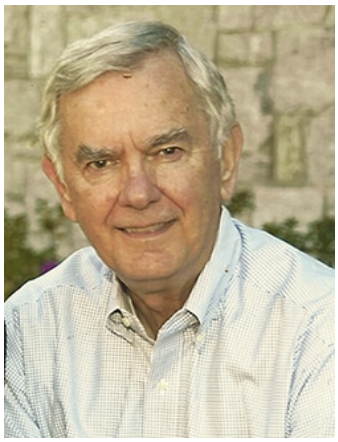
A conversation: Specimen collection and testing for SARS-CoV-2

May 2020—*Specimen collection, supplies, and serological tests were on the table when CAP TODAY publisher Bob McGonnagle spoke recently with J. Michael Miller, PhD, D(ABMM), director of Microbiology Technical Services, Dunwoody, Ga.*

Dr. Miller was with the CDC for 35 years in various roles, among them as chief of the Epidemiology and Laboratory Branch, chief of the Laboratory Response Branch, and chief laboratory science officer for the National Center for Emerging and Zoonotic Diseases. Here is what McGonnagle and Dr. Miller talked about, several weeks into the pandemic.

Have you heard about a problem with sample collection and false-negative results?



"Let's hope we will be able to stay prepared, should something like this ever occur again."
Dr. Miller

Dr. Miller: As far as everybody knows there is no "perfect" specimen. There are good specimens, some better than others. But the chronic issue we have with specimens is not so much the specimen itself but the supplies. Nasopharyngeal swabs, for example, are in short supply and that is a chronic issue.

The good news is that for some of these specimens now, patients can collect their own, and that saves the time of health care workers and some of the products that health care workers have to use.

Do you have confidence in patients' ability to collect a good specimen? Many people would worry about that.

Dr. Miller: We all worry about that, but the specimens patients can collect themselves are simple. It's just a swab in the nose. These are swabs of the anterior nares (about one cm up the nose) or a midturbinate nasal specimen, using a flocked swab, which is a little further into the nose beyond the anterior nares. And patients can collect their own specimen, or a health care worker can do that, and there are special swabs for each one of those.

For health care workers, the No. 1 specimen we need more than anything else for most testing platforms is a nasopharyngeal swab for swab-based testing. Next would be the throat swab, collected by a health care worker. The nasal midturbinate and the anterior nares specimens are also available if the nasopharyngeal specimen cannot be collected.

We also know this disease can progress to the lower respiratory tract. So some testing platforms will accept sputum, bronchoalveolar lavages, and nasal aspirates.

We know that the organism can be shed in stool so there may be a fecal-oral transmission mechanism. But the primary focus of the illness is respiratory. Upper respiratory first, and then there are some platforms that will accept lower respiratory specimens, but this is where you have to follow the directions of the manufacturer.

For testing developed in the laboratories, some protocols have been updated. They have been validated with one or more of any of those specimens. So the developers tell us the specimens of choice for their platform.

If there was a range of specimens that would be validated on an LDT, and you had no other knowledge, would you preferentially have a well-collected nasopharyngeal swab? Would that be your best specimen?

Dr. Miller: That would be the best specimen, yes. We know that the viral load in a patient is highest during the early stages of the disease, which begins in the upper respiratory tract. So that nasopharyngeal swab is going to be very important.

Many manufacturers have emergency use authorizations, and several have claimed they can use approved specimens, including nasopharyngeal aspirates, nasal aspirates. Does that make sense to you?

Dr. Miller: Yes, it does make sense, especially if their system has been validated with those specimens. And the manufacturer or developer would be able to tell us that. So a nasopharyngeal swab or a nasopharyngeal aspirate could be tested at the discretion of the developer of the test.

Can you give us more detail about what we mean by a nasal aspirate?

Dr. Miller: A nasal aspirate or a nasopharyngeal aspirate is where sterile saline is injected into the nasal or nasopharyngeal area and then it is quickly aspirated. You're washing out that area and then submitting that fluid for testing.

We have to be careful about which saline we use. For instance, phosphate-buffered saline is probably the saline of choice if saline has to be used to transport a swab, because the pH of phosphate-buffered saline is around 7.0 to 7.2. Regular saline has a pH much lower, down to 5.5 or 5.6. So we want the organism to be as intact as possible with no degradation of its RNA. We are testing for the organism's RNA, not the organism itself.

In addition to getting the specimen with a swab or a nasal aspirate, we have this question of transporting the specimens to the labs, and I've heard reports of shortages of "chemicals." Do you think in some cases they're alluding to a shortage of adequate transport media?

Dr. Miller: I'm not sure what is meant by a shortage of chemicals but there is certainly a shortage of viral transport media. Most of the tests that have been developed have been developed with the use of viral transport media of some kind. Because of that, there is a shortage of viral transport media and it's difficult for some places to get that. Now the CDC and FDA are saying that sterile saline could be used, and I think they are referring to phosphate-buffered saline that could be used as a transport medium. But many of these systems or test platforms were not validated using saline. Quick validation may be needed to ensure that the saline is okay. Personally, I think it should be all right because we're looking for the viral RNA.

Viral transport medium was designed for use by labs that are culturing viruses. So we needed intact viruses that were viable, but we don't routinely culture this virus. With PCR and nucleic acid amplification testing, we don't need a viable organism. We just need the RNA, the nucleic acid of this particular organism. The phosphate-buffered saline would provide that. It is always best to check with the manufacturer or developer.

It seems no one envisioned anything like this pandemic and so many were caught off guard.

Dr. Miller: We had not seen anything like this in a long time. Perhaps the 1918 flu pandemic had been similar. But it is hard to imagine that a virus can spread around the entire planet in a month and a half or two months and infect so many people so efficiently. It's rather scary. It's almost at the level of science fiction movies. But its real, and now we all know it's real. Let's hope we will be able to stay prepared, should something like this ever occur again.

The spread of this pathogen is much more efficient with this virus than with some others like SARS-1 and MERS. These are the kinds of events that we did tabletop exercises on with bioterrorism organisms, using the what-if scenario.

There's a lot of disaster planning, but it's just planning until the disaster happens.

Dr. Miller: Yes, it is and when it does happen, it's almost as if you're still just not ready. We have the best people in the world working in our laboratories in the United States. And they're working day and night at risk to themselves and their family, and they deserve all the credit, applause, and support we can give them–as well as the other medical staff that remain on duty.

What would you say to people who might be observing on their televisions people using drive-throughs to provide specimens? You don't know who's doing it. By and large should most people not worry about the specimen collection in those kinds of scenes, that is, whether the people are qualified to do it, whether the materials are the right materials, whether the handling and transporting are acceptable?

Dr. Miller: I have no reason to question the validity of those specimens and certainly not the qualifications of the people who are working. These drive-throughs have been set up by contract or by hospitals or whatever, and I think they're done carefully and using the right people and the right tests.

Can you talk about the serum testing for COVID-19 antibodies?

Dr. Miller: We do need some good immunological tests and several are being marketed. Most companies have not submitted an EUA for FDA evaluation because it's not required since these rapid immunological tests are not diagnostic.

But there are different things to think about with these rapid tests that detect IgM and IgG. First, we don't have data yet to evaluate how useful these tests are. We have no published research to give us confidence in the accuracy and utility of the rapid immunological tests.

It takes several days, sometimes up to 11 days, before IgM will appear after exposure, so if a patient is tested too early, there could be a false-negative reaction, which could lead to further spreading by an individual who thought he or she was not infectious.

A lot of us have concerns about cross-reactivity of these tests with the garden-variety coronaviruses that are not epidemic, those that cause the common cold. We must know if they do or do not cross react with these tests.

And if we had them, because they are not diagnostic, we have to provide a detailed disclaimer with the result as it goes to the physician, and that disclaimer is outlined on the FDA's website. It's very clear.

The immunologic tests could be useful to define susceptible individuals if they were antibody negative, versus those who have been previously infected, so they are useful for looking for the degree of infection in the population. PCR answers "Do I have it?" while immunologic tests answer "Did I have it?"

We do need them and the sooner we get trustworthy tests the better.

Can you share a couple of final thoughts or concerns or perhaps a piece of advice for people in laboratories?

Dr. Miller: I would want my technologists and I encourage my technologists where I work to become very familiar

with personal protective equipment and standard precautions. Review it over and over and over. I would stress being safe and being aware more than ever. And practicing safety with each other, talking about risk and reducing risk as much as possible. And having our laboratory managers skilled at doing risk assessments in the laboratory. What procedure, what protocol, might provide an increased risk that we have to address? Several procedures are aerosol-producing—shaking, stirring, centrifuging. So being aware of the risks is essential, and knowing the PPE and standard precautions for laboratorians is critical.

There are hundreds of microbiology specialists around our country who are invaluable sources of skill, technology information, and safety regarding this virus. And it’s a privilege for me to be among them and listen to them, and watch and learn from them. There’s good in some of this, even as we see such challenging times.