Who, what, when? Bringing order to influenza testing

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November 2016—Raquel M. Martinez, PhD, D(ABMM), is very happy in her role as director of clinical and molecular microbiology at Geisinger Health System, Danville, Pa. But in another universe she might have applied her skills to television journalism instead. That's because like any good interviewer, she not only values sensitivity and specificity but also is fond of asking crucial questions such as "When?" "Who?" and "Where?"

That Mike Wallace-like skill set was on full display during "NAATs for Respiratory Pathogen Detection: Does the How, When, and Where Matter?" a talk she gave at the ASM Microbe meeting earlier this year.

A yearly algorithm, a triage system, and a dashboard keep molecular testing for respiratory pathogens on track at Geisinger. Random-access testing and a reduced TAT are saving the health system millions, says Dr. Martinez (left), here with Barb Heiter, BS, MT(ASCP).

In her presentation and in conversation with CAP TODAY, Dr. Martinez outlined Geisinger's extensive efforts in respiratory pathogen detection, the goal of which is to determine exactly which assays should be used for respiratory pathogen nucleic acid amplification, when those assays should be performed, and in what settings, and which include the use of a diagnostic algorithm. For Geisinger, the how, when, and where do matter—and they matter very much indeed.

Geisinger, a fast-growing health network with 12 hospital campuses, aims to standardize its laboratory processes and adopt best practices in microbiology. Donna M. Wolk, MHA, PhD, D(ABMM), Geisinger's system director for clinical and molecular microbiology, elected in January 2013 to stop offering rapid antigen testing on the grounds that such testing is inferior to nucleic acid amplification testing. "Geisinger's comparison of molecular and antigen testing confirmed published reports that the antigen test's sensitivity and specificity were lacking, and we never looked back," Dr. Martinez says.

Centers for Disease Control and Prevention guidelines say antigen testing results should be confirmed with a molecular method, owing to the speed and accuracy of those molecular methods. "And we are baffled that some hospitals and many urgent care clinics and office laboratories continue to use inaccurate antigen-based methods. Antigen testing, prone to both false-negative and false-positive results, serves only to delay an accurate result and diagnosis," Dr. Martinez says. She and Dr. Wolk are committed to providing their patients and providers with faster and more accurate methods, she says, and to proving the downstream impact of rapid technology. "Our advice to

anyone fielding requests to continue performing rapid antigen testing is 'Just say no.'"

In 2009, when the laboratory still performed culture and DFA for respiratory pathogen testing, the average time to result was 67.13 hours—nearly three days. In 2011, a batch-based multiplex PCR was implemented. "We batched them once a day, Monday through Friday, and we were able to decrease our turnaround time by almost 30 hours," Dr. Martinez says. Then, in late 2012, the laboratory adopted a non-batched multiplex test for respiratory pathogens, and the average turnaround time dropped—first to 11.68 hours, then to 5.9 in 2013 by distributing technology to more of the hospitals, and then to where it stands now at the end of the 2016 respiratory season, 2.83 hours.

With the goal of reducing large-panel testing—thereby reducing costs, lowering turnaround time, and maximizing efficiency—the Geisinger laboratory collaborates with infectious disease clinicians, pharmacists, and infection prevention teams to support an algorithm that defines which patients should receive which type of nucleic acid amplification testing and at what time of year. The algorithm is revised annually before the start of flu season. Samples are collected and submitted in universal transport media, with nasopharyngeal swabs preferred for upper respiratory tract samples and 1 mL bronchoalveolar lavage for lower respiratory tract samples. Samples from inpatients, emergency room admissions and observation units, and high-risk outpatient groups are tested with a multiplex PCR panel (available year-round). Samples from low-risk outpatients and non-admitted ER patients are tested with abbreviated panel testing for influenza A and B and respiratory syncytial virus (available Nov. 1–April 30, when those viruses are highly prevalent).

Dr. Wolk (center) with Francis Tomashefski, BS, MT(ASCP), and Lisa Scicchitano, BS, MT(ASCP). Laboratories in the U.S. are often falsely labeled as cost centers, Dr. Wolk says, but she and colleagues see their lab as a "cost recovery center," and they aim to prove it for every laboratory intervention they make.

"If a patient is categorized by our providers as low risk during winter months, then providers can opt for the abbreviated panel, to lower payments for our outpatients, while still identifying treatable influenza viruses," Dr. Martinez says. "But when a patient is categorized into an inpatient or high-risk outpatient category, like those who are immunocompromised, have cardiac or lung conditions, etc., then even untreatable viruses have diagnostic impact and providers are urged to request the full multiplex panel with 20 pathogens detected."

In addition to the algorithm, Geisinger has adopted a triage system for testing to ensure the most critical patients are tested first. Specimens from the ER are categorized as the highest priority, followed by specimens from the ICU and other inpatients, followed by outpatient specimens.

Having a triage system is important, Dr. Martinez says, because while turnaround time for this type of testing can

be low, throughput can also be low. “You can only perform testing one patient at a time. So if 10 people show up in the ER and we have only two available spots, well, guess what? Eight people are waiting. And during respiratory season, it’s really important to know if someone has the flu. So clinicians are dependent on the laboratory’s result, and if the laboratory doesn’t meet their expectation, then they call us looking for their result.” Having a triage system in place helps keep everyone’s expectations in order.

After gathering performance data for the two respiratory virus seasons immediately following the implementation of non-batched testing in 2012, the Geisinger team was awarded an investigator-initiated grant to conduct a pre- and post-intervention study that would determine how Geisinger’s patient population was being affected by the random-access testing and reduced time to result. The investigators wanted to learn how the rapid testing intervention was helping the sickest patients, so the study examined the care of ICU patients who received a full multiplex test. The study’s data variables included ICU length of stay, emergency room LOS, overall LOS, antibiotic and antiviral days, 28-day mortality, ventilator days, total costs per visit, and total laboratory test utilization.

“For positive and negative results, we observed equal distributions in both groups. At that time we decided to examine the clinical and operational impact of the improvements,” Dr. Martinez says. More important, she adds, they observed equal distributions between the treatable viruses (those with influenza) and non-treatable groups. “It is important to compare data from groups of patients that are well matched in terms of treatable virus infections, age, gender, and other factors. Otherwise your conclusion can be biased.”

The downstream effects of rapid testing in the post-intervention group were dramatic. The average time in the ER decreased by almost an hour and a half. ICU length of stay was reduced by three days. Average antiviral usage days dropped by 0.6, while antibiotic usage dropped by nearly two days. Mean overall length of stay fell by two days, while relative survival rose by 10 percent.

“We documented savings associated with both positive and negative test results,” Dr. Martinez said. “For the positive tests, we saved about $9,000 per inpatient stay. For the negative tests, we saved about $8,000 per visit. Even when the laboratory accounts for the cost of testing, our data shows that the health care system still saves nearly $4 million over the two-year rapid testing period. That’s huge.”

This study, Dr. Wolk says, documents the impact that a laboratory can make in terms of patient outcomes and reducing health care costs. “We believe that laboratories in the U.S. are often falsely labeled as cost centers, but we see our laboratory as a ‘cost recovery center.’ We are confident that laboratories can continue to reduce health care costs while improving patient outcomes and care.” She and colleagues aim to prove these concepts for every laboratory intervention they make. “And we encourage other laboratories to do the same,” she says.

By substratifying time-to-result data, Geisinger was able to associate a reduction in mortality with results that were available in seven hours or less. “The Geisinger experience may not be reflective of performance in other health care systems,” Dr. Wolk says, “but the results are compelling for studies in other centers.”

What makes seven hours the magic number at Geisinger? “Geisinger Medical Center has 24/7/365 coverage in microbiology and round-the-clock, on-site providers who can make decisions about optimizing therapy and other diagnostic tests, so this could prove to be an important infrastructure,” Dr. Martinez says. Not all hospitals have hospitalists or laboratory services around the clock, and not all hospitals have infectious disease pharmacy specialists, she notes. Perhaps most important, she says, “Geisinger has many algorithms, called Proven Care, and our physicians are focused on evidence-based care and collaboration with our laboratory.”

At the start of each flu season, the diagnostic algorithm is distributed to clinicians. Given how large Geisinger is and how rapidly it is expanding, getting and keeping everyone on board with the algorithm is a perpetual challenge. New residents, new faculty, and new nursing staff are the reasons the laboratory is educating constantly. “We publish reminders in our newsletters and can monitor compliance to the algorithm. If we contact providers about compliance with system recommendations,” Dr. Martinez says, “we find there is a high level of

compliance and very little misuse of resources."
Any provider can order the full respiratory panel. "We just recommend that they don't order it if it's not going to impact a downstream clinical decision or infection prevention measures."

Dr. Martinez realizes that Geisinger is unusual in using an algorithm for respiratory multiplex testing. She pointed to an informal survey conducted recently on the ASM listserv ClinMicroNet, whose members are clinical microbiology laboratory directors. Sixty-five percent of respondents had no testing algorithm for multiplex NAAT. "A lot of places do not have the infrastructure to maintain two testing platforms and provide such an algorithm," she says. "Others think identifying all viruses is important even for outpatients. We will wait for impact studies that support those options." Until then, Geisinger's interdisciplinary teams agree the algorithm works, as does providing a lower-priced testing option for healthy outpatients with influenza-like illness.

To take the triage system a step further, in summer 2015 the microbiology team began using the Web-based AltoSoft program, which Geisinger had purchased as part of a systemwide quality improvement initiative. Technologists no longer have to look at each specimen label to determine the ordering location; rather, the AltoSoft dashboard allows them to see easily and quickly where specimens originate. The dashboard color-codes specimens by department so they're easily identified and the technologists can spot one coming from the emergency room to get it processed more quickly, which in turn has helped to reduce ER wait times and patient admission processes.

The laboratory also uses dashboards to monitor turnaround time and ensure workload is properly balanced. And dashboards in the emergency department are placed on the desktops to deliver real-time results for ER patients. "Their monitors update every 10 minutes," Dr. Martinez says.

Another dashboard pulls respiratory pathogen information from the laboratory information system and displays it in real time so viral trends can be identified. "Last year flu came late, and after April 30 our system still had a lot of flu B circulating. So we decided to postpone turning off our abbreviated panel," she says.

As Geisinger continues to grow as a system, throughput will continue to be one of the laboratory's biggest challenges, Dr. Martinez says. "The platform we use is a closed system, so it's one patient per instrument per hour. And so if we have 100 people we need to test, and our system only has x number of instruments, we can face bottlenecks." A partial solution to that lies in the triage system. "Let's say our community hospital has a sudden increase in testing," she says. "We have a rule that if they predict five hours of backlog, they can call the system reference laboratory to help test specimens and maintain the turnaround time systemwide. That way, all of our patients receive the same accuracy, speed, and technology regardless of location."

The microbiology staff take great pride in delivering results to providers and patients, she says. "In 2016 our turnaround time sets the bar for other health care systems, and we are determined to document the impact of testing in our other hospitals and possibly even for outpatients." That's their commitment, she says, to their patients, their organization, and to the larger health care system in the U.S.
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