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CLN Clinical Laboratory News

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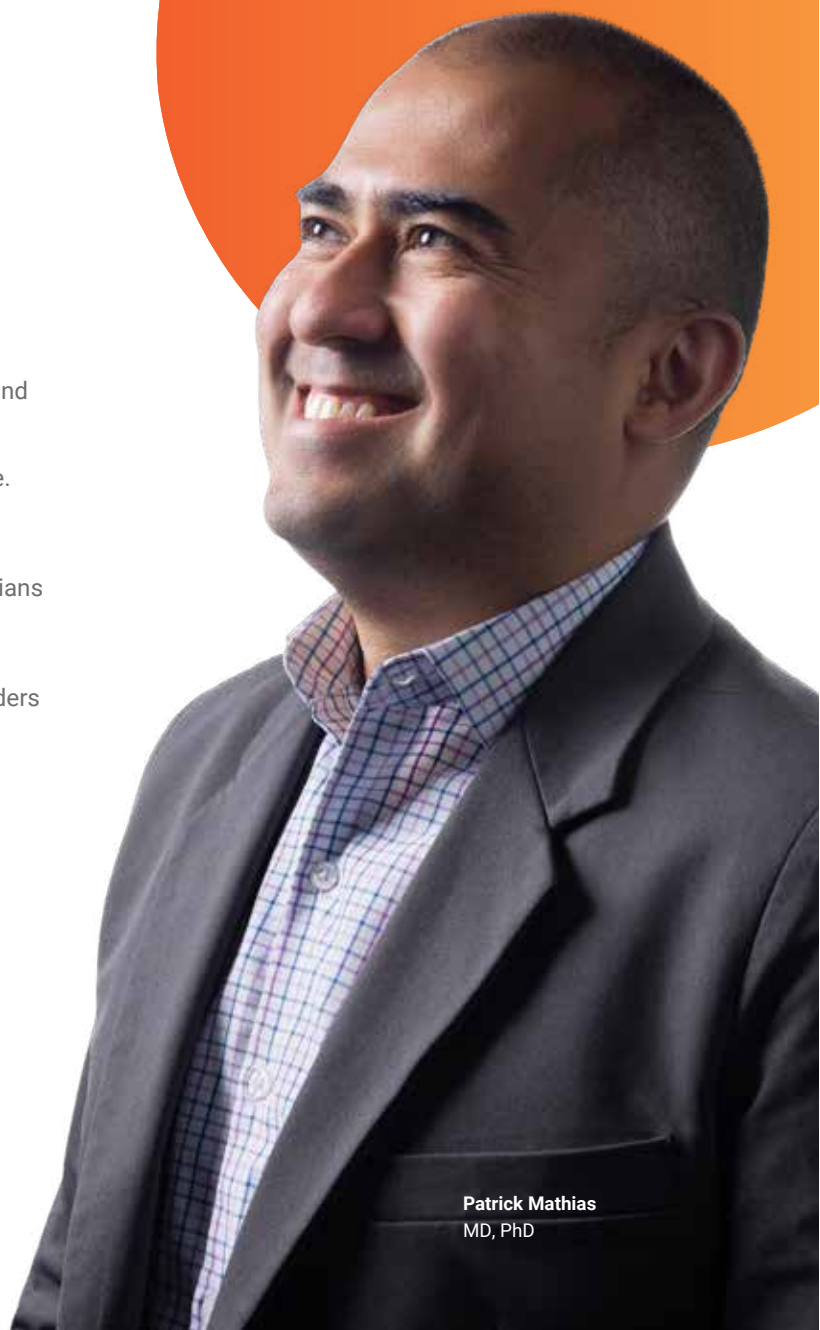

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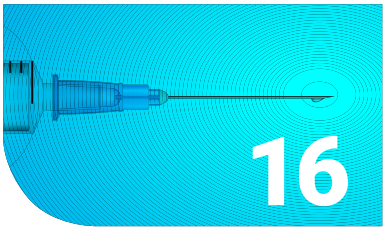

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DEPARTMENTS

"Traditional tests for [rheumatoid arthritis] detect the autoantibodies rheumatoid factor and anticyclic citrullinated peptide, but both of these may be negative in a small but significant percentage of patients."
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CMS Shifts Policy on Clinical Laboratory Director Role

The Centers for Medicare and Medicaid Services (CMS) has stirred controversy with its decision to alter regulations governing the qualifications of high complexity laboratory directors and recognize the Doctorate in Clinical Laboratory Science (DCLS) as an acceptable degree for this role. The final rule has prompted questions from key lab associations, including the Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC).

In a joint letter to CMS, the American Society for Microbiology (ASM) and ADLM voice reservations over what they see as inadequate public discourse about this shift and note that it was made without formal endorsement from the Clinical Laboratory Improvement Advisory Committee (CLIAC), which typically advises on such policies.

While ASM and ADLM acknowledge the importance of advancing education within the field, they stress the critical role of high complexity laboratory directors in overseeing complex laboratory operations, including the development and validation of laboratory developed tests (LDTs). "At a time when LDTs are facing increasing scrutiny from the Food and Drug Administration and the public, CMS must ensure that [high complexity laboratory directors] can meet these and other challenges," the associations wrote.

ASM and ADLM are asking that CMS hold a public forum conducted by CLIAC to address questions around qualifications for high complexity laboratory directors. Key stakeholders, such as the three universities that offer the degree, the CMS certifying boards, accrediting organizations, relevant professional societies, and other important parties should be invited to participate, according to the letter.

FDA PLANS RECLASSIFICATION OF HIGH-RISK DIAGNOSTIC DEVICES

FDA's Center for Devices and Radiological Health (CDRH) announced its intention to reclassify most high-risk in vitro diagnostic devices from class III to class II. The sweeping move initially targets infectious disease and companion diagnostic tests.

Reclassification would significantly streamline regulatory processes, allowing manufacturers to seek marketing clearance through the less rigorous premarket notification (510(k)) pathway instead of the premarket approval pathway that often requires clinical trials.

According to the FDA, the aim is to foster increased competition and accessibility as more manufacturers are expected to develop these tests. The reclassification proposal focuses on devices where sufficient information exists to establish what the agency calls special controls, ensuring safety and effectiveness.

This initiative aligns with CDRH's risk-based approach to device classification and periodic reviews to ensure appropriate regulatory oversight, according

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to the agency. Previous reclassification efforts have included nucleic acid and serology-based tests for hepatitis B virus, serology tests for human parvovirus B19, and cell-mediated immune reactivity tests associated with tuberculosis infections.

HHS SETTLES $4.75M CYBERSECURITY CASE WITH MONTEFIORE MEDICAL CENTER

The U.S. Department of Health and Human Services (HHS), Office for Civil Rights (OCR), announced a $4.75 million settlement with Montefiore Medical Center in New York City, covering multiple potential violations of the Health Insurance Portability and Accountability Act (HIPAA) Security Rule.

The investigation unearthed revelations that over a 6-month period, an employee at Montefiore Medical Center stole protected health information of 12,517 patients and sold it to an identity theft ring. The breach was initially brought to light by the New York Police Department in May 2015. Under the terms of the 2024 settlement, Montefiore Medical Center must implement a comprehensive corrective action plan.

In light of increasing cyber threats, OCR is urging providers to bolster their cybersecurity posture by implementing robust safeguards, including vendor oversight, regular risk analyses, audit controls, multi-factor authentication, encryption, and staff training.

OCR noted that more than 134 million individuals were affected by large breaches in 2023, an increase over the 55 million affected in 2022.

Breaking Down Body Fluids

Ping Wang, PhD, D(ABCC), FADLM

Daisy Unsihuay, PhD

The analysis of body fluids is crucial for diagnosing and managing diverse pathological processes. These fluids are categorized as off-label specimens because they fall outside the manufacturer's intended use claims. Consequently, they undergo validation procedures to meet regulatory standards, but interference studies in body fluids are typically are carried out separately during this validation process. The rationale behind this is that if accuracy studies via mixing serum and body fluid samples find no significant difference, both are considered to be similar matrices. As a result, the manufacturer's interference cutoffs for serum and plasma are transferable for body fluid testing.

A review of hemolysis, icterus, and lipemia (HIL) interference in body fluids suggests variations in the frequency and magnitude of these interferences across different fluid types (*1*). For instance, drains and pericardial fluids often yield higher H- and I-indexes compared with serum and other body fluid types. Of note, these fluids are less frequently included in validation studies compared with the more commonly used serous fluids, such as ascitic or pleural fluids. This raises questions about whether the current approach of extending HIL rules oversimplifies the complexity of body fluids, prompting considerations for the development of HIL-based body fluid specific flagging rules.

MEASURING INTERFERENCES

Studies on interference are commonly conducted to mimic endogenous interference caused by hemoglobin, bilirubin, and lipids. For hemolysis interference, hemolysate typically is prepared from red blood cells and spiked into the body fluid specimen at known concentrations. To simulate icterus interference, a solution of bilirubin conjugate is added to the fluid specimens. Reproducing interference by lipemia or turbidity is challenging due to the absence of standards that can account for the variety of lipoproteins. One approach often employed is to spike the body fluid with a lipid emulsion, such as intralipid. In all cases, the spiking solution represents 5–10% of the total volume (*2,3*). Because there are no defined total allowable error (TAE) thresholds for analytes in body fluids, conservative thresholds of 10–15% typically are adopted for the comparison with the control body fluid. Another approach for assessing interference involves dilutions using body fluids presenting naturally high HIL indexes and comparing results between the diluted and the undiluted body fluids.

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REPORTING RESULTS AND CLINICAL UTILITY

Different approaches can be taken when it comes to reporting results in the presence of interference. Some labs may opt to use the same flagging rules used for serum and release the results regardless of the magnitude of the interference with a comment indicating the type of interference and suggesting that the result

be interpreted with caution. Other labs may embark on establishing their own flagging rules to set interference thresholds that, if exceeded, will trigger review to determine if the result should be released based on clinical utility or canceled if interference is abnormally high. Given the irreplaceable and irretrievable nature of body fluids, it is important that any result reported be as informative as possible despite the interference.

Published studies on interferences in body fluids suggest that cutoff values are slightly different for certain analytes compared with serum (*2*,*3*). For example, an H-index limit causing a 10% increase in a pleural fluid protein can occur at less than 50% of the H-index listed for serum. Special attention should be directed towards lactate dehydrogenase (LDH) as this is the most affected analyte in the presence of hemolysis (similar to serum) and results spike rapidly with increasing amounts of hemolysis. On the other hand, analysis of amylase, creatinine, and lipase in serous fluids are reported to have markedly lower thresholds for icterus interference than in serum samples. In contrast, most analytes present similar tolerance as in serum for lipemic interference. Integrating these results with clinical utility is paramount to ensuring appropriate patient management. For example, the presence of hemolysis in a pleural fluid would falsely elevate LDH results and increase the risk of misclassifying a transudate (<60% URL serum) as an exudate (≥60% URL serum) using Light's criteria.

Given the irreplaceable and irretrievable nature of body fluids, it is important that any result reported be as informative as possible.

Likewise, the presence of icteric interference in pleural fluid may falsely decrease cholesterol values, increasing the risk of misclassifying an exudate (>45 mg/dL) as a transudate (≤45 mg/dL).

Creating flagging rules for all analytes and fluid types is a tough job that demands many resources from the lab, which many may not be able to afford. A possible solution to this issue could be taking an analyte- and fluid-type-specific approach to determine the scenarios where further interference studies are warranted. This would require identifying the most common interferences for each fluid type, determining the analytes with the lowest thresholds that could be affected by these specific interferences, and integrating all of this with clinical significance based on published studies. For example, a Jackson Pratt (JP) drain fluid submitted to assess for a pancreatic leakage will be prone to icterus interference. In this context, amylase has been extensively documented as an indicator of a pancreatic leak if its value is three times higher than serum. Therefore, it is more relevant to pursue icteric interference studies in amylase when validating JP drains than in pericardial fluid where clinical utility has not been reported.

Regardless of the chosen approach to reporting results in the presence of interference in body fluids, close collaboration between the lab and clinicians is essential for interpreting results, especially for analytes with significant known clinical utility.

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The Sample

Preanalytical Errors Identified Via Machine Learning Without Expert Labeling

Laboratories can accurately detect IV fluid contamination in basic metabolic panel (BMP) results using machine learning, even without curating expertly labeled training data, according to a recent report (Clin Chem 2023; doi: 10.1093/clinchem/hvad207).

Detecting IV fluid contamination is universally difficult for clinical laboratories. Contamination commonly causes preanalytical errors that can delay or misguide treatment decisions and potentially lead to patient harm.

Detecting contamination now relies on delta checks that require prior results or manual technologist intervention vulnerable to human error. Supervised machine learning may help detect contamination but requires expert-labeled training data and classifiers that can detect only anomolies for which they are specifically trained. Proposed solutions involving supervised learning algorithms have historically required a substantial investment to curate expertly labeled training data.

In response, researchers trained and tested a Uniform Manifold Approximation and Projection (UMAP) model using a combination of real patient data and simulated IV fluid contamination on a total of 25,747,291 BMP results from 312,721 patients with data in a laboratory information system.

To provide an objective metric for classification, the researchers derived and assessed an "enrichment score," comparing researchers' usual workflow using expert chart review to UMAP predictions.

UMAP embeddings showed outliers suspicious for IV fluid contamination when compared with the simulated contamination's embeddings. At a flag rate of 3 per 1,000 results, the positive predictive value was adjudicated to be 0.78 from 100 consecutive positive predictions. Of these, 58 were previously undetected by current clinical workflows, with 49 BMPs displaying 56 critical results.

The researchers said they focused on IV fluid contamination as a proof of principle and called for future studies of the UMAP model involving other body fluids, common laboratory errors like mislabeled specimens or hemolysis, and incorporation of other common laboratory panels, such as complete blood count and liver function panels.

OBESITY AND SMOKING LINKED TO BLOOD CANCER PRECURSOR DETECTION

Mass spectrometry (MS)-detected monoclonal gammopathies are associated with a broader range of modifiable multiple myeloma risk factors than what has been previously identified (Blood Adv 2024; doi: 10.1182/bloodadvances.2023010843).

Individuals with obesity are more likely to have monoclonal gammopathy of undetermined significance (MGUS), a benign blood condition that often precedes multiple myeloma, the paper noted.

MGUS has few known risk factors, and the emergence of MS for the detection of MGUS has

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provided new opportunities to determine risk factors.

Researchers conducted a screening study and an exposure survey of 2,628 individuals at elevated risk for multiple myeloma. The researchers screened their samples using MS and categorized samples with monoclonal proteins (M-proteins) at concentrations greater than 0.2 g/L as MS-MGUS. Using multivariable logistic models, the researchers evaluated associations between exposures and outcomes.

Elevated body mass index (BMI) and smoking were associated with all MS-positive cases.

After controlling for age, sex, race, education, and income, the team found that obesity was associated with 73% higher odds of having MGUS, compared with nonobese individuals.

This association remained unchanged when accounting for physical activity. However, highly active individuals were less likely to have MGUS even after adjusting for BMI class. Samples from individuals with high physical activity — defined as more than 73.5 metabolic equivalent (MET)-hours/week versus fewer than 10.5 MET-hours/week — had a decreased likelihood of MS-MGUS (OR=0.45, 95% CI= 0.24 to 0.80, P=.009).

Individuals who reported heavy smoking and short sleep (less than 6 hours per night) were more likely to have detectable levels of MGUS.

The researchers said that the presence of MGUS serves as a warning to monitor for the condition developing into more critical conditions.

Obesity was associated with 73% higher odds of having monoclonal gammopathy of undetermined significance.

POTENTIAL GESTATIONAL DIABETES MARKERS HIGHLIGHTED

A recent analysis concludes that pregnancy insulin resistance, or hypertriglyceridemia, may be useful in gestational diabetes mellitus (GDM) risk stratification (Nat Commun 2023; doi: 10.1038/s43856-023-00393-8).

Perinatal outcomes vary for women with GDM. Because the precise factors beyond glycemic status that may refine GDM diagnosis remain unclear, researchers conducted a systematic review and meta-analysis of potential precision markers for GDM.

The researchers searched for precision markers in several categories. These include maternal anthropometrics, clinical/sociocultural factors, nonglycemic biochemical markers, genetics/genomics or other "omics," and fetal biometry. Afterwards, the researchers conducted posthoc meta-analyses of a subset of studies with data on the association of maternal body mass index with larger than average offspring or large-for-gestational age (LGA).

Unsurprisingly, the researchers found that high maternal weight is a risk factor for offspring born larger for their gestational age. Women with GDM and above-average weight/obesity versus women with GDM and healthy BMI are at higher risk of larger-than-average offspring (OR 2.65; 95% CI 1.91, 3.68), and LGA (OR 2.23; 95% CI 2.00, 2.49).

Researchers found other promising markers. Lipids and insulin resistance/secretion indices were the most studied nonglycemic biochemical markers, with increased triglycerides and insulin resistance generally associated with greater risk of offspring macrosomia or LGA. Most studies examining lipids in association with adverse perinatal outcomes have measured a standard lipid panel that includes total cholesterol, LDL and HDL cholesterol, and triglycerides. Half of the studies reported that higher triglycerides, independent of BMI, were associated with larger than average offspring or LGA, with fewer studies finding that higher LDL or lower HDL was associated with neonatal size. Not all studies included in the review reported positive associations, and many factors, such as differences in timing of blood collection and variability in the distribution of characteristics across studies, could explain inconsistencies. Few studies examined the joint effects of multiple lipid subclasses.

The researchers noted gaps in the literature. These include inadequate data to determine whether a predominant defect in insulin secretion without excess insulin resistance is related to adverse perinatal outcomes, associations between adipokines and adverse perinatal outcomes among women with GDM, and genetic markers that predict adverse outcomes.

The What, Why, and How of Gender Cultural Competency

Clinical laboratories should explore the latest resources in training for phlebotomy staff to take the lead in providing equitable care for all of their patients.

Cultural competency in healthcare is the ability of health systems to provide care to patients with diverse values, beliefs, and behaviors, including tailoring delivery to meet patients' social, cultural, and linguistic needs (*1*). Some prefer the term "cultural humility," which implies a commitment to learning and improvement rather than mastery (*2–3*).

Improving the cultural competency of providers may help improve care outcomes among marginalized populations (*4*), including sexual and gender minorities, such as those who identify as lesbian, gay, bisexual, transgender, and queer (LGBTQ). These populations face significant health disparities as well as discrimination, ignorance, bias, and even abuse from healthcare providers (*5*). Focusing on improved knowledge of gender diversity is especially important as social acceptance and awareness of transgender individuals have lagged behind the acceptance of people with diverse sexualities (*6*).

Although efforts have been made in the healthcare community to promote quality educational resources for healthcare professionals about cultural competency, they primarily have focused on education for students and patient-facing advanced medical professionals, such as medical students, physicians, nurses, and dentists. Educating laboratory medicine professionals, especially patient-facing staff such as phlebotomists, on how to interact with

BY GABRIELLE WINSTON-MCPHERSON, PHD, DABCC, AND HENRIETTA (FASANYA) MAKU, MD, PHD

gender-diverse patients is a significant step towards improving healthcare for this patient population (*7*).

EDUCATION FOR THOSE WHO NEED IT MOST

It is crucial that phlebotomists are fully equipped to interact with transgender patients in a professional, courteous, and dignifying manner. In the field of phlebotomy, there are multiple barriers to quality care for transgender patients, such as a lack of understanding of appropriate terminology, possible discrepancies between legal and preferred name and gender, and challenges with urine collection instructions (such as inappropriate gendered instructions)(*8–10*).

Educating phlebotomists on appropriate gender terminology and how to have respectful interactions with transgender patients creates an environment of inclusion and openness for these patients. This improves care by decreasing the anxiety and avoidance associated with interacting with the healthcare system (*9–11*).

Members of the transgender community who are prescribed gender-affirming hormonal therapy will require a significant amount of interaction with phlebotomists, especially during the evaluation of therapeutic hormone concentrations (*12*). Ensuring that patients are comfortable in their healthcare environment and maintaining a mutually respectful relationship with providers at all levels of care is essential to improving patient outcomes for gender-diverse people.

Members of the transgender community who are prescribed gender-affirming hormonal therapy will require a significant interaction with phlebotomists.

HOW TO DEVELOP EDUCATION ON CULTURAL COMPETENCY

While phlebotomy staff must demonstrate gender-cultural competency, how to provide adequate education remains a challenge. To date, no universally accepted standard dictates what or how phlebotomy staff should be taught about conducting culturally appropriate interactions with members of the gender-diverse community. This means that details of the staff training process are decided by their respective institutions, often at the department level.

Fortunately, there are some general guidelines that institutions can tailor for their staff. The World Professional Association for Transgender Health Global Education Institute (WPATH GEI) has a robust certification program that strives to advance knowledge, skills, and cultural awareness around four core competencies: the caregiver/care receiver relationship, content knowledge, interdisciplinary practice, and professional responsibility. Structuring a phlebotomist-focused transgender cultural education program around these four competencies is an excellent place to begin.

Mandi Pratt-Chapman, PhD, and colleagues also published consensus recommendations for developing and implementing an LGBTQ cultural competency education program (*13*). The consensus standards were determined by a group of experts with diverse professional roles, work settings, gender identities, sexual orientations, and racial or ethnic identities. They summarized five key recommendations for all training initiatives:

1) Training must be audience-specific, which may require conducting a needs assessment. Additionally, the goals of the training should be clearly delineated and applicable to the

Table 1. Phlebotomy Training Resources

Resource	Organization	Website
Transforming healthcare: A guide to best practices in LGBTQA+ cultural competency training	Whitman-Walker Health Institute, The National LGBT Cancer Network	https://culturalcompetency.org/curriculum-fundamentals/
Advancing effective communication, cultural competence, and patient-and family-centered care for the lesbian, gay, bisexual, and transgender (LGBT) community	The Joint Commission	www.jointcommission.org/lgbt
Affirmative services for transgender and gender-diverse people: Best practices for frontline health care staff	The Fenway Institute	www.lgbtqiahealtheducation.org/publication/affirmative-services-for-transgender-and-gender-diverse-people-best-practices-for-frontline-health-care-staff

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learners, and it is critical to communicate why the education is vital for the learners specifically.
2) The curriculum should include foundational concepts (e.g., social determinates of health, disparities, and intersectionality), terminology (e.g., transgender, gender-expression, and dysphoria), and methods to avoid stereotyping and be resilient in challenging situations.
3) The education ought to employ effective modes of delivery by using multiple strategies for interactive learning (multimedia, case studies, narrative, and self-reflection).
4) Choose trainers with expertise in applicable sexual and gender minority healthcare topics and try to include trainers with diverse lived experiences and skill sets. Importantly, the trainers should be able to respond to strong emotional reactions.
5) Evaluate the education to assess effectiveness.

The recommendations by Pratt-Chapman and core competencies from WPATH GEI provide an excellent framework for developing a transgender-oriented cultural competency education program, but they omit the specific content needed to populate the training. Several reputable organizations provide this information for use and adoption (Table 1).

A CALL TO ACTION

Cultural competency education in phlebotomy is the responsibility of the lab medicine community. We understand the unique challenges this may present to phlebotomists, and how their typical practices —showing respect by using the terms "sir" or "ma'am," for example —may not work for gender-diverse patients. Additionally, there are regulatory concerns related to patient identification when the preferred name and legal name do not match. It is the task of laboratory leaders to ensure phlebotomy staff have the tools they need to overcome these challenges and interact with gender-diverse patients in a respectful and affirming manner.

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From ensuring proper instrument function to quality control, laboratories are using point-of-care testing technology to boost efficiency and patient safety.

THE VALUE OF

REMOTE MONITORING IN POINT-OF-CARE TESTING

BY ALICE PEDERSEN, MBA, MLS(ASCP)

When asked why point-of-care (POC) testing is gaining popularity, the most common answer is real-time test results; next is cost efficiency and ease of use. But there are so many more benefits of POC. With ever-advancing technology and interface capabilities, and when utilized properly, POC can be used by labs to remotely monitor and offer support in multiple areas, such as instrument functions, regulatory compliance, and patient safety.

While there are numerous choices of interface systems in the market, I am most familiar with Telcor because it is the system used at my institution. And after speaking with POC coordinators from other organizations, I realized that many of us follow the same daily, weekly, and monthly tasks. I wonder how many of us truly understand the significance of these routine tasks and how they benefit the clinical staff and, ultimately, patients?

MONITORING ESSENTIAL INSTRUMENT FUNCTIONS

One of the daily tasks POC coordinators do is checking instrument functions in the interface system — in our case, Telcor's QML. We check to see when the instruments last communicated with the system. From the time stamp, we can determine if there is a potential issue with the interface connections. We then contact the unit if their instrument has not communicated for some time.

The specific time frame is dependent on the instrument type and facility location. For example, Inform II, ID NOW, Coaguchek, and iSTAT instruments should always stay connected. On the other hand, we have found that Cliniteks sometimes take a while to connect or reconnect, especially in rural sites where interface connections or Dynamic Host Configuration Protocol (DHCP) IP addresses are not as abundant. We typically wait a couple of days prior before contacting the units for Clinitek connections.

The benefit of this monitoring process is detecting potential issues before they become significant problems. It can be either the interface or the instrument that is having issues. For example,

a common cause for Inform II meters not communicating with our system is that the meter is not sitting and charging in the dock properly. This enhanced feature of remote monitoring enables our POC team to proactively contact the units before they even realize the problem — or contact us — due to instrument trouble.

REMOTE QUALITY CONTROL REVIEW

Reviewing quality control (QC) performance and results is another daily task. We review QC performance for all interfaced instrument types, including those instruments that have QC lockout. This is to ensure instrument settings have not been changed in error. Though many instrument types have QC lockout, there are still some that do not, such as iSTAT or ID NOW. During the daily monitoring/review, we confirm that QC was repeated with acceptable results if there was a QC failure. If there are no acceptable repeat QC results, we check to see if any patients were tested during that timeframe.

We have noticed that for Cliniteks, if a QC is repeated within a minute of the failed result, the repeat result sometimes does not cross over to the QML system. In this case, we check the instrument on-site to see if the QC was indeed repeated with acceptable results.

QC review also helps monitor operator performance. If we see the same operator repeatedly failing QC, we may reach out to see if they would like retraining or need other assistance. At one of our sites, we recently noticed an increased number of QC results not crossing into the system, even though review of the Clinitek results in the instrument on-site showed they had been performed. After investigating, we discovered that if the operator scanned the 2D barcode on the QC vials, the results would not cross from the instrument to QML. To resolve the problem, we recommended the site black out the 2D barcodes on the QC vials and instructed staff to manually enter the QC lot number.

For iSTAT, we monitor in QML to confirm that QC frequency was within the 31-day timeframe and to ensure compliance with the individualized quality control plan. We also review cartridge lot numbers used for patient testing and confirm that QC was indeed performed on each new lot prior to patient testing. This monitoring process ensures regulatory compliance, instrument performance, and patient safety.

In addition to QC review, we also review monthly wipe tests for instruments such as Liat and ID NOW. Wipe tests must pass in order to continue patient testing. This ensures regulatory compliance and protects against contamination.

MANAGING OPERATOR ACCESS AND ASSIGNMENT

The next routine monitoring task is to add, renew, or remove operators from the system. Many of the interfaced instrument types in use do have operator lockout. Due to the number of sites we oversee, we synchronize the sites to seven competency cycles. Regardless of when new hires start, their competency cycles get synchronized to their department. To monitor training for manual tests, we grant access to interfaced tests only after the manual test training has been completed as well.

Before granting access, our POC team checks the learning management system (LMS) to confirm if the operator has completed both components of the course: an online course and a hands-on observation checklist, both completed by an approved POC train-the-trainer. Upon completion, unit managers can validate the training in the LMS.

We grant permanent staff instrument access by their badge ID barcode. Traveling staff are granted instrument access based on a temporary barcode we create.

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WE REVIEW QC PERFORMANCE FOR ALL INTERFACED INSTRUMENT TYPES, INCLUDING THOSE THAT HAVE QC LOCKOUT.

For nonwaived instruments, we monitor and assign courses for initial, 6-month, and annual competencies accordingly. Unit managers also confirm that operators of nonwaived instruments have fulfilled the diploma requirements. All these steps are implemented to ensure all operators performing patient testing are trained properly. This translates into better patient safety and more accurate, reliable results.

In addition to ensuring appropriate training, we also assign the specific locations where the operators perform testing. This is especially important for the nonwaived test platforms, where competency must be completed at each individual site. At the time of assignment, we also set the access expiration date to ensure annual competency is completed to retain access.

EXCEPTIONS OR RESULT CHARTING ISSUES

Each day, our POC team reviews exceptions where the test results are not posted to patient charts due to a variety of reasons, such as scanning the wrong label, instrument error codes, or the presence of critical results or emergency barcodes. There are multiple reasons a sample label scan might be incorrect, such as the encounter label being wrong due to a patient registration error, or scanning a label not associated with the correct patient encounter.

The system automatically stops the questionable result from being delivered if the patient scanned did not have a valid encounter for that date and time. This is a safeguard against results charting to the wrong patient. Emergency barcodes are used for cases where patients have not yet been registered but need immediate assistance. In this case, the unit provides the test date, test time, patient name, date of birth, and the patient MRN or account number to the POC team. Once we obtain the needed information, we add the result to the patient chart.

USING INFECTION CONTROL REPORTS

Due to feedback and observations, we started compiling monthly infection control reports for some of our sites to ensure proper glucose meter cleaning between patients. This process was recommended by the hospital infection control team. There were concerns that the portability of the glucose meter may spread disease from one patient to another.

Using the QML software, we can pull monthly data of the glucose results by site. We analyze this data using a Microsoft Excel macro. The final report shows the percentage of tests that were not in compliance with the glucose meter cleaning policy. This is the number of tests where the test time between patients was less than 4 minutes.

To ensure proper cleaning and sanitation, the meter needs to be wiped and left to air dry for 4 minutes. This cleaning/drying time is dependent on the bleach wipe type. Though this method is not perfect, it does offer a minimal check to assess compliance with the proper cleaning time.

The report also includes the list of units and operators that were not in compliance. Each month, these reports are sent to the infection control team, compliance team, and managers of each facility. They use the information to educate their team and to take needed action to improve patient safety.

ADDING UP THE BENEFITS

The POC functions mentioned above provide a general picture of the benefits to the healthcare system. With the current monitoring process, we have been able to view instrument functions, QC review, operator access, and resulting issues. We also have been able to gather data and create reports to meet the specific needs of different testing sites. As technology continues to advance, these monitoring capabilities will enable POC to further improve its capacity to ensure compliance and patient safety.

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A destructive new drug is exacerbating the fentanyl crisis, but clinical labs have ways to help treat and protect patients.

THE TOOLS TO BEAT TRANQ

BY JEN A. MILLER

As the opioid crisis continues along its destructive path, a new factor has entered the fray to make drugs more lethal: xylazine. The drug, which is also known as "tranq," has traditionally been used in veterinary practice as a tranquilizer but is now being mixed with fentanyl, placing people who use drugs at a higher risk of adverse effects.

Joshua DeBord, PhD, senior scientist at the Center for Forensic Science Research and Education, suspects that tranq is added to fentanyl to do one of three things: "Increase the euphoria, increase the sedation, or increase the potential addiction," he said. It's also possible that makers of the drug believe it somehow prevents overdoses caused by fentanyl when used in combination.

The mixture of fentanyl and tranq, like other emerging novel psychoactive substances (NPS), is also created to avoid detection, said Harvey W. Kaufman, MD, medical director and head of the Health Trends research program at Quest Diagnostics. "We're seeing a shift towards these synthetic drugs that are being developed by innovative chemists as a way to evade detection through traditional drug testing."

A GROWING PROBLEM IN U.S. DRUG SUPPLY

In a recent report, Quest Diagnostics found xylazine in nearly 1 in 12 samples of fentanyl, making it the most popular NPS drug in the U.S., particularly in the eastern part of the country. Five percent of those samples were positive for other NPS drugs.

In addition, Quest found that 37.7% of fentanyl-positive specimens were also positive for xylazine, and that 97.7% of specimens positive for xylazine were also positive for fentanyl. "They're so common already everywhere that no one's immune at this point. Every part of the country has been exposed to relatively high levels of these NPS drugs," Kaufman said.

Because xylazine is still relatively new in the drug market, it can be hard to recognize and treat — and it's having devastating effects. Because it's not an opioid, Narcan doesn't work in reviving people, and thexylazine injection itself can also cause recalcitrant skin ulcers and gruesome necrotic wounds.

Xylazine has never been studied clinically in humans, so it's still a mystery just how much of the drug is required to cause terrible consequences, said Adina Badea, PhD, DABCC, director of toxicology at Rhode Island Hospital and assistant professor of pathology and laboratory medicine at the Warren Alpert School of Medicine at Brown University. For example, "we don't know how much xylazine it takes for someone to develop skin ulcers," she said. People who use xylazine can also have an "almost sleep-like sedation, they can collapse in an uncomfortable position," she said, which can lead to compartment syndrome, requiring limb amputation. "There's a lot we don't know."

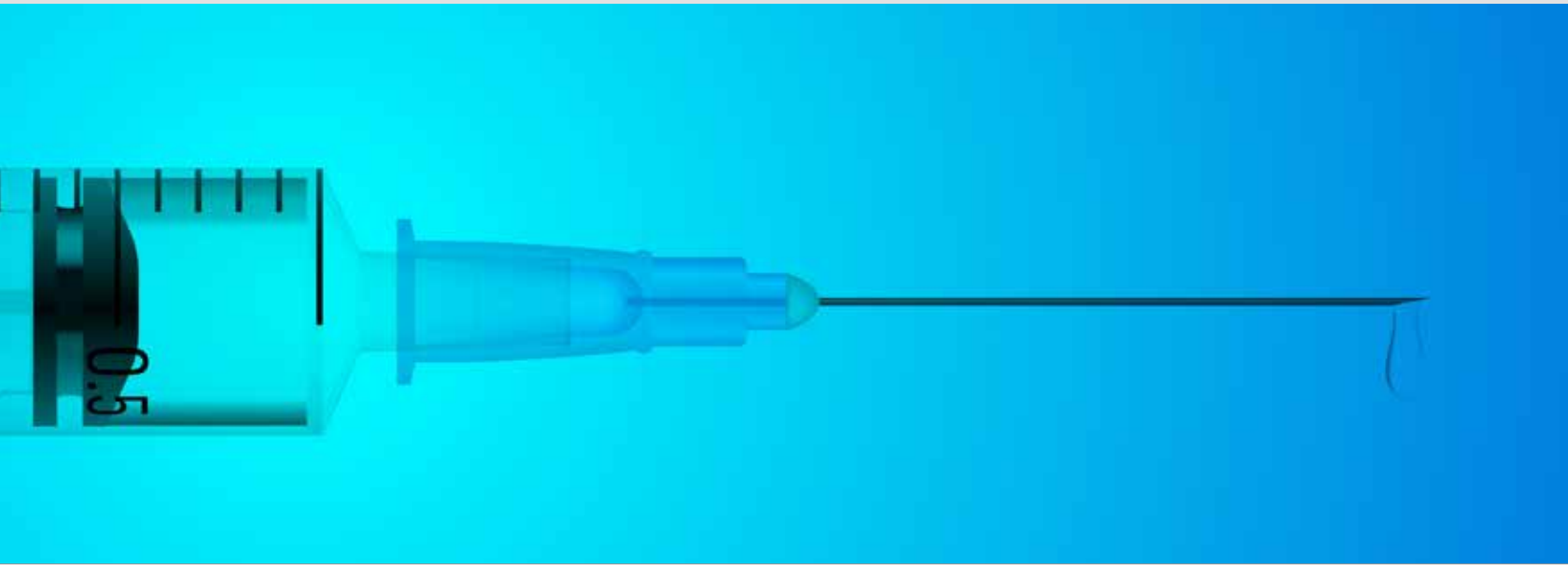
TESTING FOR XYLAZINE IN THE CLINICAL LAB

Although xylazine was designed to evade drug tests, clinical laboratorians have been catching up. "We've seen significant utilization, more than we anticipated," Jennifer Colby, PhD, DABCC, FADLM, scientific director at Premier Biotech, said of her company's test. Most of their customers are coming from the addiction treatment and substance use disorder space. They perform liquid chromatography-mass spectrometry to test for the presence of xylazine and related metabolites.

Like Quest, Premier Biotech found that not all fentanyl contains xylazine, but "when xylazine is present, fentanyl is almost always present," Colby said.

That can help avoid unnecessary testing when xylazine is unlikely to be present. "In terms of testing, we get a lot of orders for xylazine on people who have no history or no recent history of fentanyl use. If the fentanyl screen is negative, the xylazine screen almost always is going to be," Colby said.

Rhode Island Hospital offers a comprehensive drug screen for xylazine in urine and serum with liquid chromatography-high resolution mass spectrometry, said Badea. "The nice thing about an



untargeted method on a high-resolution mass spectrometry platform is that you can very easily add compounds to the list that you are monitoring," she said.

Still, it took some time for the test to catch on with emergency department physicians, and to educate clinicians about xylazine and how it might present. "Mass spec assays in general take a longer time to perform, because they have a relatively intense sample prep, so we wait to batch samples — although this assay was designed to be faster," she said, with results taking 1–2 hours once the sample arrives at the lab.

Over time, physicians began to use the test more as they became more familiar with it, saw more people being affected by xylazine, and realized they could still deliver results to patents after they were discharged, she said.

The first adopters of their test were pediatric physicians "because kids get into everything," she added. "A lot of the times with kids, the amounts of drug present are not high enough to trigger a positive result on a typical immunoassay drug screen, even if they are exposed to a drug the test is designed for. But the clinical impact is still profound, so this is where a mass spec test with increased sensitivity, specificity, and a more comprehensive panel can be really impactful."

Modern clinical and toxicology labs have the equipment to test for xylazine, said DeBord. "There is nothing especially challenging about the compounds, but labs must make the financial investment to expand their testing capabilities," he said, adding that he believes it may not be worth

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the investment if a lab is already testing for fentanyl and there is no established use of xylazine in the area.

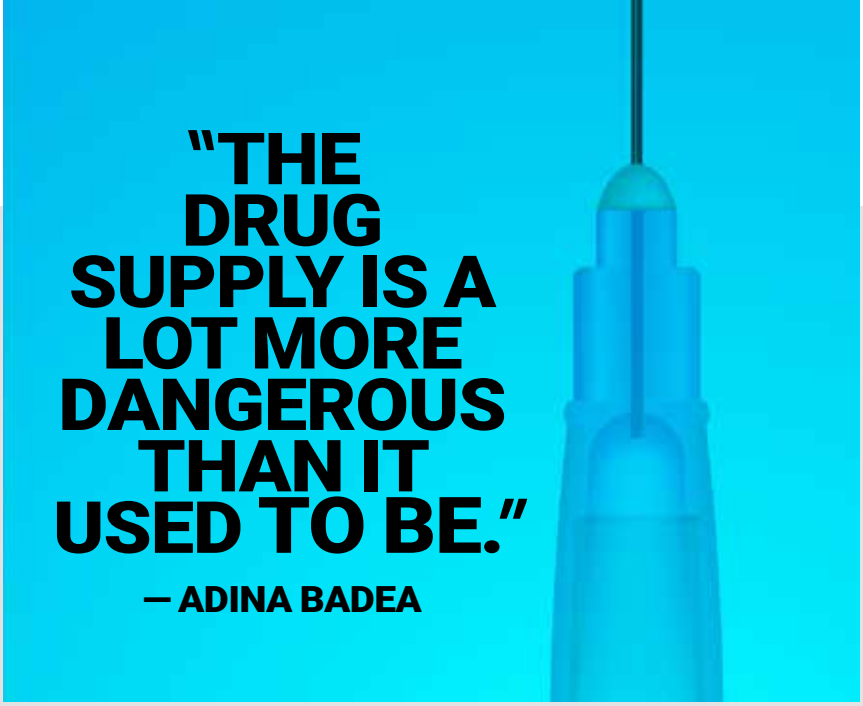
WORKING IN THE PUBLIC HEALTH SECTOR TO TEST FOR XYLAZINE

While collaborating with physicians is important for xylazine testing, so is partnering with the professionals who interact the most with drug users.

"There's an opportunity for significant interplay between the people who are doing the testing in biological samples and the people at the front lines doing harm reduction work, where they're providing xylazine test strips so that users can test their actual drugs," said Colby. County health departments also have a lot of information on what's being found in drugs, which can help "to determine if it's appropriate to offer a xylazine urine test."

Rhode Island Hospital is part of a 2-year program called testRI that tests used equipment, such as pipes and syringes, which are donated from community members or local organizations. In the first published results, which appeared in the International Journal of Drug Policy and involved 125 samples, they found fentanyl in 67.2% of samples and xylazine in 41.6% (2023; doi: 10.1016/j.drugpo.2023.104118).

But they don't just publish those results in medical journals. Instead, the Rhode Island Department of Public Health publishes test results for specific samples, anonymously, every 2 weeks on the Prevent Overdose RI website (https://preventoverdoseri.org/local-drug-supply/#tests).



"Some participants told us they showed their testing results to their sellers," said Badea.This information is critical "to inform people that the drug supply is a lot more dangerous than it used to be, and they should be taking some precautions before they use, such as not using alone," she said.

THE FUTURE OF NPS DRUGS

While the medical and laboratory community is now aware of the xylazine problem, it's not the only NPS drug, and may not be the most common one for long. Which drugs are used most changes quickly. For example, in their report, Quest found that the rate of heroin-positive samples dropped off to 0.4% in 2022. Their data suggests that fentanyl's superior potency and lower cost is pushing heroin out of the nation's drug supply.

"This is going to continue to evolve," Kaufman said. "We're going to continue to look at other compounds that are going to be identified in the ensuing months and years, and modify our test offerings, as we've done over time to meet what's actually being used."

The harm reduction movement needs to continue to be a key player too, said Colby, since these professionals see the effects of drugs firsthand. "There's a potential to partner with people on the front lines who know what's going on with users, whereas we're measuring downstream," she said.

Clinical laboratorians should also stay on top of NPS trends in other geographic areas, which might indicate that a new drug is going to hit their market soon. Badea, for example, said she first learned about xylazine by reading news reports of what was happening in the substance use disorder community in Philadelphia. Then, she said, "with untargeted data collection on high resolution mass spec platforms you can retroactively survey your data to see if this has been present in your patient samples, but you just weren't seeing it because you didn't know to look for it." If so, you can add that compound to the list of drugs you're testing for. "I find it very useful to further keep up with how the drug supply is changing, and how fast it's changing."

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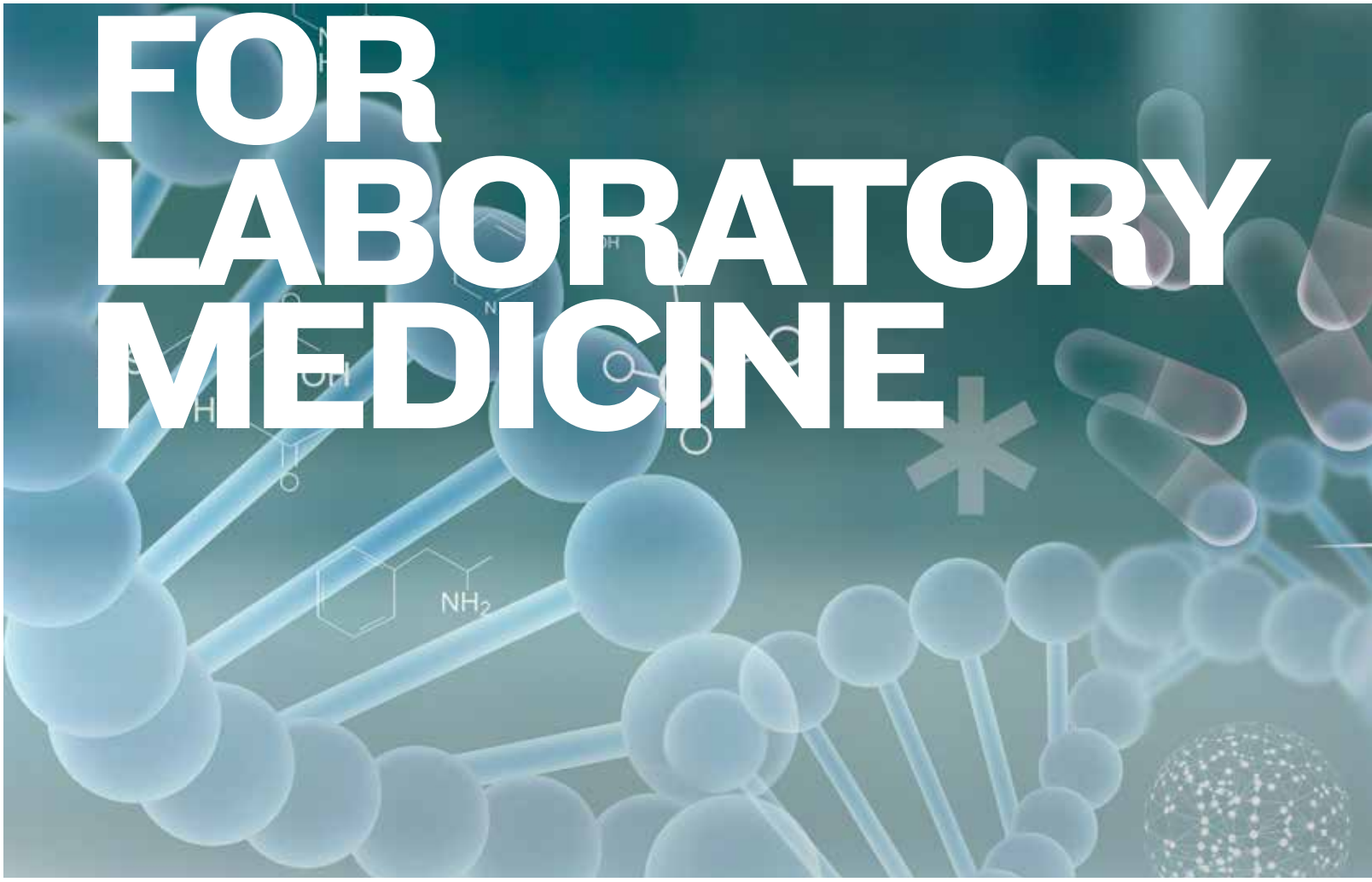
WHAT LIES ON FOR LABORATORY MEDICINE



A conversation with Jason Park, MD, PhD, editor-in-chief of *Clinical Chemistry*, who tackles AI, publishing, and the future of laboratory medicine.

BY JEN A. MILLER

Jason Park, MD, PhD, FCAP, DABCC, is the Robin M. Jacoby, PhD Professor of Biomedical Science and a professor in the department of pathology with an adjunct appointment in the Eugene McDermott Center for Human Growth and Development at the University of Texas Southwestern Medical Center. He is also the clinical director of the advanced diagnostics laboratory at Children's Health, Children's Medical Center Dallas. Park has been an active laboratory medicine community member since 2004 with more than 250 publications and 14 patents to his name.

Park is also currently the editor-in-chief for the journal *Clinical Chemistry*, widely considered the preeminent journal of laboratory medicine, published by the Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC).

THE HORIZON

We recently spoke to Park about trends in the field, where it's heading in the future, and what young clinical laboratorians should keep in mind as they progress in their careers.

Can you tell us about your goals and why you went into laboratory medicine?

Back in the '90s, I was in my thesis laboratory in graduate school, and that laboratory had spun out a cancer biomarkers company. From that point in time, I became very interested in biomarkers, diagnostic technologies, and in the commercialization and clinical use of those technologies. I was fortunate that I was able to continue that type of work during my pathology residency.

While there, I met a mentor and a friend who became very influential to me: Larry Kricka, DPhil, FACB, FRSC, former president of the association and an international leader in clinical chemistry and molecular diagnostics. Notably, he had not one or two but multiple successes in commercializing his inventions in analytical technology. Through Larry, I was introduced to ADLM, and I really learned, not just about discoveries and research, but also

about the importance of being part of organizations and collaborations. It's thanks to him that I developed this love for the discovery and development of diagnostic technologies.

As the editor in chief of *Clinical Chemistry*, what do you see as the 5-year goal for the journal?
The journal will continue its leadership as the preeminent journal in laboratory medicine and will also continue as a forum for all aspects of laboratory medicine. Over the last 20 years, the journal has come to focus not just on clinical chemistry, but also on other areas of the clinical laboratory, such as mass spectrometry and molecular diagnostics. It has also covered a wide range of diseases — everything from cancer to clinical microbiology. Over the next 5 years, the journal will continue to grow in these areas, and we are actively working on establishing the journal's role as a leading publication in emerging areas such as artificial intelligence.

Speaking of AI, what do you think of large language models (LLMs) such as ChatGPT, and what do you expect their immediate and long-term impact to be?
LLMs are probably the best example of how AI can become rapidly implemented once it's shown to be useful. Over the course of the last year, everyone noticed that LLMs such as ChatGPT were rapidly adopted. Anyone who has family members or close contact with people in school, anyone from middle school through university and graduate school, they know this type of technology was

NEW TECHNOLOGIES IN PROTEOMICS, GENOMICS AND AI ARE ALL GOING TO LEAD TO RAPID CHANGE IN THE ROLE CLINICAL LABORATORIES PLAY IN HEALTHCARE SYSTEMS THROUGHOUT THE WORLD.

As you scan the laboratory medicine field, what new trends do you see emerging?
Over the past decade and certainly the past year, not just in the professional realm but in all parts of society, we have recognized that AI will be significant. In laboratory medicine, this significance will permeate every aspect of our practice — everything from education to professional training to quality control to scientific publication. We've seen such a rapid rate of adoption of AI that I'm really uncertain what the next 3 years will be like. But I'm certain that they will be different, and I'm certain that over the course of the next years and next decade AI will be central to radical change in all areas of medicine, not just laboratory medicine.

used within months of it being deployed. These technologies have demonstrated their usefulness as everything from study aids to writing tools. They became adopted at such speed that educators and students have not yet fully adapted to this type of change.

I think that specifically in the professional environment over the past year, we have seen LLMs make a dramatic impact on how research studies are designed, how discoveries are made, and how publications are assembled or written. ChatGPT and other LLMs are the forerunners of many more technologies that will come out over the next 5 years.

Is there space in the field for a more concerted international approach to laboratory medicine?
I'll look at this from the journal and society perspective. As we know, ADLM is an international organization that has long been part of education and collaboration not only within the United States community, but also the international community. *Clinical Chemistry*, a journal of ADLM, has been part of that international outreach and collaboration.

By identifying how practices may differ in different countries and different regions of the world, we can find best practices and then achieve those best practices through things such as standardization and harmonization.

In your opinion, what can the laboratory medicine community do nationally and internationally to best prepare for the next epidemic in order to prevent a global pandemic?
From the journal's perspective, I was fortunate to be part of the journal when Nader Rifai, PhD, was editor in chief in the late days of 2019 going into 2020. Rifai did a number of important things in terms of identifying that this was a significant crisis, even in the early days of December 2019, and decided that as a journal, our role should be to disseminate information rapidly. This was important and successful because, if we

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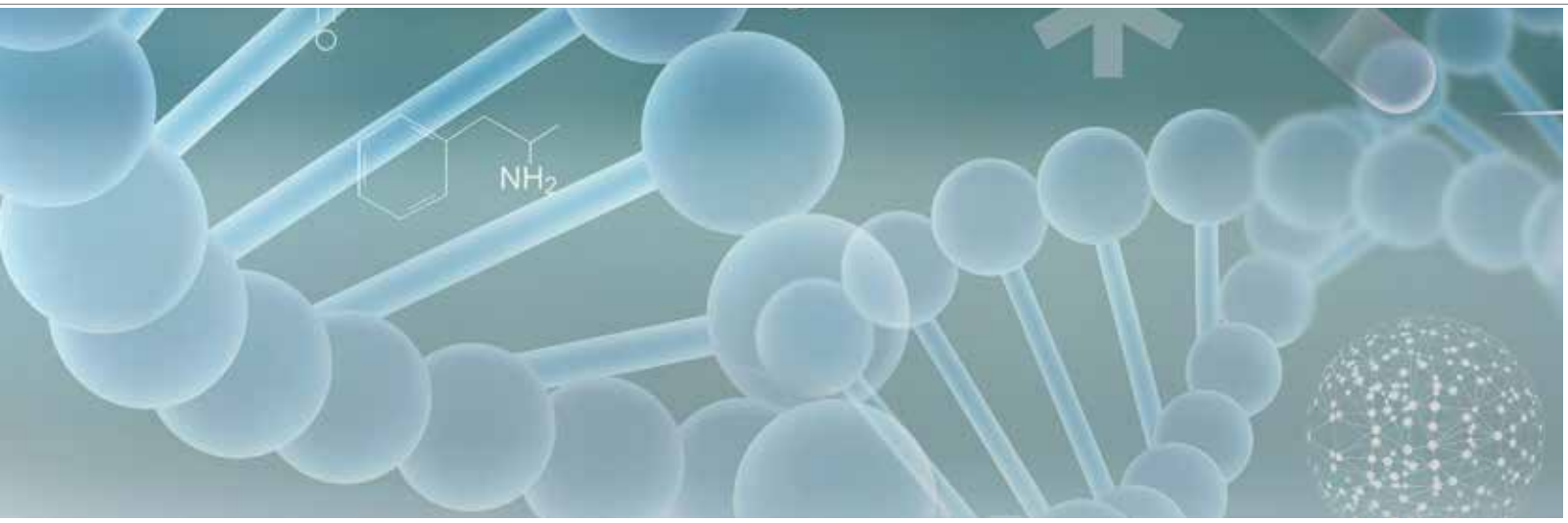

look at those early publications in *Clinical Chemistry* on COVID-19 from January 2020, those studies were widely cited, not just in scientific publications by other journals but also in the general news media.

The journal as a scientific voice has the ability to identify topics of growing importance, such as regional epidemics, and to publish research and expert commentaries on those epidemics. The journal can also widely disseminate that information, so that people are aware of what is going on. The dream would be to mitigate the next global pandemic by rapidly communicating critical information reviewed by experts.

What hurdles do you see facing laboratory medicine in the next 5 to 10 years?

New technologies in proteomics, genomics and AI are all going to lead to rapid change in the role clinical laboratories play in healthcare systems throughout the world. A major challenge for the laboratory medicine profession will be to maintain relevance in this period of change. During any period of rapid technological change in history, there has been an emergence of new disciplines and new jobs. On the flip side, there are career disciplines that become obsolete during those times of change. Laboratorians need to embrace and adopt new technologies in order to maintain expertise, relevance, and for our field to continue to thrive.

If you could magically make something happen in the laboratory medicine field, what would you like to see?

In an ideal world, we would provide excellent patient-centered care without financial or regulatory burdens. Unfortunately, the reality is that to provide excellent clinical care, we need to be adept at the financial and regulatory demands of providing a clinical service.

Based on your success, what information would you pass along to early career laboratory medicine professionals?

I think that one of the many strengths of laboratory medicine as a career is that it can be a very long and enjoyable one – a career can last decades. Given this long career trajectory, which hopefully many of us will have, it's helpful to identify and work towards both short-term and long-term goals. Having this combination of goals that can be achieved over varying periods of time can lead to different types of professional experiences and different rewards. Short-term goals could be things like achieving something personally in terms of a publication or implementing a change within the workplace. A long-term goal could be preparing to lead a work group or a society as an officer and then becoming involved with things like scientific journals.

Another important thing I've recognized over the last couple of years through my career and through watching the careers of my colleagues is that it's important to be open to changing career directions. As opportunities emerge, or unanticipated life events happen, it's important to be open to changing and redefining personal success and goals. It's important not to be so fixed on those goals that you can't adapt. There are always new ways of finding personal success, especially in laboratory medicine.

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AN INTERVIEW WITH NATHAN A. LEDEBOER, PHD

Implementing Molecular Testing for Gastrointestinal Infections in Clinical Practice

By Jen A. Miller

FOCUS ON MOLECULAR DIAGNOSTICS

Molecular diagnostic technologies have revolutionized testing for gastrointestinal infections in many areas of clinical practice. But they haven't entirely kicked other kinds of diagnostics off the field — at least not yet.

We spoke to Nathan A. Ledeboer, PhD, professor of pathology at the Medical College of Wisconsin and associate chief medical laboratory officer for Froedtert and the Medical College of Wisconsin, about the role of molecular testing in this area today, figuring out the reimbursement piece of the puzzle, and what the future might hold.

What are the most common gastrointestinal infections affecting patients under your care?
Let's break this down into those patients who have had gastrointestinal-related illnesses in the U.S. and those who may have traveled. We tend to see both.

Among those that acquire it in the U.S., there's community-acquired and healthcare-acquired gastrointestinal illnesses. The two most important things that we deal with in the area of healthcare-acquired infections are *C. difficile* and norovirus.

When we think about community-acquired pathogens, the most common ones we see are those you would expect: *Salmonella*, *Shigella*, Shiga toxin-producing *E. coli*, and *Campylobacter*. We also see a fair amount of community-acquired norovirus, but we don't test for that frequently.

With travelers, it will depend upon where they have been. If they've traveled to a developing nation, we most commonly see traveler's diarrhea, which is usually *Enterotoxigenic E. coli*.

What are the advantages of using molecular tests for detection of gastrointestinal pathogens?
There are two really significant advantages. First and foremost is the turnaround time. We've moved gastrointestinal pathogen testing from a rather passive process under culture with turnaround times of 2–3 days to getting results in as little as 2–3 hours with molecular testing.

It's also improved sensitivity. For example, with Shiga-toxin producing *E. coli*, we see differences of sensitivity of 50% or greater. With *Campylobacter*, *Salmonella*, and *Shigella*, that improvement can be from 10% up to 30–40%.

There's also a third advantage I see. It's increasingly more difficult to find staff in the clinical laboratory. Being able to perform these tests with a molecular approach helps. Working up lots of negative stool cultures is generally not something people want to do in the laboratory, and it also takes a lot of time. So, addressing this with a more straightforward approach to testing can help with staffing challenges as well.

What have you learned since implementing molecular testing for gastrointestinal infections in routine practice?
We've talked about the improvements in sensitivity, and we've talked about the improvements in turnaround times — both very impactful for patient care. However, we're still facing a reimbursement picture that has become significantly more challenging.

When many of these molecular tests emerged, in most cases we were able to get paid for what we tested. Today that is certainly not the case, and it will vary depending on where you are in the country. Developing a reimbursement strategy and ensuring that your payers buy into that is incredibly important.

Along the lines of reimbursement, with a test that is primarily run in the ambulatory environment, laboratories also need to take into consideration the patients' cost. In areas where you have many patients who may be on a high deductible healthcare plan, depending on the size of the panel you are running, that patient may be facing a bill ranging from $100 to $500 to even $800. Patients push back significantly when they get a large bill from their healthcare center. The pushback comes to places like primary care offices and urgent care providers. Then they push back on the laboratory test menu.

I believe laboratories need to develop a high level of understanding

how reimbursement works in their markets. Really doing what you can to address costs for patients and the healthcare system while also performing testing at a high level of quality is important. Balancing those is a huge challenge.

Are there specific patient populations that see most benefit from molecular diagnostic testing?
Everybody benefits from a better turnaround time. Everybody benefits from a higher degree of sensitivity.

One of the groups which I believe has really experienced a great deal of advantage is immunocompromised patients, who come in with a couple of days of diarrhea. The clinical team is really trying to determine whether it is infectious or if there is another underlying condition or cause. If our clinical partners can quickly rule out an infection, that helps them a great deal.

Do you think that molecular testing will replace more traditional methods like culture and microscopy in the near future?
I don't think that they'll entirely replace culture and microscopy, but I think it will change the order.

For gastrointestinal illness, as a screen we've already seen a significant shift towards molecular testing. Cost, however, can be and will continue to be important and can be a driving factor in why some health systems, clinics, and laboratories continue to choose culture.

For gastrointestinal illness, as a screen we've already seen a significant shift towards molecular testing.

That's something we really do have to continue to address. How do we provide this level of testing and make it affordable to patients so we make it easy to do the right thing?

There will also continue to be value in performing culture for certain scenarios. For example, many daycare facilities and schools will require a negative test if a child has been diagnosed with Shigella. You can't necessarily do that with molecular tests because we know DNA can hang out in the stool for an extended period.

We continue to need isolates to do good public health, and in order to do good epidemiology and susceptibility testing. Getting isolates is important for that. In the near future, and even intermediate future, we're going to continue to need culture.

What do you see as the future of molecular testing?
I think we're going to see a couple of different trends. Costs are coming down as testing becomes more democratized. That's a good thing. We are also seeing increased adoption.

I believe we will see the biggest advancement in the antibiotic-resistance space, and in the future push further and further into next generation sequencing. I think that's going to be an area where we're going to see a great deal of development and investment in hospitals.

The other thing that really needs to be considered is whether we can, as a field, get together with our insurers and start to develop guidance around what's going to be paid regardless of what you test for. It allows us as healthcare providers to focus on what we need to do in the best interest of the patient.

Some of the testing panels will probably change over time. For example, for an immunocompromised patient, the clinician will want to be a bit broader in workup of this patient. For patients with travel or exposure to an environmental source where parasites would be in the differential, molecular testing for the appropriate array of parasites could be selected by the provider.

With a healthy adult, maybe we are only interested in the big four, versus an elderly patient in a nursing home where we're concerned about the spread of norovirus. If we can start to think about reimbursement a bit differently, we can then start to think about what we test for in the context of the patient. Instead of developing panels based on what we can and can't get paid for, we can instead build panels for patients' underlying disease state and what is needed for patient care.

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AN INTERVIEW WITH DAVIDSON HAMER, MD , FACP, FIDSA, FASTMH, FISTM

How PCR Testing Enhances Surveillance Capabilities for Gastrointestinal Pathogens

FOCUS ON MOLECULAR DIAGNOSTICS

By Jen A. Miller

PCR testing has become increasingly important for gastrointestinal pathogens. These tests are also key in surveillance to detect what kinds of pathogens affect a particular population, and as a frontline tool in detecting foodborne and waterborne outbreaks.

We spoke to Davidson Hamer, MD, FACP, FIDSA, FASTMH, FISTM, professor of global health and medicine at the Boston University of School of Public Health and Chobanian & Avesidian School of Medicine, and adjunct professor of nutrition at the Tufts University Friedman School of Nutrition Science and Policy, about how molecular tests such as PCR are used in this disease area right now, and what their role could be in the future.

What gastrointestinal pathogens are most common cause of outbreaks in the U.S.?

Norovirus, nontyphoidal *Salmonella*, and *Campylobacter jejuni* are all common. There are a host of others, too. Listeria occurs less commonly, but it has a much higher risk of death associated with it. We also see an entire range of different *E. coli* strains, including enterohemorrhagic *E. coli*, which are toxin-producing.

How are these infections transmitted?

They're mostly foodborne, but some are also waterborne and even human-to-human. We see it rarely, but there's also animal-to-human transmission.

Who is at higher risk of gastrointestinal infections?

To start, younger children are at higher risk because they don't have immunity, or their immune systems have not yet developed. Older adults are also at risk. In general, anybody with any underlying disorder that predisposes them to more severe diarrhea, like someone with uncontrolled HIV, is also at risk, as are those who are immunocompromised, like transplant patients. Anybody with an immune system deficit is going to be at higher risk.

Do tests based on PCR improve clinician's approach to care?

In the U.S., there are many hospitals and some bigger group practices that use multiplex PCR to diagnose diarrheal infections. It's really revolutionized how we test these patients.

In the past, testing required either cultures or enzyme immunoassays for certain organisms, and it was a lot harder to make a diagnosis. A lot of times, we still do not make etiological diagnoses, but increasingly we do. The advantages of these assays are that they are very sensitive, and they're multiplex, so they've helped us offer a specific diagnosis to a lot more patients than we could in the past. Some of these multiplex panels have 22 different pathogens all on one panel. Some of them break them down by category. For example, our hospital breaks them down into bacterial, viral, and protozoa. If you think something is really likely to be viral, you might limit your test to those.

That's in high-income countries. In low-income countries, PCR tests are sometimes used for field surveillance, or trying to understand the etiology of diarrhea in different populations. But this testing is relatively expensive, so it's done less frequently. On other hand, people are increasingly using multiplex PCR platforms for diagnosis of intestinal parasites, and trying to define at the population level what the relative prevalence of a parasite is.

These tests are more sensitive than classic methods and are so sensitive that you might find people have a very small amount of a parasite. What does that mean? It's not quantitative most of the time. Stool exams quantify how many eggs per gram of stool to get an idea of the intensity of infection. That's hard to do with PCR unless you have quantitative PCR, but even that has limitations.

When used for surveillance, PCR tests help increase the likelihood of identifying a specific pathogen, but multiplex PCR tests are used much more on a clinical basis. For certain diarrhea pathogens in the U.S., there's required reporting, where hospital laboratories connect to the department of public health and share their data.

When used for surveillance, PCR tests help increase the likelihood of identifying a specific pathogen.

An etiological specific diagnosis will be made if there's a reporting requirement for state-level surveillance systems that then report to national surveillance systems.

How do molecular tests impact outbreak response?

Molecular tests can facilitate more rapid identification of potential outbreaks. Say you're looking for Campylobacter. This is a fastidious organism: You need certain media and days to grow it. If you get a stool sample and run a multiplex PCR assay, you will have results within hours, or within a day at most. If there's an outbreak going on, you might get an inkling of what pathogens are responsible, faster.

But tying it together — actually knowing it's an outbreak — is a different thing. There need to be a number of cases or some aspect of surveillance that allows you to connect the dots to say "Oh, we've seen so many cases of this, this is above the baseline, looks like we have an outbreak."

That's easy if, for example, a group of people at one church dinner all got sick. But there's a disconnect if it's an imported food from another part of the world that is sent to 10 different states and there are sporadic cases. That takes a little bit more work to identify.

PCR might be how the first few cases are identified, but if it's bacterial, the next step is going to be culture and then possibly sequencing. Now, laboratories often perform whole genome sequencing in order to identify a common link among specific pathogens in geographical locations.

What is the impact of implementation of PCR-based tests for GI pathogen detection on public health?

For individual clinicians, it's become an important and helpful tool to identify potential causes more rapidly for diarrhea in individual patients. Because that data is usually fed into our public health systems, it may also be helping to strengthen them in terms of capacity to identify specific pathogens and to identify outbreaks earlier.

How do you think this technology will progress over the next 10 years?

It's likely that the tests will become less expensive, so we'll be using them more widely for clinical purposes. Some institutions may also perform active population surveillance by taking samples from all patients presenting to emergency rooms with diarrhea to understand what they have.

Lower costs could make molecular testing available in more low-income countries, where there's a much greater burden of foodborne and waterborne pathogens in particular.

One of the limitations for PCR is resistance testing. A PCR test can tell you which bacteria or virus is present, but if you really want to understand the bacteria's resistance patterns, you need to grow it.

Many places now have a process for stool specimens that are PCR-positive for Salmonella or Listeria. The laboratory will try to grow the organism in a specialized culture. If they can grow it, they can perform antibiotic susceptibility studies on it, and they potentially have it for sequencing, too.

You've worked with the World Health Organization on maternal, newborn, and child health. What is a pressing issue in that realm right now?

In the U.S., Listeria is an important pathogen to know in pregnancy because it can lead to pregnancy complications, more severe disease, and potentially death. Pregnant women are at greater risk of having a more complicated course of Listeria. Identifying Listeria and making sure there's early and effective treatment for pregnant women who are affected is extremely important.

Overuse of antibiotics for childhood diarrhea is another major problem. Many types of watery (nonbloody) diarrhea resolve on their own with just oral rehydration, yet in many parts of the world they are treated unnecessarily with antibiotics. This is one of many drivers of antibiotic resistance worldwide.

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BY SHANNON STASI, MS, LCGC

Optimizing Oncology Test Stewardship: Paving the Path for Precision Care

When the Seattle Children's Hospital stewardship program launched in 2012, all testing related to cancer was excluded from review given its complex, time-sensitive, and critical nature. However, with the increase in availability of molecular tumor next-generation sequencing (NGS) panels, we could no longer ignore this testing domain. We learned that there are unique considerations for biomarker testing review that can present challenges to standard stewardship strategies (Table 1).

By 2016, we expanded our insurance preauthorization policy scope and test review criteria to include tumor NGS panels. This required a dedicated integrated system of pathologist review and laboratory genetic counselor support to adequately assess clinical utility, test selection, and specimen criteria and navigate insurance preauthorization nuances.

At that time, the bulk of testing served patients with central nervous system (CNS) tumors based on the available evidence, including the 2016 World Health Organization (WHO) Classification of CNS tumors, which required molecular testing for the diagnosis of many CNS tumor types.

We formed a monthly molecular brain tumor board, consisting of neuro-oncology, pathology, molecular pathology, genetic counseling, neurosurgery, and a

Table 1. Special Considerations for Stewardship Review of Biomarker Testing in Cancer

Urgency	Most biomarker testing is needed to guide treatment decisions, provide a diagnosis, and/or allow for enrollment in clinical trials.
"Repeat" Testing	The same biomarker test may be necessary either in a recurrent or new specimen, at certain intervals in the setting of minimal residual disease monitoring, and/or when there have been updates to technologies.
Specimens	Pathology tissue may be limited, stored in a way that limits testing options, and/or need to be sent paired with a normal sample. Additionally, samples such as bone marrow and others used for RNA-based testing have sample stability limitations.
Implications for inherited cancer risk	Potential germline variants may be identified incidentally from biomarker testing. Prior to biomarker testing, the chance for an inherited cancer risk should be considered.
Reference lab selection	There are many academic and commercial options that vary in reporting practices (Are variant allele frequencies or germline variants reported? Are therapeutic implications included?), methodology utilized (exome-based, ability to detect copy number variants/fusions, etc.), turnaround time, billing practices, and more.
Rapid increase in biomarker testing volume and complexity	As a result of precision medicine research and technology development, there likely will continue to be a significant increase in available biomarker testing options.
Insurance	A scarcity of insurance policies and non-specific CPT coding, combined with some of the considerations above, can negatively affect insurance authorizations and reimbursement.

research coordinator to review results. This group also dealt with ordering and insurance logistics, and it facilitated several research projects that informed internal ordering pathways for clinical and research tumor testing. We also used data from this work to justify institutional support for an integrated genetic counselor in the multidisciplinary neuro-oncology clinic.

As the stewardship program evolved, so did the number of available testing options and indications in oncology. From 2017 to 2019 we began triaging minimal residual disease (MRD) testing requests, developed DNA/RNA testing protocols in patients with acute myeloid leukemia and acute lymphoblastic leukemia, and guided the transition from research to clinical testing across all cancer types.

We also created molecular tumor boards for hematologic malignancies and non-CNS solid tumors. Like the molecular brain tumor board, these meetings were led by stewardship pathologists and included lab genetic counselors.

The release of the 2021 edition of the WHO Classification of CNS tumors prompted a new strategy to support the increase in testing volume and options. By this time, all miscellaneous genetic tests from hematology-oncology and any defined single gene or panel order underwent stewardship review. We observed an increase of approximately 300% in oncology preauthorization requests from 2016–2023 (Figure 1).

There might not be a more perfect pair than a pathologist and a lab genetic counselor to lead oncology test stewardship efforts.

Stewardship Strategies—A "Yes, And" Approach

There might not be a more perfect pair than a pathologist and a lab genetic counselor to lead oncology test stewardship efforts. As a first step, identify your champions. Collaboration with oncology providers and pathologists was critical to our program's success. If there are tumor boards at your institution, ask to be on the invite list. If molecular tumor boards don't exist, start one! Also born from the complexities of precision oncology care is a similar role to the lab steward, commonly referred to as a precision medicine steward or biomarker navigator (*3*). This emerging role will offer lab stewardship programs more opportunities for collaboration in the future.

Below I'll address a few of the considerations unique to stewardship of biomarker testing.

Urgency

Yes, testing is urgent — and there are opportunities to obtain preauthorization to protect the patient and institution financially. There often is time to process an insurance preauthorization while performing other first-line therapies or imaging. Education and collaboration are key, and once scenarios such as these have been identified, hospitals can implement processes to support preauthorizations and prevent orders from falling through the cracks. Documenting the recommended preauthorization and testing plan in the tumor board summary supports care teams in executing next steps.

And, when in doubt, send it out! Like other institutions, we have recently transitioned biomarker test ordering from the provider to the pathologist in cases where the results are needed to confirm diagnosis that cannot be made from radiography or histopathology alone (*2*). In these cases, there is no time to wait for preauthorization; however, stewardship interventions are still important. Templates allow pathologists to take ownership of documenting medical necessity within the preliminary pathology report and the integrated molecular diagnosis in the final report. This documentation may be useful for a patient's future testing and may be needed at the time of insurance claims review.

"Repeat" Testing

MRD monitoring is difficult to preauthorize and track. Yes, this testing typically requires insurance preauthorization like other genetic testing, and there are many tools you can implement to

make this less painful. For example, consider using a tracking database that allows for easily viewing order dates of service and prior preauthorization requests. Create Epic SmartPhrases or templates to submit MRD preauthorization requests to the payor and your insurance processing team so they know the request is not a duplicate. Defining these orders in the electronic medical record can help streamline billing workflows.

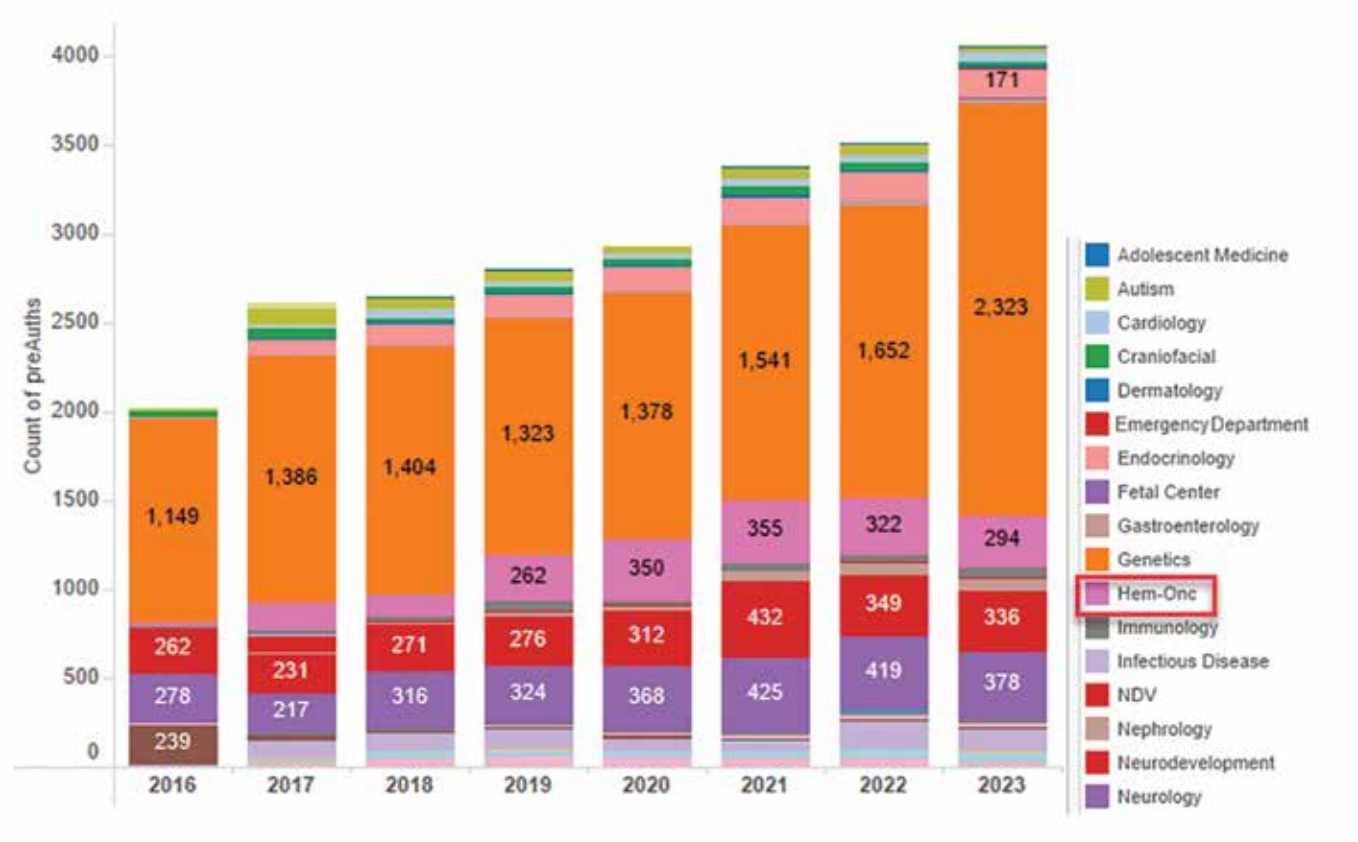
Templates help with other situations as well. As a stewardship consultant reviewing the same test on a patient, it can be challenging to determine testing rationale each time. We helped develop medical necessity and testing plan templates and shared them with the ordering teams. Now, a quick look at a single note gives us details to efficiently triage the order.

As a stewardship consultant reviewing the same test on a patient, it can be challenging to determine testing rationale each time.

Implications for Inherited Cancer Risk

The potential for identifying germline variants from biomarker testing raises additional considerations for the stewardship process, including pre-test counseling, sample requirements, and order details. We

Figure 1. Preauthorization Requests Over Time by Provider Specialty



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leveraged the relationship between our stewardship lab genetic counselor and oncology department to create two embedded clinical genetic counselor positions within hematology-oncology and collaborate to align clinical practice with lab stewardship philosophies.

Conclusion

To borrow a phrase from Taylor Swift, cancer is in its molecular diagnostics era. We need to shake it off (the past, that is) and embrace new models of stewardship interventions and strategies for biomarker test coordination. Pathologists are now directly involved in the ordering of molecular testing: This practice change is a perfect opportunity for stewardship team engagement to guide new workflows, and ensure patients get the right test, even in a time crunch.

"In recent years, there has been a revolution in our knowledge of the genetic drivers of pediatric cancer," said Bonnie Cole, MD, a pathologist and clinical assistant professor at Seattle Children's. "It is now our job to use this knowledge to precisely tailor diagnosis and treatment for every single one of our patients."

Another colleague, Sarah Leary, MD, MS, an attending physician and medical director of the pediatric brain tumor program at Seattle Children's, underscored the need for teamwork. "For practicing oncologists, collaboration with laboratory medicine is crucial to understanding the implications as well as limitations of ever evolving testing options."

I encourage lab stewardship teams to remain flexible, count the small wins, when in doubt send it out, and acknowledge that a one-size-fits all approach will not be successful.

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BY SUSAN SCHOWALTER, MS, LCGC

Not Just Kitting Around Part 2: Accommodating the Increasing Demand for Alternate Sample Coordination for Genetic Tests

Since the start of the COVID-19 pandemic, the demand for alternative sample collection for genetic testing has been on the rise. Despite the return to prepandemic norms for many of the clinics at our institution, the requests for alternate sample kits have continued to grow.

In our first article about alternative sample coordination in 2021, we were sending out around 98 kits per month (*1*). As of November 2023, we sent out an average of approximately 228 kits per month, a 233% increase from 2021. The COVID-19 pandemic was the catalyst for what has become a persistent demand for this service.

With more experience coordinating these alternative sample kits (and higher volumes), new challenges have arisen. In a recent review of our current alternative kit coordination process, our team identified some of the major pain points, along with their associated costs, in supporting targeted efforts at process improvement.

Incorporating alternate specimen collection for genetic testing is an important step for our institution to increase access to this essential testing (*2*). The following sections outline aspects of our current process where we are exploring possible improvement options to maximize access to genetic testing and minimize wasted work and resources.

Home Collections: Are They as Easy as We Think?

Although home collections can certainly provide an easier collection experience by removing the need to commute to a lab and for needle pokes, they also can introduce new challenges. This option requires patients and their families to take on the responsibility of correctly collecting, labeling, and sending a specimen back to our institution within a preauthorization window for testing to be completed.

A recent research project completed at our institution by genetic counseling assistant Alexis Olsen showed that 5% of all the alternate specimen kits we send out to families must be resent at least once (*3*). The reasons for over 70% of the kits needing to be resent include collected samples being deemed insufficient in quality, patient collection errors, and shipment concerns (see Figure 1). Each of these three identified categories points to aspects of the home kit collection process that may prove more difficult than anticipated (*3*).

Anecdotally, our laboratory tech teams have seen alternative specimen kits returned to the lab with varying issues, ranging from all samples being labeled with the proband's name to saliva kits with distinctive colors suggesting potential food or drink contamination. While we have made efforts to provide thorough instructions (with translations available in more than 20 different languages) in each kit, some patients and families still have difficulty understanding or finding the time to collect samples that will be usable.

Ensuring families return kits to us is another area of difficulty we have identified. In a 6-month timeframe, all the kit tracking numbers were reviewed to determine how many of the return-to-lab labels had been activated. Our team found that 15–20% of the kit labels we had provided for a return shipment had not been scanned into our couriers' system. While we cannot determine the specific reasons why these kits are not returned, it seems feasible that getting a package to a mail carrier drop box can be a challenge, especially if it is a stop outside of a normal routine.

Whom Are Kits Sent To?

Of the approximately 1,900 kits we sent out in 2022, approximately 80% were sent to collect comparator samples for a proband's test. There has been a rise in the utilization of trio-based genetic tests, like exome or genome, due to increased diagnostic yield (*4*). While probands occasionally have residual DNA from previous tests, comparators almost always require specimen collection. It is noteworthy that while inclusion of comparators is incredibly valuable from a clinical perspective, there are no

LABORATORY STEWARDSHIP FOCUS

charges associated with sending comparator kits to families. At least 80% of the kit services being provided are therefore not billable.

Where Are We Sending Kits?

Another layer of cost we have assessed is where families receiving these kits are located. The majority of our alternate specimen kits are being overnight shipped to and from addresses within the greater Seattle area. Our current cost for shipping these kits has been over $100,000 in just one year.

We certainly want to have the option of shipping kits to families who cannot travel easily to our main campus and satellite clinics, but we should also evaluate less costly alternate options than overnight shipping of kits to our local patients and families.

Proposed Process Improvements

The above findings collected from our review of the current alternative specimen collection process have given us many possible directions for implementing targeted process improvements.

One improvement we have explored is developing inclusion criteria to send alternative specimen collection kits. While the criteria can still be relatively broad to ensure access for families that need it, we could also provide more guidance around which cases might not need to use this option. Clear, outlined criteria can help families and providers understand in which circumstances remote specimen collection will make testing easier and in which circumstances it may truly not be the best option for efficient testing. It is noteworthy that venous blood has traditionally been the tissue of choice because the yield of DNA is quite high compared to noninvasive alternatives (5).

We also have explored the possibility of having pick-up and drop-off locations in the phlebotomy area on the main campus for alternative specimen kits. This could create a pathway for local patients and families to use alternative specimen collection kits without the need to ship kits to and from local addresses.

Finally, we are looking into ways in which we could collaborate more with our most used reference laboratories. Many large reference labs already have extensive systems for coordinating alternative specimen collection kits. Rather than using our internal resources, we might be able to use the processes reference labs already have in place and supplement those offerings to best support our patients.

Alternative specimen collection kits have redefined our genetic testing process over the past three years, and they are likely here to stay. We hope sharing our experiences with alternate specimen coordination can provide useful information for other institutions working with alternate specimen kits in the interest of sustainable, accessible, and patient-centered genetic testing.

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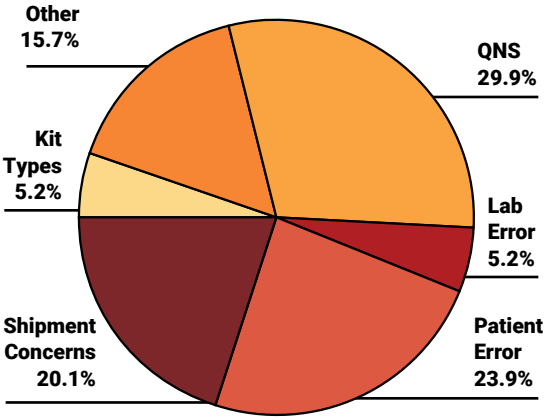
Figure 1. Kits Re-Sent Based on Reasoning 2021–2022



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Regulatory Roundup

New Genetic Test Helps Spot Risk of Opioid Use Disorder

The Food and Drug Administration (FDA) recently approved the first genetic test for risk of opioid use disorder.

The AvertD test sold by AutoGenomics should be used prior to a first exposure to oral opioid pain medications in patients being considered for a 4- to 30-day prescription for treating acute pain. The test may help patients who are concerned about being treated with an opioid for acute pain make better informed decisions, according to an FDA announcement.

The prescription-use only genetic lab test involves a cheek swab and is only for patients 18 years and older who have no prior use of oral opioid analgesics, not for patients treated for chronic pain. For example, adult patients scheduled for surgical procedures might be eligible for this test.

As part of the approval, AutoGenomics will train healthcare providers to use the test appropriately and conduct a large post-market study assessing device performance in patients. The company will regularly report to the FDA on the progress of the study.

THE FDA AUTHORIZES CHLAMYDIA AND GONORRHEA TESTS WITH AT-HOME SAMPLE COLLECTION

LetsGetChecked's Simple 2 test, the first test for chlamydia and gonorrhea with at-home sample collection, recently received Food and Drug Administration market authorization. The over the counter Simple 2 test is intended for use in adult patients aged 18 years and older. It uses vaginal swabs or urine specimens, as appropriate, to detect the presence of the bacteria *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, which cause chlamydia and gonorrhea, respectively.

The test can be purchased without a prescription. Results are delivered online, with follow-up from a healthcare provider in cases of positive or invalid test results.

COMPANION DIAGNOSTIC APPROVED FOR AN ADVANCED BREAST CANCER

Foundation Medicine has announced Food and Drug Administration (FDA) approval for its FoundationOneCDx as a companion diagnostic for AstraZeneca's Truqap (capivasertib) in combination with Faslodex (fulvestrant).

Fulvestrant has been contemporaneously approved for treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations in adults. Approved treatment follows patient progression after at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

Research has shown that adding capivasertib to fulvestrant therapy resulted in a significant improvement in progression-free survival among patients with HR-positive, HER2-negative PIK3CA/AKT1/PTEN-altered advanced breast cancer whose

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disease had progressed during or after previous aromatase inhibitor therapy with or without a CDK4/6 inhibitor.

According to FoundationOne, the test will be the first FDA-approved test to identify this new, prevalent subset of breast cancer patients for treatment with capivasertib.

ACUTE INFECTION AND SEPSIS TEST SYSTEM RECEIVES FDA BREAKTHROUGH DEVICE DESIGNATION

Inflammatix recently announced Food and Drug Administration (FDA) breakthrough device designation for its TriVerity test system for acute infection and sepsis.

Currently under development, the TriVerity test system includes the Myrna instrument and the TriVerity test for adult emergency department patients with suspected acute infection or sepsis.

The TriVerity test provides three independent readouts that reflect the likelihood of a bacterial infection, the likelihood of a viral infection, and the risk of severe illness based on the need for critical organ support within 7 days of presentation to the emergency department, according to Inflammatix.

As a breakthrough device, TriVerity is expected to be eligible for the Centers for Medicare and Medicaid Services New Technology Add-On Payment Program, which will enable future Inflammatix hospital customers to receive a partial subsidy for purchases of TriVerity acute infection and sepsis tests performed on admitted patients for up to 3 years. The company won the Association for Diagnostics & Laboratory Medicine Disruptive Technology Award for its system in 2019.

QIAGEN STI ASSAY GETS FDA CLEARANCE

The Food and Drug Administration (FDA) has cleared Qiagen's NeuMoDx CT/NG Assay 2.0, which directly detects bacterial infections involving *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.

These common bacterial sexually transmitted infections are mostly asymptomatic and generally curable with single doses of antibiotics.

This FDA clearance expands the test menu of the company's NeuMoDx Molecular Systems in the U.S. The clearance also builds on the 16 European Union CE-marked in vitro diagnostic tests available on these systems, including assays for transplant-associated viruses, respiratory infections, bloodborne viruses, and sexual and reproductive health.

FDA 510(K) CLEARANCE GRANTED FOR MULTIPLEX MOLECULAR PLATFORM AND HSV AND VZV ASSAY

QuidelOrtho Corporation has received Food and Drug Administration 510(K) clearance for its iSavanna PCR platform and Savanna HSV 1+2/VZV in vitro diagnostic test for the detection and differentiation of herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), and varicella-zoster virus (VZV) nucleic acids.

The nucleic acids are isolated and purified from swabs obtained from symptomatic patients' cutaneous or mucocutaneous lesion specimens.

QuidelOrtho said the Savanna multiplex molecular platform enables analysis of up to 12 pathogens or targets, plus up to four controls, from a single test run in roughly 25 minutes, depending on the assay. Its integrated sample prep combined with rapid real-time PCR amplification and detection technologies is designed to aid syndromic testing in hospitals and moderate-complexity labs, with the goal of eventually making syndromic testing accessible in physician offices, urgent care clinics, and other point-of-care locations.

DISINFECTOME RECEIVES CHINESE APPROVAL FOR NEW SEQUENCER

Disinfectome recently announced that its Difseq-200 sequencer gained approval from the Chinese National Medical Products Administration.

The Difseq-200 is a compact and flexible desktop sequencer that uses both probe-anchored synthesis and DNA nanoball sequencing technology. This sequencer can work with an automated preprocessing instrument, nucleic acid extractor, an automated library preparation, and the Gensis bioinformatics analyzer to conduct in-hospital next-generation sequencing and provide a personalized report to guide the use of precision drugs.

Difseq-200 is suitable for comprehensive clinical applications, including prenatal screening, tumor variant detection, and pathogen identification, according to the company.

Industry Playbook

Quest and Scipher Collaborate on Rheumatoid Arthritis Diagnostics

Quest Diagnostics and the precision immunology company Scipher Medicine have announced a collaboration with the goal of advancing precision medicine for rheumatoid arthritis (RA).

Under the multi-year collaboration, Quest will provide RNA extraction and next-generation sequencing services for Scipher's PrismRA test. The assay is a blood-based molecular signature response classifier that predicts patients' responses to tumor necrosis factor inhibitor (TNFi) therapy and helps them avoid unnecessary dose escalations or drug cycles.

Quest also will provide specimen collection at approximately 7,300 of its locations — including physicians' offices and patient service center locations — and through courier logistics services that include transport of patient specimens between Quest and Scipher laboratories and provider sites.

The collaboration centers on Quest's next-generation sequencing capabilities at its advanced laboratory in Marlborough, Massachusetts. Quest will extract and sequence RNA from PrismRA blood specimens to identify approximately 24 molecular traits associated with response to TNFi therapies. RNA transcripts in the blood can be incorporated into Scipher's molecular classifier analysis, which predicts the biology that underpins drug response.

Scipher will incorporate this molecular data with patient data and results of anticyclic citrullinated peptide, an RA antibody marker, from testing at its North Carolina laboratory. Through electronic health records, physicians receive a personalized report with a score indicating predicted response based on analysis of the complete set of laboratory and patient data.

Previous data published by Scipher indicates RA patients with moderate and high disease activity, whose treatment was guided over 6 months by PrismRA, had a nearly two-fold clinical improvement in Clinical Disease Activity Index scores, compared to patients whose therapy was not guided by PrismRA results, according to Quest.

ROCHE TO ACQUIRE LUMIRADX POINT-OF-CARE TECHNOLOGY

Roche Diagnostics announced an agreement to acquire parts of LumiraDx's point-of-care technology.

According to Roche, the transaction is part of its plan to enable more patient-centric healthcare in multiple care settings, including the home, pharmacy, general practitioner's office, emergency room, and intensive care unit. The acquired technology platform offers a wide range of immunoassay and clinical chemistry tests on one portable device. These tests can be stored at room temperature, enabling convenient handling in a range of decentralized healthcare settings, according to Roche.

By leveraging its extensive global reach and established affiliate network, Roche will be able to drive access to timely, accurate diagnostic results when and where patients need them most, the company added.

Close of the transaction is expected by mid-2024, according to Roche.

ATALAN ADDS TRICORE TO ITS CLINICAL PARTNERSHIP

Atalan, a clinical partnership that provides doctors and medical centers access to a vetted network of clinical laboratories,

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recently announced the addition of TriCore to its network.

TriCore adds to Atalan's list of College of American Pathologists ISO 15189-accredited providers.

Atalan's network of laboratories share the ability to eliminate excess capacity, reduce costs, and improve profit, according to the company. This arrangement allows labs to expand their reach and foster collaborative innovations, the company said.

TriCore is an independent, not-for-profit clinical laboratory providing more than 2,900 full-service, state-of-the-art laboratory tests to healthcare professionals and their patients. TriCore also offers analytics and research services supporting healthcare and scientific organizations worldwide.

According to Atalan, it vets its growing list of laboratory partners to add to the cumulative strength of the network.

In less than 30 minutes, the [SwiftX-traction kit] extracts DNA from various challenging sample types in just a few steps.

EUROIMMUN AND XPEDITE DIAGNOSTICS PARTNER ON POC DNA EXTRACTION

Euroimmun, a franchise of Revvity, and Xpedite Diagnostics recently announced a strategic partnership to offer faster and easier protocols for DNA extraction at the point of care.

Current users of the Euroimmun EUROArray diagnostic platform will receive the EUROArray SwiftX-traction Kit for rapid manual DNA extraction, the company said. In less than 30 minutes, the kit extracts DNA from various challenging sample types in just a few steps. The new extraction method is currently under validation in combination with several CE-marked EUROArray products.

Xpedite Diagnostics intends to register the extraction kit itself as a CE-IVD, according to Euroimmun.

Xpedite Diagnostics officials said that the EUROArray SwiftX-traction was tailored specifically to the needs of users of the EUROArray diagnostic platform and is based on their SwiftX Toolbox.

CENTOGENE AND LIFERA ENTER COLLABORATION

Centogene, a rare disease company that focuses on neurodegenerative diseases, and Lifera, a biopharmaceutical company wholly owned by Saudi Arabia's Public Investment Fund, have announced a joint venture to increase local and regional access to multiomic and genomic testing.

The resulting Lifera Omics will provide this testing to health systems, biopharma clients and institutions with patients in Saudi Arabia, and countries of the Gulf Cooperation Council (GCC).

The joint venture will build a laboratory and bioinformatics infrastructure that leverages the Centogene Biodatabank, which the company said is the world's largest real-world integrated multiomic data repository in rare disease biobanks globally.

The joint venture is intended as a vehicle for large national screening and genomics programs. Patients in Saudi Arabia and the GCC, a rapidly growing region with more than 56 million inhabitants, will have increased access to advanced, effective diagnostic offerings. These diagnostics are the core of Lifera's strategic objective to contribute to improving national resilience and health outcomes in Saudi Arabia, according to the companies.

Index to Advertisers

Ask The Expert

Alternative Markers of Rheumatoid Arthritis

James D. Faix, MD

Why do we need alternative markers of rheumatoid arthritis (RA)?

A. Diagnosis of RA can be difficult because other disorders cause similar symptoms, especially early in the course of disease. Traditional tests for RA detect the autoantibodies rheumatoid factor (RF) and anticyclic citrullinated peptide (CCP), but both of these may be negative in a small but significant percentage of patients with RA. We need better markers that can close this gap and help predict which patients need early intervention, target treatment, and improve our ability to monitor therapy.

What other autoantibodies have been proposed as markers of RA?

The most common methods for measuring RF are turbidimetry and nephelometry, but these primarily detect IgM RF. The use of enzyme immunoassay allows differentiation of RF into IgM, IgA, and IgG classes. Detecting IgA and IgG RF in addition to IgM RF does not increase diagnostic sensitivity, but it may add specificity when combined with IgM RF and anti-CCP.

Modern anti-CCP assays detect many different (and proprietary) peptides. The general term anticitrullinated protein antibodies, or ACPA, has been proposed as a name for these markers. Citrullination refers to the modification of an arginine residue to citrulline via enzymatic deimination. The enzymes that create citrulline (peptidyl arginine deiminases or PADs) are active in synovial inflammation and the production of antibodies against these altered proteins is characteristic of RA. With regard to alternatives to the anti-CCP assay, most of the focus has been on developing tests that detect antibodies to individual proteins that have been citrullinated or that have undergone a different posttranslational modification.

Assays are commercially available for antibodies specific for citrullinated alpha-enolase (a glycolytic enzyme) and citrullinated vimentin (a cytoskeletal protein). There are two different antibodies to citrullinated vimentin. Inflammatory cells in RA not only citrullinate vimentin, but the protein also undergoes somatic mutation, increasing the number of arginine residues and therefore the degree of citrullination. The original antibody, called anti-Sa, targets wild-type citrullinated vimentin. Antibody against the mutated version of citrullinated vimentin, called anti-MCV, has been shown to be much more sensitive and may be the best alternative marker for identifying patients who may be anti-CCP negative.

The other major type of posttranslational modification in RA is carbamylation, in which nonenzymatic conversion of a lysine residue produces homocitrulline. Antibodies to carbamylated protein are not as sensitive as anti-MCV, but they may be a useful alternative marker to help confirm the diagnosis.

What other types of alternative markers have been proposed?

Two markers of joint inflammation and bone erosion have been investigated. Matrix metalloproteinases (MMPs) contribute to joint destruction in RA, primarily by degrading cartilage. Serum levels of MMP-3, the major MMP present in RA synovia, and 14-3-3 eta, a chaperone protein present in the inflamed joint and also detectable in serum, correlate with disease activity in early RA and also with disease progression. These markers may be helpful additions to conventional monitoring with C-reactive protein. 14-3-3 eta also shows high sensitivity and specificity for RA and can help identify RA patients who are negative for RF and anti-CCP.

What new markers of RA are on the horizon?

The search for other antibodies to specific citrullinated proteins continues. Antibodies to PAD4, the enzyme that creates the citrulline residue, may also have prognostic value. Analysis of RNA transcript expression may help determine whether patients are likely to respond to biologic disease-modifying antirheumatic drugs. Finally, a study presented at the recent American College of Rheumatology meeting reported that epigenetic features of almost 1,000 genes showed discrimination between patients with and without RA. The ultimate alternative RA marker may wind up being a molecular genetic one.

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Undetected Point-of-Care Hypoglycemia Can Be Life-Threatening to the ICU Patient

Bedside glucose testing is one of the most commonly performed tests in the hospital and many clinicians take the accuracy and reliability of these results for granted. However, certain glucose meters have interferences from medications and other endogenous factors that can cause erroneous glucose meter results. Five recently published papers have reported that inaccurate results from these meters have led to improper treatment, such as giving insulin to a patient who is hypoglycemic, which can cause catastrophic outcomes including death. This is an ongoing, real-life problem, with erroneous glucose meter results and inappropriate insulin administration.[1-5] In addition to adverse events, meter errors can cause increased length of stay and increase the cost of hospitalization.

This seminar will show how better patient outcomes are achieved through improved glucose meter accuracy, discuss factors which can affect the accuracy of some glucose meters and how to avoid them, and review implementation of an interference-free bedside glucose testing system which protects patients and providers.

Topics

- Using comparative reference methods to evaluate glucose meter systems
- Evaluating glucose interferants (e,g., hematocrit, other sugars, acetaminophen, ascorbic acid)
- Preventing glucose meter interferences and adverse events
- Implementing a hospital-wide POC glucose testing program that includes critically ill patients
- FDA and CMS regulations for glucose meter use with critically ill patients

Educational Credits

This program has been approved by the American Association of Critical-Care Nurses (AACN) for 2.5 CERPs, Synergy CERP Category A, File Number 24813. Approval refers to recognition of continuing education only and does not imply AACN approval or endorsement of content of this educational activity, or the products mentioned. This program offers 2.5 hours of P.A.C.E. continuing education credits.

Speakers

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