Labs size up options for unpredictable flu

Charna Albert

December 2019—There aren't good flu seasons; there are just varying degrees of how bad they are.

That's the message the CDC wants people to hear, says Lynnette Brammer, MPH, lead for the CDC's domestic influenza surveillance team. It's what laboratories know well and why platforms, panels, and prescribing patterns are top of mind.

Brammer

The 2018–2019 flu season was unusually long, Brammer says. "That was probably the biggest standout. Influenza-like illness was elevated for 21 weeks. Our previous long was 20."

When the season began, H1N1 viruses were predominant, Brammer says. "It looked like it wasn't going to be a terrible season. And then it switched over to H3N2, which made the season long. We had never seen a season where we had two pretty much equal influenza A waves, but we did last year. And we didn't have much B activity, which we frequently see toward the end of the season."

The lesson reinforced by the last flu season? "Flu is unpredictable. I don't think any of us understands the interplay of factors well enough to say, 'This happened because of this,'" Brammer says of last season's atypical influenza A pattern. "The best explanation I have is, 'It's flu, and flu is unpredictable.'"

As for this season, "Here in the U.S., we've seen the H3N2 viruses, H1N1 at a slightly lower level, and influenza B viruses. We've got everything out there; all our options are open," she said in an interview in late September.

Australia's flu season this year, reported to be severe, was actually moderate but early, Brammer says. "It did happen early, so activity was high for the time of year it was happening, and from what I understand there were increases in testing. When you only look at positives, it looks bad, but people were just testing more," she says, adding that in general, "there is more and more testing done."

As a whole the Southern Hemisphere was a "mixed bag."

"In South America, some countries saw more H1 than H3, some saw more H3 than H1, some saw more B than others." Australia was H3 predominant, she says, and New Zealand had more B than A. "So there's just a mix. It's hard to say this probably predicts what we're going to see because sometimes it does and sometimes it doesn't."

Meanwhile, laboratories are weighing options and making changes.

For Arkansas Children's at Little Rock and Springdale, the goal was to pilot a CLIA-waived rapid molecular PCR influenza A/B test (to replace the Quidel Sofia Influenza A+B fluorescent immunoassay) in the emergency department by the end of 2019, most likely the Cepheid Xpert Xpress Flu, said Sherry Childress, BSMT(ASCP), section manager of molecular diagnostics and immunology, and Bobby L. Boyanton Jr., MD, pathologist-in-chief and section medical director of molecular pathology, in a recent interview.

"This rapid molecular flu test will be used for patients presenting with influenza-like illness who are not sick enough to be admitted," Childress says. "For patients with bronchiolitis or sick enough to be admitted, the BioFire

FilmArray respiratory panel will be the front-line test."

"We initially considered the Cepheid Xpert Xpress Flu/RSV test," Dr. Boyanton adds. "However, RSV is not the only respiratory virus that causes bronchiolitis. Our emergency room physicians felt the BioFire Film-Array panel was more helpful in this setting."

Childress (l), Dr. Boyanton (r)

The laboratory implemented the BioFire panel first, "but the Sofias came on board through point of care," Childress says. If the point-of-care program hadn't purchased the Sofias, there's a good chance the laboratory would already have implemented rapid molecular testing, she says. "In truth, the pieces weren't all put together as part of the big picture right from the beginning."

Between 2018 and 2019, the laboratory upgraded to the BioFire Film-Array Respiratory Panel Two (RP2) and high-throughput Torch system. This allowed interfaced results with the laboratory information system, automatic verification of negative specimens, and trained staff on off-shifts to provide around-the-clock testing.

Before implementing the Torch and RP2, the molecular laboratory day staff fed RP tests through two FilmArray instruments. The RP test had a 65-minute run time, Childress says. "We could only do about 16 tests on the extended day shift, and we'd always have a substantial test queue each morning. The RP2 assay, which we validated with the new Torch instrument, runs in 45 minutes. With four modules on our Torch, we could run up to 45 assays on day shift."

The laboratory began offering 24/7 RP2 Torch testing at the beginning of 2019 and it has become a "fast favorite," Childress says. "Of course, now we've given a mouse a cookie. Within a couple months of 24/7 coverage, emergency department staff were calling the lab to ask for results, indicating they couldn't let patients go home until RP2 testing was complete." Test use from January to August 2019 increased 45 percent compared with the same period in 2018.

Autoverifying negative specimens, which went live in August, is a first for the molecular lab, Childress says. "Lab technicians no longer have to go into the laboratory information system [Epic Beaker] and manually verify negative test results. We're surprised by the difference even this small change has made in workflow. Our average TAT is currently 1.4 hours, and that's without offering the test on a stat basis."

Dr. Babady

Memorial Sloan Kettering Cancer Center has used only the BioFire Film-Array respiratory panel since 2011. "During the outrageous 2017–2018 flu season, we were on calls every day trying to result things," says Esther Babady, PhD, MSK's director of microbiology services. That flu season sparked closer consideration of flu testing algorithms.

“Should we implement flu RSV separate from the respiratory panel?” In a cancer hospital, “should we only test for flu,” especially if the patient is going to be admitted and put in isolation because of respiratory symptoms? “Should we know what it is? And that conversation has been ongoing.” For now, patients get the full panel. “And as it gets faster,” Dr. Babady says, “there’s less incentive to add an algorithm to make it more complicated.”

MSK implemented the BioFire RP2 assay and Torch system in 2018 in conjunction with other changes: MSK’s laboratory moved at the end of 2017 from the main hospital to a new location only a few blocks away—but a sufficient distance in busy Manhattan to affect TAT significantly. “Most clinicians were quite familiar with how long the BioFire panel takes to run and expected results in 90 minutes or less. Because of the move we added 20 minutes, 30 minutes, sometimes an hour for the specimen to get to the laboratory,” she says. “The experience made everyone start thinking about implementing flu testing options outside the lab.” Part of what makes the Torch system attractive, she says, is that laboratory leadership is comfortable implementing the platform outside the clean microbiology lab and training non-microbiology staff to run it.

The plan is to install a Torch in 2020 at a new inpatient/outpatient center that will open in January at 74th Street, 10 blocks from the main laboratory. “That’s the first step in bringing micro outside the comforts of the clinical micro lab,” she says.

In the next few years, Dr. Babady and colleagues will think about a strategy for implementing CLIA-waived testing, with the aim being to provide the same level of care throughout the MSK system. If all of the challenges are addressed and the testing is implemented well, she says, “it can have a positive impact on any sort of algorithm we could put together.”

“One and done” is what made the Roche Cobas Liat appealing to the laboratory at Highpoint Health, a 79-bed acute care hospital in Lawrenceburg, Ind., says laboratory director Sandy Hoff, MLS(ASCP). “We realized we could provide better treatment to the patients.” Two were purchased in 2017 for testing ED patients. “The physician director was more confident that he was treating patients appropriately because of the test’s specificity and sensitivity” and despite the 2018–2019 flu season giving the two Liats “a run for their money,” Hoff says. An added bonus, she says, is that the Liat also performs a group A strep nucleic acid assay. “It provides results in a time frame that works with the ED. Patients can be tested and sent home with the appropriate treatment. They really appreciate that,” she says of the ED physicians and the lab’s switch from the prior antigen test. “It also helps with antimicrobial stewardship.” The lab now has a third Liat. “The ER collects the swabs, and they tube them down to us. The turnaround time is short and allows us to complete the test during the ED visit.”

Hoff

The laboratory also recently acquired the BioFire and added the RP2. “We’re trying to educate the physicians not to double test: ‘Don’t order the flu if you’re going to order the RP2 testing on it. Just order the RP2 if that’s what is needed. But if it’s flu season and it looks like flu, order the Liat,’” the lab advises.

Highpoint Health decided to expand its use of the Liat after Roche released its CLIA-waived version, so 23 Liats were placed in Highpoint Health-owned physician offices in fall 2019. Point-of-care staff will monitor for false-positives and other potential problems. “I think there might be a little sticker shock, but they’ll realize the value of treating quickly and appropriately and not using the antivirals when they’re not needed. That will come with time,” Hoff says.

NorthShore University HealthSystem in suburban Chicago implemented the Cobas Liat influenza A/B and RSV assay

in all urgent care centers and EDs during the 2017–2018 season. This followed the laboratory's study of 620 patients from January to June 2017 in which it implemented the Liat assay at one urgent care center and compared antimicrobial prescribing for respiratory disease with that of five other NorthShore urgent care centers that continued to use the Quidel QuickVue Influenza A+B assay, with confirmatory PCR testing for negative results (Benirschke R, et al. *J Clin Microbiol.* 2019;57[3]:e01281-18).

The centralized clinical laboratory evaluated the negative rapid antigen specimens by batched reflex confirmatory PCR testing using the DiaSorin Molecular Simplexa Flu A/B and RSV assay. Median TATs for specimen collection to result verification for the Quidel assay were 16 minutes and for the Liat 29 minutes (results were available during the patient visit). For the reflex PCR in the central lab, the median TAT was 21 hours.

Dr. McElvania

Liat testing resulted in a 12.5 percent increase in antiviral prescriptions for patients with positive results, from 69.9 percent with rapid antigen testing and reflex PCR to 82.4 percent with Liat, according to the study. Only 2.3 percent of patients who tested negative by Liat were prescribed antiviral medication, compared with 13.1 percent using the rapid antigen test with reflex PCR. "Both were statistically significant improvements in prescribing patterns," the authors write. "Our results suggest that the higher sensitivity and negative predictive value provide confidence in the test results provided during the patient encounter, thus positively impacting antimicrobial stewardship."

Antimicrobial stewardship is one reason why Erin McElvania, PhD, a coauthor of the study, believes rapid molecular PCR testing is worth its price. Moreover, a Liat test isn't necessarily more expensive than the cost of rapid antigen testing along with PCR testing to confirm negative results. "It's going to be somewhat institution-dependent, but at [NorthShore] we specifically priced our Liat at the same level as our batched PCR testing," says Dr. McElvania, director of clinical microbiology at NorthShore.

On the other hand, says coauthor Robert Benirschke, PhD, director of POC testing at NorthShore, for hospitals in a resource-limited environment, or where a large number of patients are paying out of pocket, rapid molecular PCR testing may be prohibitively expensive.

"The cost is a lot cheaper if you perform rapid antigen testing without backing it up with PCR," Dr. McElvania says. "It just has horrible sensitivity. But if the difference is between having zero testing and rapid antigen, I'd probably go with rapid antigen."

Charna Albert is CAP TODAY associate contributing editor.