New requirements for molecular micro waived testing

Karen Lusky

September 2019—Four new checklist requirements for waived molecular-based microbiology tests have been added to the CAP point-of-care testing, limited service laboratory, and immunology accreditation program checklists, as part of the 2019 checklist edition released this month.

“The CAP has decided to improve patient care by providing additional safeguards that wouldn’t necessarily be performed otherwise,” says Bobbi Pritt, MD, MSc, DTM&H, chair of the CAP Microbiology Committee and professor, Mayo Clinic Alix School of Medicine.

Dr. Pritt and other members of the Microbiology Committee have noticed that even though the new cartridge-based waived molecular tests are self-contained, and the risk for nucleic acid leakage and contamination is low, nucleic acid contamination can occur. They have seen false-positive and -negative results, even with the purportedly low-risk molecular tests. Although the tests are waived, “we feel like there is still quality assurance and quality control that should be performed around them, as a best patient practice, knowing that this will be going beyond what the basic requirements may be,” says Dr. Pritt, who is director of Mayo’s clinical parasitology lab and co-director, vector-borne diseases laboratory services.

The committee was asked what requirements from the microbiology checklist should be made part of the POC testing checklist, and they worked with members of the Checklists and Point of Care Testing committees to make the selection. “It was a nice collaboration between our three committees,” Dr. Pritt says, “trying to use all of our different CAP expertise to decide what is applicable, what’s doable, what applies to day-to-day testing in a point-of-care setting.” They modified the four requirements “to be relevant to the point-of-care testing environment.” (The microbiology checklist can be used for both waived and nonwaived testing.)

Dr. Karger

The first waived molecular tests became available within just the past few years, says Amy Karger, MD, PhD, vice chair of the CAP Point of Care Testing Committee and medical director, West Bank Laboratory, University of Minnesota Health. “Since this is new technology, we have to adapt our checklists to reflect the different risks that come with molecular testing that aren’t seen with immunoassay testing.” Those who perform the testing must be educated about the risks for false-positives, she says.

The first new checklist requirement, POC.08675 Quality Monitoring Statistics, calls for written procedures to monitor for the presence of false-positive results (owing to nucleic acid contamination, for example) for all molecular microbiology tests. The note says, “Examples of this may include review of summary statistics (eg, monitoring percentage of positive results relative to current local and regional rates and increased positive Strep results above historical rate within a run or over multiple runs), performance of wipe (environmental) testing, review and investigation of physician inquiries, and use of process controls to minimize risk of contamination.”

Molecular platforms amplify genetic material from an organism, and because of that amplification step, Dr. Karger says, “you just need a little bit of material to contaminate a sample and create a false-positive.” Environmental contamination is a worry in POC testing, says Sheldon Campbell, MD, PhD, a member of the Checklists Committee, “where neither the staff nor the environment is set up for contamination control.”

If one patient's swab is placed on a counter and it contaminates the counter surface, and another patient's swab is then placed on the same counter, the second swab could pick up genetic material from the first swab. If the first patient was highly positive, the result for the second patient who might be truly negative will be a false-positive, which is why, Dr. Karger says, the first checklist requirement cites wipe testing in the note.

Wipe tests, like any procedure, must be well thought out and require skill to be done well, says Dr. Campbell, professor of laboratory medicine at Yale School of Medicine. "You wipe potentially contaminated surfaces and put the swab into your molecular test to see if you are getting positives from your environment as opposed to from patients."

A point-of-care coordinator or supervisor who is observing and overseeing the staff's workflow should determine whether to do wipe testing, Dr. Karger says, though it's preferable to teach the best practice of not putting exposed samples where they could deposit genetic material. "If you have robust procedures in place where something like that wasn't happening, then perhaps you wouldn't feel like you needed to do wipe testing as a routine part of the process. That said, I do think occasional checks with wipe testing is a good idea." If a clinic found that it was seeing a much higher rate of positives, Dr. Karger says, then wipe testing would be part of the investigation to identify the source of the contamination.

A test could become contaminated if people are administering influenza immunizations and a vial of influenza vaccine leaks onto the area where influenza PCR testing is performed, Dr. Pritt says. Testing is often performed in a small area, in which the same counter might be used to prepare vaccines. "We want to raise awareness that those types of activities should be done in separate areas," she says. "These aren't just little boxes they can put on their countertop and put in a sample and get a result and not really think about it. They have to think about the entire process from start to finish."

Dr. Campbell

They have to understand, too, the risks associated with a false-positive. When patients present with respiratory tract symptoms and fever, Dr. Campbell says, the potential diagnoses include bacterial pneumonia, flu, congestive heart failure, and other conditions. If a molecular flu test is a false-positive owing to contamination, "providers may not work up other problems. They could treat the person for flu and send them home when the person has a bacterial pneumonia." Or a patient with a false-positive result could be treated unnecessarily, with Tamiflu perhaps. "That medication has side effects," Dr. Karger says.

The second new checklist requirement, POC.08690 Specimen Handling Procedures, calls for written procedures to prevent specimen loss, alteration, or contamination during collection, transport, processing, and storage. Collection, processing, and storage must follow the manufacturer's instruction, the note says, and limit the risk of preanalytical error. "For example," the note says, "there must be a procedure to ensure absence of cross-contamination of samples during processing/testing for respiratory specimens tested at the point-of-care that may be sent to the laboratory for further testing. It is also essential to follow the manufacturer's instructions for the handling of wastes (eg, used test cartridges) to prevent contamination."

Dr. Pritt says the CAP wants point-of-care labs to think of their entire workflow and have procedures in place to prevent loss, alteration, or contamination. "If they are going into that specimen and taking out an aliquot, are they doing that in a sterile manner? How do they prevent someone from contaminating that specimen?" Someone without laboratory training may not think of those things, she notes.

The cartridges contain amplified DNA that can cause false-positives, Dr. Campbell says, so it's critical to make sure they are disposed of in medical waste without harming the cartridge.

The third new checklist requirement, POC.08715 Safe Specimen Handling/Processing, says there must be written policies for safely handling and processing samples from patients with suspected infection due to avian influenza, SARS, Ebola, or similar emerging pathogens. The note says the policies may be part of an institution's plan but that the plan must address point of care specifically.

Dr. Pritt

The Microbiology Committee recognized that if a member of a community traveled recently and has become ill, he or she may go to the local emergency room, which may be performing waived molecular testing, or the person may just visit a local walk-in care clinic and not communicate that they traveled, Dr. Pritt says. "There have to be ways to still do the general testing required, such as influenza PCR, but the health care staff need to realize that if a patient just returned from the Middle East and had exposure to MERS, there are different considerations for obtaining and testing specimens. They may not even want to test the specimen there," she says, referring to the point-of-care setting. "That would be the type of discussion they'd need to have with their health care institution, and have a written plan in place for how to deal with specimens from patients with suspected infection with emerging pathogens."

The hope of the committee members, Dr. Pritt says, is that when an institution is creating its plan for high-consequence pathogens, that point-of-care settings be considered. "I do a lot of work with high-consequence pathogen planning at the institutional level. Measles is one of these pathogens," she says, "and we realize that people with measles feel relatively well." Because of this, they may have just a rash and slight fever and go to their local physician's office or an emergency or walk-in clinic, rather than the main hospital where the specimen will be sent to the microbiology laboratory. "We want to raise awareness that all institutions need to consider their point-of-care tests because that's where the patient may show up first—the point-of-care site."

The fourth new checklist requirement, POC.08730 Final Report, calls for the report to include a summary of the test method and information regarding clinical interpretation, if appropriate. The note says that for tests that may be performed by either direct antigen or molecular-based methods, including the test method in the report is important for result interpretation. "The report must include a brief description of the method if the methodology is not explicit in the test name," the checklist says.

Direct antigen tests for influenza have variable sensitivity, Dr. Pritt says, ranging from less than 40 percent to upwards of 95 percent, compared with molecular-based methods, for which the sensitivity is 95 percent or higher. "Now that we are starting to get into all of these options—antigen tests, PCR tests—it's important to include the method in the name or description of the test on the report, so that clinicians reading the report can use this information to interpret the significance of the result. For example, if a patient was tested by a less sensitive influenza antigen detection method, then it may not be safe to rule out influenza in that patient."

Group A strep antigen tests also have variable sensitivity—around 80 percent. "Some providers and laboratories prefer to use a diagnostic algorithm where a rapid test may be performed initially, and if negative, a second more sensitive test is performed," Dr. Pritt says. "Others prefer to use the most sensitive method first, which is generally a nucleic acid amplification method, but this may not always be easily and rapidly available."

Dr. Campbell says there was an "argument for access" with the antigen tests. "Back in the day, when there was

nothing but the antigen tests, I think they had a role, but that role is fading because there are better alternatives. The molecular tests cost more, yes, but you can charge more or bill more for them in environments where that matters, and the performance is markedly better."

Any lab using waived molecular-based microbiology tests in a CAP-accredited laboratory would have to comply with the requirements, says Lyn Wielgos, MT(ASCP), checklist editor for the CAP Accreditation Programs. "For example, if a chemistry department decided it wanted to put that instrument in its chemistry laboratory, it would be given an additional checklist that has the applicable requirements, such as the immunology checklist, to use for inspection."

Wielgos notes that supervisors in many labs have been asked to oversee multiple areas. So the labs may be performing testing in areas where one would not expect it to be done. "But it's not uncommon for an immunology laboratory to have a serology section that's doing different types of infectious disease testing that might include anything from the antibody testing to the direct antigen or the waived molecular method."

People working in limited service labs, Dr. Pritt says, might ask why they need to meet the requirements and contend with what they could see as a more complicated checklist. "The answer we would give is that these limited service labs are now doing fairly complex tests. Even though the tests are waived and easy to perform, the technology behind them is complicated and uses molecular-based amplification methods that may be prone to contamination."

"We are not requiring a lot of additional things," Dr. Pritt continues. There is no additional training. "We are not saying that you need a unidirectional workflow like with a negative pressure room and that sort of thing. But we want labs to be aware of the risks and have a procedure for preventing contamination, keeping an eye out for it, and being able to detect it."

Point-of-care testing in large health systems overseen by pathologists is the right model, says Dr. Campbell. "These are relatively simple tests, but a lab person ought to be involved in that testing," as far as education and developing practices and procedures. "Good laboratory practice is its own discipline," he says. "You wouldn't turn untrained lab people loose on a nursing process. You don't let untrained nursing people loose on a lab process."

Physician offices that perform CLIA-waived testing are required to have a CLIA certificate of waiver and are not inspected routinely by the CMS. "There's no enforcement at all in that kind of setting," he says. "The rules for waived tests are basically that you have the certificate of waiver, and you are supposed to follow the manufacturer's instructions."

Does he view that as a problem? Dr. Campbell quotes what he says is his favorite phrase in the medical literature; it's from an article on the Oregon Health Plan: "Cost, access, quality—pick any two" (Bodenheimer T. *N Engl J Med.* 1997;337[10]:720–723). "In the case of waived testing," he says, "we are giving priority to access, with some probable compromise in quality." That isn't necessarily wrong, he adds, but a lab professional ought to be involved. "Mandating it, regulating it, and making it happen could severely impair access. There's always a tradeoff. There is never a slam dunk 'this is the right way to do things' with no downsides," he says.

A decade ago, there were fewer analytes and no molecular tests at the point of care. "Ten years ago, I made jokes about it: 'One of these days, we will have molecular tests at the point of care. Ha, ha, ha,'" Dr. Campbell recalls. "I knew we would eventually but it was a long way off, and molecular tests at that time were hard to do in your lab, let alone in the clinic." Now the tests are performed by people on the floors who have no training in laboratory practice. That, he says, needs to change. There either has to be "a regulatory switch, so that trained laboratory people have a role in these things, or a switch in training, so that nursing education and physician education incorporate some accountable component of good laboratory practice."

"This is the beginning, not the end, of the move of molecular and other cutting-edge laboratory methods into the point-of-care setting."

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