Lab’s respiratory panel found to curb antibiotic use

Anne Ford

January 2014—Fewer children with respiratory disease symptoms hospitalized from the ED without a diagnosis, less antibiotic use, and a favorable ratio of reimbursement to expense. That’s what the laboratory at Children’s Healthcare of Atlanta is seeing, said Beverly B. Rogers, MD, chief of pathology, in a Nov. 5 webinar, “Focus on FilmArray: One New Technology Applied to Classic Clinical Problems.” Presented by CAP TODAY and made possible by an educational grant from BioFire Diagnostics, the webinar centered on the multiplex PCR system from BioFire that tests for viruses, bacteria, yeast, and antimicrobial resistance genes.

Stevenson

BioFire marketing director Wade Stevenson explained how FilmArray works. “It does sample prep, it does amplification, and it does detection” in one benchtop instrument, he said, adding that “it is capable of testing for dozens of targets, all in one reaction.” The user injects water into the FilmArray’s reagent storage device, then injects the sample and loads the instrument. At that point, the FilmArray performs the sample extraction and preparation, extracting and purifying total nucleic acids before delivering those acids first to a multiplex PCR chamber and then to a PCR array.

The Food and Drug Administration has cleared two panels for Film-Array: respiratory and blood culture identification. “We’re real excited,” Stevenson said. “We just finished our clinical trial for our gastrointestinal panel. We’re writing up the 510k submission now.” At BioFire, the hope is to have FDA clearance for the GI panel by mid-2014. “And then deeper in our pipeline, we have a meningitis panel for which we’re just now ramping up to begin clinical trials,” early in 2014, “and then [even] deeper in our pipeline, a lower respiratory panel.”

Dr. Rogers

Children’s Healthcare of Atlanta—a pediatric children’s health care system consisting of three hospitals and five community urgent care centers—began performing respiratory panel testing in July 2012 and has implemented eight FilmArray instruments across its two largest hospitals.

“Currently, most of the testing for the FilmArray respiratory panel is requested from the emergency department, and oftentimes these are children who are undergoing admission for respiratory disease,” Dr. Rogers said. Her laboratory has done more than 5,000 FilmArray respiratory panels since January 2013. “The throughput is one test per instrument, and so in order to handle the volume we have—which is extremely large, given the size of our health care system and the fact that we are a pediatric population—we need the additional instrumentation to run these tests 24/7.” The laboratory uses FilmArray to test for flu A and B, RSV, parainfluenza 1-4, human

metapneumovirus, adenovirus, coronavirus, rhinovirus, enterovirus, *M. pneumoniae*, and *Chlamydophila pneumoniae*. Because bronchoalveolar lavage specimens aren't validated on FilmArray, "we still do culture, but we also ask the pulmonologist, at the time of gathering the BAL, to please go ahead and swab the nasopharynx, so we can do a FilmArray as well."

Between August 2011 and mid-January 2012, that is, before Children's Healthcare began using Film-Array, the primary virus detected was RSV—"not a large surprise in a pediatric hospital," Dr. Rogers said. "We ran 426 panels during that time, but compare that with what happened once we brought on the Film-Array." Between mid-August and late December 2012, "for the Film-Array we ran 1,080 panels, because that many more were requested. In addition, we could detect viruses such as human metapneumovirus. One of our oncologists said, 'I had no idea that I should ever order a human metapneumovirus PCR, but indeed, that's what my kid had.'"

For a closer look at the effect of the FilmArray respiratory panel on patient care, Dr. Rogers pointed to a study, "Implementation of Film-Array respiratory viral panel in a core laboratory improves testing turnaround time and patient care" (Xu M, et al. *Am J Clin Pathol.* 2013;139[1]:118–123).

The study examined the experience of Seattle Children's Hospital, which implemented the FilmArray in its core laboratory, ran it 24/7, and gathered the resulting data for four months. During that time, test volume doubled and average turnaround time was 1.6 hours (as compared with seven hours for a direct fluorescence assay). Of 97 children with influenza A or influenza B seen in the emergency department, 45 percent were discharged with a diagnosis of influenza, and another 52 percent were given that diagnosis within three hours after discharge. "This means that the kids could receive oseltamivir. Fifty-two of 97 received the script in the ED, and another 27 received the script within three hours," Dr. Rogers said.

As for how FilmArray has affected patient care at Atlanta Children's, Dr. Rogers has enough data to tell the story and is gathering more. She and her colleagues are looking at cases of acute respiratory illness in hospitalized children three months or older, "because children under three months of age were treated on protocol regardless of FilmArray result," she said. "We wanted to get kids whose physicians would make a decision, based on the results of the respiratory panel, whether or not to treat with antibiotics."

Between November 2011 and January 2012, batch PCR (run once daily) was used on 361 samples, of which about 60 percent were positive, with a mean time to result of 19 hours. "Only 14 percent of the kids had a result returned when they were still in the emergency department," Dr. Rogers said.

"Now fast forward to when we have the FilmArray respiratory panel," she continued.

"Again, this is a time when we were looking at viral targets only." Between November 2012 and January 2013, the number of tests increased to 766, of which about 80 percent were positive, with a mean turnaround time of six hours and results available in the ED prior to hospitalization 52 percent of the time.

Dr. Rogers and her colleagues found that implementing the Film-Array respiratory panel reduced antibiotic use. Children with a negative panel result and a time to result of four hours or less spent, on average, 3.15 days on antibiotics, while children with a positive panel result and a time to result of four hours or less spent an average of 2.66 days on antibiotics. In contrast, in "kids who had a result turnaround greater than or equal to six hours, we didn't see that effect" of decreased antibiotic use. "So basically, the expanded panel's great," she said. "And turning it around in a short amount of time also really impacts patient care." This made it possible to justify additional technical staff for off shifts, she said.

Dr. Rogers and her microbiology manager have devised a ratio of reimbursement to expense, that is, the reimbursement received for a test compared with the cost of performing that test. "So a higher ratio means you get more reimbursement per cost," she said. "When we used ASRs, the ratio was 1.58 for patients covered by Medicaid. Then if you add in parainfluenza, it went down to 1.46. For the FilmArray respiratory panel, at a time when we were reporting less than 12 viral targets, because additional targets were still being validated, the ratio was 1.21. But as you increase the number of viral targets you report, and as you add in the bacterial targets, then what you get is really a much more favorable ratio of reimbursement to expenditure, which makes a hospital

administration happy."

To validate the assay, Dr. Rogers and colleagues used the Zeptometrix NATrol Respiratory Verification Panel (catalog No. NATRVP-IDI). A positive and a negative are provided for each target. They tested 24 samples, with four positive results and 20 negative results per organism. Correlation with the Zeptometrix verification panel was 100 percent.

Quality control is run once per week. "But we're actually thinking about decreasing that," Dr. Rogers said, "because, quite honestly, nothing has ever failed," and once a week is not required.

The CAP offers three proficiency testing Surveys—IDR, ID2, and IDO—each of which contains components of the respiratory panel. BioFire is the largest peer group in the IDR (Infectious Disease Respir-atory Panel) Survey, with 103 participants.

The FilmArray assay is considered moderate complexity, so it can be run by someone with a high school degree and appropriate training (assuming state regulations don't supersede this requirement). "Given that someone with a high school degree can perform this test, it is an instrument that could quite likely be placed in the front end of a laboratory, where specimen processing techs might do your rapid streps, that type of thing," Dr. Rogers said. At Children's, the FilmArray instrument sits between the microbiology laboratory and the core laboratory, with "either microbiology or core lab techs performing the tests."

A study to determine and quantify the complexity of FilmArray compared with direct fluorescent antibody found that the former required technologists to touch the instrument and related materials about 100 times, as compared with 300 times for DFA (Wang J, et al. *J Mol Diagn.* 2012;14[6]:748).

That finding, said Dr. Rogers, "leads us to say that the FilmArray instrument further simplifies respiratory viral testing by making it possible to move previously highly complex testing into the routine clinical laboratory, or even at the point of care. . . . Given the fact that you can turn it [the respiratory panel] around in an hour and a half, and it's a definitive test, it's just far superior to anything else out there, I think."

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Anne Ford is a writer in Evanston, Ill. The full webinar, including Frederick Nolte, PhD, on rapid identification of positive blood cultures, is on the Web at captodayonline.com.