you're trying to solve.

Dr. Wierzbowski: Lastly, can you comment on what is happening internationally in terms of serology testing for the novel coronavirus? And what is important to keep in mind in terms of the performance of these serology tests?

Dr. Tipples: I can't comment on serology too much outside Canada, other than, yes, some publications come out about the use of whether it's point-of-care testing, serology or other applications for serology in other jurisdictions. All I'll say is that when you're interpreting these publications or these investigations, you have to be very, very careful in the interpretation of those results. What was the specific population that tested? Which was the test that was used? Because all of that's going to factor into the reported results. You have to understand that what's coming out of one jurisdiction may be very different that comes out of a different jurisdiction. It all returns to the appropriate design of serosurveys, and the proper use of serology is incredibly important.

There's a fair amount of work underway right now to evaluate the different commercial serological tests that are out there for COVID. And, before the implementation of any of those, the lab has to evaluate and validate that assay and test thoroughly, to make sure that you understand the sensitivity, that you know the specificity of the test before you use it. Also, as much as possible, you want to be using the best tests that are out there - highly sensitive and highly specific. So, there's work currently underway both within Alberta, within other provinces and collaboratively across Canada to evaluate different serological assays.

Shivoan: That was Dr. Alexandra Wierzbowski's phone interview with Dr. Graham Tipples, the Medical Scientific Director of Alberta's Provincial Public Health Laboratory. If you have other public health questions on COVID-19, please submit them to nccid@umanitoba.ca. Production of this podcast has been made possible through a financial contribution from the Public Health Agency of Canada, but the views expressed here do not necessarily represent those of the agency. The host organization at the NCCID is the University of Manitoba. Learn more at nccid.ca.