May 2023

CLN Clinical Laboratory News

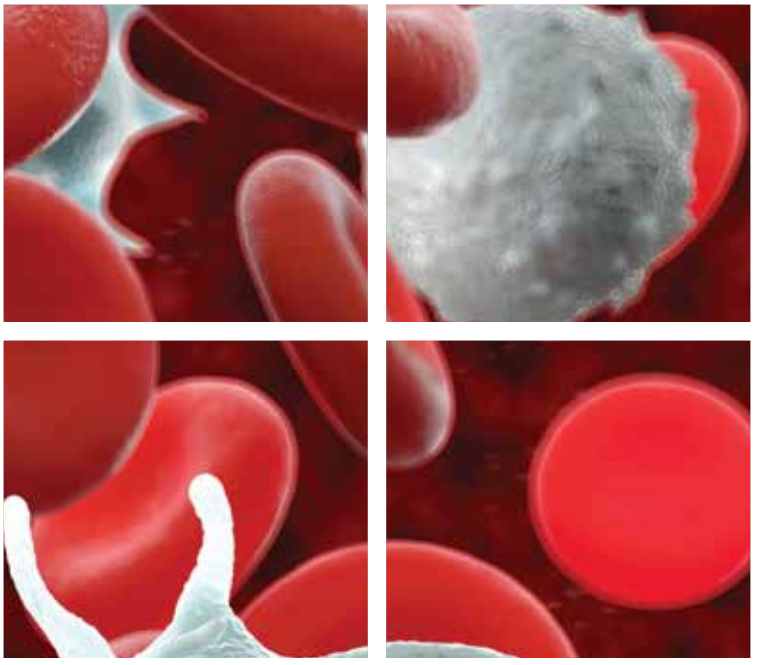
CONTINUOUS GLUCOSE MONITOR MISMATCH

36–43%

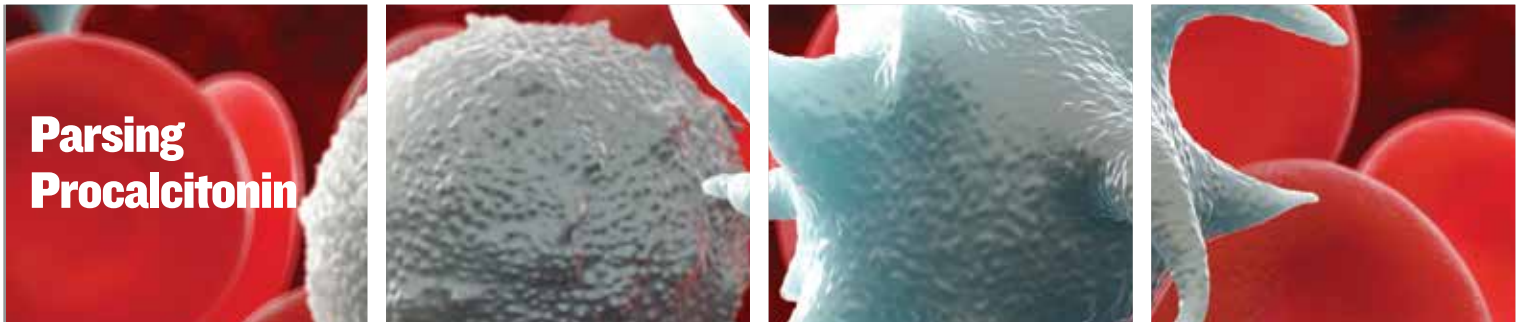
Percentage of patients with clinically significant difference between glucose monitor interval and HbA1c

PAGE 6

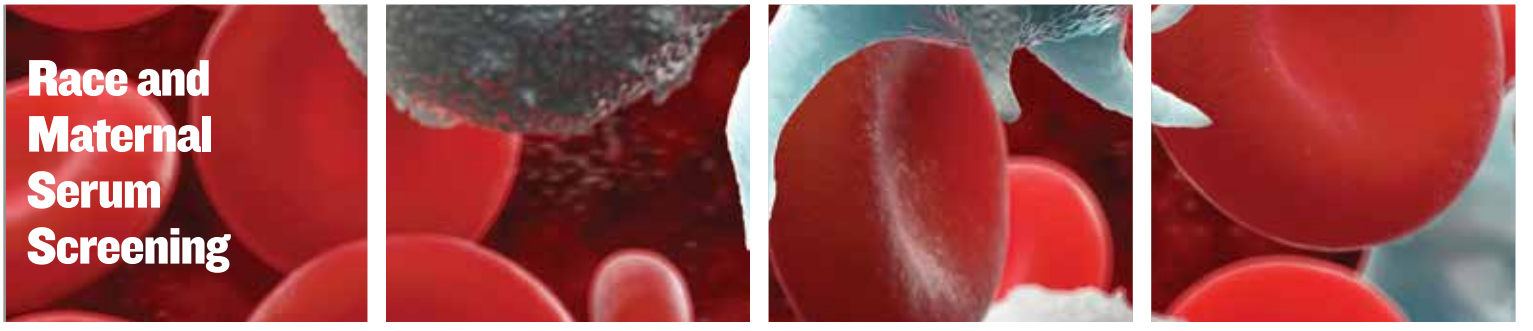
Modernizing Viscoelasticity Testing



Parsing Procalcitonin



Race and Maternal Serum Screening



AACC Better health through laboratory medicine.

VANCE ST. CAPITAL

As an experienced manufacturer of microfluidics and microplates, PDC is an established partner to life science companies. Combining an ability to produce complex micro geometry with an understanding of material characteristics, PDC is well-positioned to support various applications in point-of-care (POC) testing, immunoassay, clinical chemistry, and molecular diagnostics.

pdc

www.plasticdesigncompany.com

We'll be at booth #4522 at AACC!

Advancing Life Science Innovation

Partner with Vance Street Capital and its industry leading, life sciences companies to bring your vision to life. Our portfolio of companies thrive on finding creative solutions to your most complex challenges, from high throughput screening, to point of care diagnostics, to wearable monitoring.

EXCEL SCIENTIFIC

innovize. let's make it better

pdc Plastic Design Company

At Vance Street Capital, our mission is to partner with entrepreneurs who are great at solving customer challenges and help them scale their business. We invest heavily in our companies with deep operating resources to accelerate growth and unlock untapped value.

15304 Sunset Blvd, Suite 200 Pacific Palisades, CA 90272 | +1.310.231.7100 vancestreetcapital.com

CLN Clinical Laboratory News
www.aacc.org

Subscriptions
AACC
900 Seventh St., NW, Suite 400
Washington, DC 20001
Phone: +1 202.857.0717 or +1 800.892.1400
Email: custserv@aacc.org

Editorial Correspondence
Bill Malone, Managing Editor
Phone: +1 202.835.8756 or +1 800.892.1400
Email: bmalone@aacc.org

Clinical Laboratory News is published monthly (10 times per year—Jan./Feb., March, April, May, June, July/Aug., Sept., Oct., Nov., and Dec.) by the American Association for Clinical Chemistry. 900 Seventh St., NW, Suite 400, Washington, DC 20001. Phone: +1 202.835.8756 or +1 800.892.1400 Fax: +1 202.877.5093. POSTMASTER: Send address changes to AACC, 900 Seventh St. NW, Suite 400, Washington, DC 20001.

Design and Production Management
Melissa H. Miller Designs

On the cover: FG Trade / iStock

Features

Departments

Instruments that can perform online mass spectral matching will be most effective for identifying new designer drugs.
p32

Federal Insider

AACC Reignites Fight to Counter Lab Payment Cuts

AACC is renewing its support of the Saving Access to Laboratory Services Act (SALSA), which would reform the Medicare clinical laboratory fee schedule (CLFS). The current payment methodology set forth in the Protecting Access to Medicare Act (PAMA) has resulted in deeper lab payment cuts than Congress intended, said an AACC letter to Representative Richard Hudson (R-N.C.), a member of the House Energy and Commerce Subcommittee on Health.

The bill was reintroduced this year by Sens. Sherrod Brown (D-Ohio) and Thom Tillis (R-N.C.), along with Reps. Richard Hudson (R-N.C.), Bill Pascrell, Jr. (D-N.J.), Gus Bilirakis (R-Fla.), Scott Peters (D-Calif.), and Brian Fitzpatrick (R-Pa.).

PAMA, which was passed in 2014, directed the Centers for Medicare and Medicaid Services (CMS) to rebase the CLFS to reflect private sector payment rates. However, nearly all the data used to set the new fees comes from large commercial laboratories, which can perform testing at sharply reduced costs due to their economies of scale. This has resulted in significant reductions in payment rates that are adversely affecting all laboratories.

According to the Medicare Payment Advisory Commission, the CMS cuts have reduced reimbursement to hospitals and physician offices for testing services by 9% and 6%, respectively. This trend is expected to continue and may force some labs, particularly those in rural and underserved areas, to curtail or eliminate testing.

The SALSA bill would deal with several deficiencies in the earlier PAMA statute, according to the letter. These include the use of statistical sampling to ensure that CMS obtains more representative payment data for setting fees, providing greater price stability by placing limits on payment increases and decreases, and reducing the administrative burden on laboratories.

Lab professionals are encouraged to use AACC's Laboratory Voice tool to write to their members of Congress: www.aacc.org/advocacy-and-outreach/laboratory-voice

AACC JOINS COALITIONS TO PUSH FOR CDC FUNDING

AACC is working with several coalitions to advocate for greater funding from Congress for the Centers for Disease Control and Prevention (CDC).

The largest initiative, called the CDC Coalition, includes 143 other members and is calling for $11.581 billion for CDC programs in the FY 2024 Labor, Health and Human Services, Education and Related Agencies appropriations bill.

"Due to years of underfunding, many CDC programs have not received the resources that are needed to address the many health challenges we face as a nation, resulting in many of CDC's most effective prevention programs not reaching all states and communities," wrote the coalition in a letter to Congress.

The coalition noted that CDC serves as the "command center" for the public health defense system against emerging and reemerging infectious diseases, as well as man-made and natural disasters. CDC also faces other "unprecedented challenges and responsibilities," such as chronic disease prevention. At AACC's urging, CDC also has been supporting harmonization of clinical laboratory results.

Separately, AACC has joined with a group of professional societies, academic institutions, and companies that are urging Congress to provide $175 million in funding for the Advanced Molecular Detection (AMD) program at CDC. The funding aligns with the level authorized in the Tracking Pathogens Act, which was enacted as part of a year-end legislative package in 2022.

The AMD program uses cutting-edge genomic and bioinformatic technologies to detect and respond to infectious disease threats, including the ongoing COVID-19 pandemic.

Beyond pathogen surveillance, the program also informs vaccine development, helps to identify and track antimicrobial resistance and foodborne illness, and informs the development of diagnostics for new, existing, and emerging diseases.

The program also has expanded training for public health and laboratory professionals in genomics and bioinformatics.

Rawpixel/iStock

Nova Biomedical's Educational Webinar Series Presents:

Glucose Meter Accuracy and Capillary Blood Testing In The ICU: Why It Matters

Bedside glucose testing is one of the most performed tests in the hospital. Many clinicians take the accuracy and reliability of these results for granted; however, hospitalized patients can have interference from medications and other endogenous factors that can cause erroneous glucose meter results. Inaccurate results can lead to improper treatment, such as giving insulin to a patient who is hypoglycemic, which can have catastrophic outcomes. This is an ongoing, a real-life problem, with recent published reports of death and disability due to erroneous glucose meter results and inappropriate insulin administration[1-5]. Aside from these events, hypoglycemia can cause increased length of stay and increase the cost of hospitalization.

This webinar will present outcomes achieved through improved glucose meter accuracy, factors which can affect accuracy of some glucose meters, how to avoid glucose meter errors, and how to implement a bedside glucose testing system which protects patients and providers. By the end of the presentation, attendees will be able to:

- Explain factors that impact the accuracy of glucose meters in the hospital and critical care environment.
- Describe variables that can affect the efficacy of hospital glycemic control protocols.
- Discuss the impact of improved glucose meter accuracy on patient outcomes.
- Review capillary glucose accuracy data for one device when used with critically ill patients.

Primary Presenter
Brad Karon, MD, PhD
Professor of Laboratory Medicine and Pathology
Chair, Division of Clinical Core Laboratory Services
Mayo Clinic, Rochester, MN

Next Generation Hospital Glucose/Ketone Meter

In this presentation, Dr. Naveen Bangia will discuss the clinical importance of blood ketone testing in adult and pediatric critical care patients. A point of care method for monitoring glucose and ketones in critically ill patients will also be presented.

Presenter
Naveen Bangia, PhD
North American Director of Medical and Scientific Affairs
Nova Biomedical

Webinar Dates:

Thursday, June 8, 1:00 PM ET • Thursday, June 22, 1:00 PM ET

Register Now:

novabiomedical.com/glu-icu-cln

This program offers 1 hour of P.A.C.E. continuing education credits. Nova Biomedical is approved as a provider of continuing education programs in the clinical laboratory sciences by the ASCLS P.A.C.E.® Program.

This program has been approved by the American Association of Critical-Care Nurses (AACN), for 1.00 CERPs, Synergy CERP Category A, File Number 24553. Approval refers to recognition of continuing education only and does not imply AACN approval or endorsement of the content of this educational activity, or the products mentioned.

nova® biomedical
novabiomedical.com

References:
1. Orija, et al. DOI: https://doi.org/10.1016/j.aace.2020.11.030T
2. Krabbe, et al. DOI: https://doi.org/10.1515/cclm-2020-1445
3. Katzman, et al. DOI: https://doi.org/10.1177/1932296820932186
4. Lachance, et al. DOI: https://doi.org/10.1186/s13256-021-02869-4
5. Daan Ten Berge, et al. DOI: https://doi.org/10.7759/cureus.28615

Bench Matters

How Project Management Helps You Keep Up With Laboratory Projects

PeopleImages / iStock

By Anu S. Maharjan, PhD, DABCC, FAACC

Laboratory medicine involves carefully analyzing analytes from various biological matrices and provides timely reporting to support patient care needs. Along with the daily tasks of patient specimen processing, clinical laboratories have evolved and adapted to changing processes of quality, regulation, and specimen handling. With ongoing advances in the field of lab medicine, laboratorians need to carefully utilize their time and resources to keep a well-organized workplace.

Laboratorians receive various types of training in their clinical areas of expertise—state and federal regulation, laboratory finance, and laboratory management. However, there is still room for improvement in project management—particularly in developing a project vision and goals and measuring success.

Project Managers and Teams

Hospitals and reference laboratories have started using project management teams to steer expansive projects such as building a new laboratory, bringing in new automation, or transitioning to a new laboratory information system. Completing these vital projects requires buy-in from key stakeholders within the organization or institution. The project outline explains the overall vision, promotes collaboration among stakeholders and laboratorians, and provides a blueprint on how the project will be implemented.

A key component of a successful project management team is the project manager, who uses different tools to keep all stakeholders accountable for their tasks at hand and to monitor the timeline. The project manager also ensures there is clear communication between the manufacturer and the team members at the institution.

How to Choose a Project Management Tool

Project management tools are not only for large projects, though. Laboratorians can use them on a

smaller scale to improve efficiency and sustainability of tasks that laboratories handle every day. Project management tools can help organize project discussions and track multiple projects at once. On an individual level, these tools also can help laboratorians stay on task, track progress, and measure success.

Project management tools include software such as Smartsheet, Microsoft Project, Asana, ClickUp, Monday, or Wrike. These can be used for free or purchased for advanced features. While each company's software has a different outlook on project management, the basic idea of managing projects is the same.

One of the most important features of any project management tool is the ability to track progress against a timeline. One of the best ways to do this is using a Gantt chart. Digital project management platforms allow the project manager to add their team members' names and emails to a centralized location. Instead of emailing about different projects, a project manager can communicate through this one platform with many individuals about different projects simultaneously. The platform is further populated with messages between team members, resulting in more dynamic and interactive discussions about the project. Additionally, images, emails, and ideas can be linked to a specific task, which allows everyone to view and contribute to their colleagues' thoughts.

Viewing different projects on one platform can help each member of the team to monitor their individual progress through the Gantt chart and focus on the deadlines or mileposts most relevant to their work. Software programs also provide tutorial videos on creating your own Excel project management sheet that can incorporate a Gantt chart and allow users to monitor their timelines. Whether a person uses a subscribed project management software or a free version, the most important lesson is to communicate with each other via the platform or discuss the tool during meetings.

Adjusting Project Management to Suit Your Team

When using project management tools, it is helpful to go over pending projects with your team on a regular basis; a project management tool cannot be a substitute for all communication.

Whether a person uses a subscribed project management software or a free version, the most important lesson is to communicate with each other via the platform or discuss the tool during meetings.

In our laboratory, we worked on a robust contingency plan for situations where we do not have operable analyzers. Using a project management tool, we planned out our contingency phases in several rows and assigned different team members based on the task. We tracked our progress, added important attachments to tasks, and turned on automatic alert emails when row changes were made. However, we noticed alert fatigue after a couple of days, so we customized the program to send alerts only once a week.

The pace of the project picked up when we started discussing the itemized list during lab meetings. In our setting, we found it helpful to review management sheets for 10–15 minutes during laboratory meetings. Any updates made to the management tool automatically sent a weekly email notification to the assigned person, reducing email redundancy. Using dashboards and their visual representation of priority projects has helped us reach team goals in a timely manner.

Anu S. Maharjan, PhD, DABCC, FAACC, is assistant professor (clinical) at UConn Health in Farmington, Connecticut.
+EMAIL: amaharjan@uchc.edu

The Sample

Glucose Management Indicator May Be Unreliable

The glucose management indicator (GMI)—an estimated measure of hemoglobin A1c (HbA1c) recommended when managing diabetes with continuous glucose monitoring (CGM)—may be an unreliable measure of type 2 diabetes glycemic control and should be interpreted cautiously, new research says (Clin Chem 2023; doi: 10.1093/clinchem/hvac210).

HbA1c has its own limitations: It does not characterize variability or acute spikes in glucose, and it may be less reliable with altered red cell turnover and certain comorbidities, such as some types of anemia or chronic kidney disease. GMI is derived primarily in young adults with type 1 diabetes, so GMI's performance in patients with type 2 diabetes is poorly characterized. Yet clinicians increasingly rely on it for these patients.

In response, the researchers prospectively studied 144 adults with a mean age of 59.4 years with obstructive sleep apnea and type 2 diabetes who did not use insulin. After measuring HbA1c at the study screening visit, participants simultaneously wore two CGM sensors (Dexcom G4 and Abbott Libre Pro) for up to 4 weeks—2 weeks at baseline and 2 weeks at the 3-month follow-up visit. The researchers calculated GMI using CGM data from each sensor.

The mean difference between HbA1c and GMI was just 0.12–0.14 percentage points, or approximately 2 mmol/mol. However, the two measures were only moderately correlated (r = 0.68–0.71), and researchers found substantial variability in GMI across measurements of HbA1c (root mean squared error: 0.66–0.69 percentage points [7 to 8 mmol/mol]). Between 36% and 43% of participants had a clinically significant, absolute difference between HbA1c and GMI of 0.5 percentage points or more, and 9% to 18% had an absolute difference greater than 1 percentage point. Discordance was higher in the Libre Pro than the Dexcom G4.

LC–MS/MS ASSAY SHOWS PROMISE FOR ANTIDEPRESSANT TESTING

A new automated liquid chromatography tandem mass spectrometry (LC-MS/MS) assay can simultaneously quantify four different classes of antidepressants commonly prescribed to women, according to recent findings (Sci Rep 2023; doi: 10.1038/s41598-023-29229-0).

While the percentage of patients using prescribed antidepressants has skyrocketed, finding suitable treatments remains a long trial-and-error process to deal with side-effects and determine overall treatment efficacy. The challenge increases for women who become pregnant. In response, studies have focused on effective methods to quantify and monitor a wide range of antidepressants that clinicians prescribe specifically to women.

In the current study, researchers validated an automated triple

martin-dm / iStock

quad LC–MS/MS-based assay for simultaneous quantification of the antidepressants, developed a prototype kit using a small sample volume with minimal sample preparation, and compared the assay to previously reported studies in terms of precision and accuracy. The researchers focused on the simultaneous detection of the norepinephrine-dopamine reuptake inhibitor (NDRI) bupropion; selective serotonin reuptake inhibitors (SSRIs) citalopram, olanzapine, sertraline, and vilazodone; the tricyclic inhibitors (TCIs) desipramine and imipramine; and the serotonin and norepinephrine reuptake inhibitor (SNRI) milnacipran.

Using a small 20 µL serum sample, the researchers measured the drugs across a range of 1.0 to 230 ng/mL. The method exhibited a linearity of R2 greater than or equal to 0.99 when detected in multiple reaction monitoring mode (MRM) and percent coefficient of variation (CV) of less than or equal to 20% for all analytes across the board. When compared with existing commercial kits available outside of the United States, the prototype kit proved easily automated with minimal sample loss.

They said that their prototype has potential as an automated method for quantifying antidepressants in postpartum mothers and infants, determining how much of the drugs may be passed on during the nursing period, and monitoring postpartum depression.

INSULIN PUMPS EFFECTIVE IN YOUTHS WITH TYPE 1 DIABETES

Even as the data from continuous glucose monitoring (CGM) has come under scrutiny, new research shows that using insulin pumps with real-time CGM is associated with more frequent meeting of clinical and time-in-range targets and lower probability of severe adverse events compared with other treatment modalities (JAMA Netw Open 2023; doi: 10.1001/jamanetworkopen.2023.0077).

In adults with type 1 diabetes, use of real-time CGM, compared with intermittently scanned CGM, has been associated with improved glycemic control and outcomes.

Researchers aimed to assess real-world data on how CGM affected time-in-range clinical targets among youth with type 1 diabetes. Their multinational cohort study included 5,219 children, adolescents, and young adults under age 21 with type 1 diabetes for at least 6 months. Participants, who provided CGM data, were divided into four treatment modalities: intermittently scanned CGM with or without insulin pump use, and real-time CGM with or without insulin pump use.

Participants' median HbA1c level was 7.4%. Treatment modality was associated with the proportion of individuals achieving recommended clinical targets. Users of real-time CGM concurrently with an insulin pump were most likely to achieve targets for more than 70% time-in-range, less than 25% above, and less than 4% time below clinical target ranges. CGM and pump users had the adjusted highest time in range and were the least likely to experience severe hypoglycemia and diabetic ketoacidosis events.

The proportion of participants achieving the recommended more than 70% time-in-range target was 36.2% for real-time CGM plus insulin pump use (95% CI, 33.9%–38.4%), 20.9% for real-time CGM plus injection use (95% CI, 18.0%–24.1%), 12.5% for intermittently scanned CGM plus injection use (95% CI, 10.7%–14.4%), and 11.3% for intermittently scanned CGM plus insulin pump use (95% CI, 9.2%–13.8%).

The proportion of participants who were 25% of time above target range included 32.5% of those using real-time CGM plus insulin pump (95% CI, 30.4%–34.7%) and 12.8% of those in the intermittently scanned CGM plus insulin pump groups (95% CI, 10.6%–15.4%). Proportion of participants who were less than 4% time below range target included 73.1% of the real-time CGM plus insulin pump group (95% CI, 71.1%–75.0%) and 47.6% of the intermittently scanned CGM plus insulin pump group, (95% CI, 44.1%–51.1%). Adjusted time in range was highest among real-time CGM plus insulin pump users at 64.7% (95% CI, 62.6%–66.7%).

The findings suggest that concurrent real-time CGM and insulin pump use should be more readily available to youths with type 1 diabetes, the researchers said.

As this biomarker becomes more established in the U.S., experts weigh in on how to optimize its use for different clinical indications and patient populations.

THE ULTIMATE GUIDE TO Procalcitonin Testing

BY JEN A. MILLER

Procalcitonin (PCT) is a blood biomarker whose concentrations rise in response to systemic inflammation caused by bacterial infection and sepsis. In recent years, the Food and Drug Administration (FDA) has approved new PCT assays and expanded indications for PCT tests that allow healthcare providers to use this biomarker as both an antimicrobial stewardship tool and to predict 28-day mortality in sepsis patients.

But PCT has limitations, the assays for it can be expensive to run, and studies on its efficacy in specific age groups, including pediatric and neonatal patients, have produced mixed results. In light of the rapid adoption and expansion of PCT testing in healthcare—fueled by those FDA approvals and the COVID-19 pandemic—AACC recently issued new guidance for both clinicians and laboratory professionals on how best to use PCT tests.

While there has been an avalanche of studies proving PCT's effectiveness in the realms of antimicrobial stewardship and sepsis, "there wasn't really a good, comprehensive review from a laboratory-based body, where we could rigorously look at the studies but also limitations of the lab test itself to make recommendations as a whole on how to use this test," said Alison Woodworth, PhD, DABCC, FAACC, clinical director of global laboratory services at CTI Clinical Trial & Consulting Services, and an author of the guidance.

That is, until now.

THE CHALLENGES OF PCT TESTING

Despite their global popularity, PCT tests are still relatively new in the U.S., with FDA only starting to approve them for antibiotic stewardship in 2017.

"These tests have been used for many years in Europe, but they weren't available in the U.S.—particularly as FDA-approved or FDA-cleared assays—on the routine analyzers that most of us have in clinical laboratories," said Allison Chambliss, PhD, DABCC, FAACC, associate clinical professor of pathology and laboratory medicine at the University of California Los Angeles David Geffen School of Medicine, and an author of the guidance.

Interpreting results, especially deciphering what they mean in relation to both sepsis mortality risk and antibiotic stewardship, is not straightforward either, especially for nonlaboratorians. Because of this, Chambliss said, "we thought it was important to pull the literature together, especially clinical trials that had been done in Europe to support the FDA approval and bring PCT over to the U.S."

Another challenge of testing for PCT is that it's "fairly expensive," said Angela Fung, PhD, FCACB, clinical assistant professor at the University of British Columbia and clinical chemist at St. Paul's Hospital, and reimbursement is not always guaranteed. "Despite the published trials, the effectiveness of PCT in real-world implementation requires collaboration and practical considerations such as developing testing protocols (i.e., who is tested and how frequently); interpretation guidance (e.g., determining different cut offs); and test utilization strategies to determine when to approve or cancel tests and which also have to include education," she said.

At the start of the COVID-19 pandemic, when clinicians and laboratorians were desperately trying to find any test or treatment that could help care for patients who were sick with the virus, PCT tests were also thrown into the fray for patients who had tested positive for SARS-CoV-2, Fung said.

The newness of PCT assays, combined with their use during COVID-19, has led to them being ordered in situations where they may not be appropriate.

Interpreting results, especially deciphering what they mean in both sepsis mortality risk and antibiotic stewardship, is not straightforward.

"A lot of residents started to order PCT based on different hospital practices," she said. "We spend a lot of effort educating about appropriate test utilization."

RECOMMENDATIONS FOR USE IN ADULTS AND CHILDREN

While clinical trials on PCT testing done in Europe have been helpful in establishing its effectiveness in sepsis guidance and antibiotic stewardship, there are limitations in what those results can tell healthcare providers and laboratorians in another country. Most of the trials were done with one particular test, and on adults. "Anybody who wanted to use PCT, that's all they had to go off of," Chambliss said, even though there are differences in available PCT assays and what their results mean. "Using the same test in the same lab and watching the value either rise or fall using the same test—that is much more powerful than using a single cutoff from these trials as a guide to management," she added.

One of the benefits of the new AACC guidance is that it distinguishes between different clinical indications of use, she said. "Are you looking to diagnose the patient? Looking to determine when to start antibiotics or, more importantly, when to stop antibiotics? The cutoffs are different," Chambliss said.

PCT testing is also not as well studied in children, which is why the AACC guidance includes a special section on its use in pediatrics and neonates. While PCT assays have been used to test for severe bacterial infections in children—including bacterial meningitis, urinary tract infections, sepsis, and bacteremia—the utility and accuracy of these tests have not been as closely evaluated in children as in adults.

Plus, PCT cutoffs in adults don't always mean the same thing in children, especially newborns, as PCT is high for the first 48–72 hours of a baby's life. "If you're measuring PCT in a baby who doesn't actually have a bacterial infection, but you're using reference ranges and rules that were established in adults, you might misinterpret that result as elevated," Chambliss said. That can lead to unwarranted and potentially harmful treatment.

While studies have been done on PCT levels in children, the authors of the AACC guidance didn't feel that these studies were large enough to determine standard levels that can be applied across different pediatric patient populations.

"We stress in the document that it's important to either establish pediatric intervals or at least acknowledge these limitations with interpretative information to ensure that clinicians are not misinterpreting elevated PCT in those age groups," Chambliss said.

It's also worth noting that, although COVID played a role in the surging popularity of PCT assays in practice, the team that wrote AACC's guidance did not include that as part of the guidance, as PCT is considered a marker for bacterial, not viral infections. Instead, the guidance authors focused on respiratory diseases in which PCT has been more widely studied, including bacterial pneumonia.

PARTNERING WITH PROVIDERS TO IMPLEMENT THIS GUIDANCE

Making sure that PCT assays are used for the right patients and interpreted in the right way can be challenging, especially since the assays are new, evolving, and might have been overused during COVID. This guidance should help, its authors say.

"One of the biggest issues in implementing these tests is that people will just implement them and not do it correctly," said Woodworth. "There can be a big misunderstanding about what the results mean." That's especially true if clinicians are ordering PCT assays without the laboratory's input or without asking clinical laboratorians for help interpreting the results, since many factors and conditions can lead to PCT levels being different from one patient to another. For example, someone with a chronic illness may have an elevated inflammatory response and a higher PCT baseline than other patients. PCT also can spike due to surgery or giving birth, and may not be an indication of a bacterial infection right after those events.

"It really isn't a single measurement but a monitoring over time," said Woodworth. "We really want to help laboratories and also clinicians set up programs to establish when to measure PCT, how frequently they should measure it in what patients, and then also provide them with cutoffs in terms of concentrated PCT in the bloodstream that might predict severe disease or the need to change treatment."

That's why the AACC guidance also includes a section on how PCT testing should be incorporated into broader antimicrobial stewardship efforts. "The laboratory and these antibiotic stewardship clinicians, infectious disease clinicians, and pharmacists should work together so that we can present laboratory data in a way that supports the optimal use of these tests and optimal use of antibiotics," Chambliss said.

As laboratories implement PCT assays and add this biomarker to their test menus, "it's really important to determine how the results are going to be displayed and what kinds of interpretative comments go with the test results," she said. "Hospitals and laboratories should develop interpretative algorithms, and many have."

As a healthcare system introduces a PCT assay as a testing option, "rather than just validating the test and opening it up for ordering, we should make sure we're providing effective interpretative information and that we're involving appropriate stakeholders so that information will be seen and followed," Chambliss added.

As an example, at St. Paul's Hospital in Vancouver, British Columbia, PCT tests are strictly used for ICU patients suspected of having bacterial infection and for the purpose of antibiotic stewardship only. "There's a protocol in place for daily rounding with the infection control and antibiotic stewardship teams to look at the PCT result and look at the clinical picture together" in order to determine antibiotic therapy discontinuation, Fung said. That and cancelling tests for unapproved clinical indications and situations goes a long way in making sure PCT assays are used and interpreted in the right situations and in the right ways.

Jen A. Miller is a freelance journalist who lives in Audubon, New Jersey.
+TWITTER: @byJenAMiller

Previous page and left: Sasiistock / iStock

Why Labs Should Partner with Payers and Providers

As clinical laboratories explore ways to add value to healthcare, some are partnering with providers and payers. In doing so, they not only improve care while lowering costs, but also earn the lab more leverage with healthcare administrators and managed care organizations.

A number of laboratories are becoming more proactive in the services they offer to clinicians, said Andrew Fletcher, MD, MBA, CPE, CHCQM, FCAP, founder of Eutiologic Consulting in Salt Lake City, a consulting company focused on laboratory stewardship and quality. Fletcher advocates for labs to figure out ways they can provide added value not only to providers, but also to managed care companies.

"Labs tend to look inward at ourselves. We're not good at looking outward and seeing the bigger picture," said Fletcher, who worked at ARUP Laboratories before starting Eutiologic. "We need to ask ourselves: How does the laboratory affect the cost of care? How do we take it to another level? How does the laboratory drive the cost of care for the entire healthcare system?"

Jon Harol, president of Lighthouse Lab Services, a consulting company based in Charlotte, North Carolina, agreed, noting that labs already provide a lot of value to the health system, but they need to be able to demonstrate it and tie it to healthcare outcomes.

"Labs need to do a better job of advocating for the value that they bring to healthcare, and they need to speak the language of healthcare outcomes," he said.

Fletcher's own experience demonstrates that laboratory intervention can be helpful in improving care and reducing costs in many different areas, including shortening length of stay, both for inpatients and in the emergency department (ED). While working at ARUP, he realized that for patients coming to the ED for chest pain, providers often were running creatine kinase-MB tests every 8 hours—when the patients first arrived and twice more over the next 16 hours. However, because of Medicare rules regarding observation, part of that time when patients were in the ED was not reimbursed.

Through these collaborations, clinical laboratories can use their expertise and data to improve outcomes, save money, and increase their influence within the healthcare system.

BY KIMBERLY SCOTT

The Role of Labs in MIPS

In addition to helping payers and providers in managing population health, clinical laboratories also can play a role in helping providers receive incentive payments under Medicare's Merit-based Incentive Payment System (MIPS).

MIPS is part of Medicare's Quality Payment Program, which rewards physicians for the value of care they provide rather than the volume of care they provide. Payment adjustments are based on performance points scored according to national benchmarks. Each performance year, an eligible clinician's MIPS final score determines their future Medicare Part B payment adjustments.

"We work with a large managed care organization that decided it wanted to capitalize on its MIPS scores," said Jon Harol, president of Lighthouse Lab Services, a consulting company based in Charlotte, North Carolina. "Lab testing was a big part of that. They increased testing for diabetes. They also used a lot of home testing to reach patients who were home-bound. The physicians were all a part of that, and it helped them improve their MIPS incentive bonus."

Although it seems likely that the MIPS system will continue, a study published Dec. 6 in the Journal of the American Medical Association calls into question whether the program is working as intended (JAMA 2022; doi:10.1001/jama.2022.20619). Researchers analyzed more than 80,000 primary care physicians enrolled in MIPS and concluded that the program's accuracy in identifying high-versus-low performing providers was really no better than chance.

The researchers are not certain why MIPS scores may not capture clinical performance. However, they suspect there is inadequate risk adjustment for physicians who serve more medically complex and socially vulnerable patients, and that smaller, independent primary care practices have fewer resources to dedicate to quality reporting, leading to low MIPS scores.

"MIPS scores may reflect doctors' ability to keep up with MIPS paperwork more than they reflect their clinical performance," wrote Amelia Bond, PhD, an assistant professor of population health sciences at Weill Cornell Medicine in New York City and author of the study.

Fletcher recommended that the ED use cardiac troponin tests instead, which are run every three hours (hours 0, 3, and 6). This allowed for faster diagnosis and reduced the time that patients spent in observation. High-sensitivity troponin tests, which can be run every hour, can save even more time and result in an even quicker diagnosis, thus improving patient outcomes.

"The laboratory actually helped shave time off the length of stay," Fletcher noted, adding that these types of initiatives give labs leverage when it comes time to make decisions about budgeting within a health system or even in contract negotiations with payers.

"Most of the time labs don't have a seat at the table when it comes to decision-making in the hospital," he said. "But if the lab can actually show data on how they reduced length of stay and saved money for the system, they can get a seat at the table."

LEVERAGING LONGITUDINAL DATA TO IMPROVE CARE

TriCore in Albuquerque, New Mexico, is one of the labs leading the way in leveraging clinical laboratory results to improve patient care. The Rhodes Group, an analytics company owned by TriCore, works with managed care organizations to provide laboratory-generated clinical insights into specific conditions and to help the payers improve the health of certain populations.

In the area of prenatal care, for example, Rhodes conducted a study over 11 months to examine the benefit of laboratory-generated clinical insights on prenatal care quality metrics and clinical outcomes, explained Richard VanNess, Rhodes director of product development. Measures included early identification of pregnancy and births to facilitate care, care gaps with prenatal laboratory testing, ED visits, preterm births, and neonatal intensive care unit (NICU) admissions and length of stay.

Once Rhodes helped to identify gaps in care, payers were able to work with providers to ensure that those gaps in care were closed, resulting in improved outcomes, according to a study published in 2021. Women with ongoing prenatal care had fewer ED visits (17% vs. 23%) and NICU admissions (11% vs. 18%) compared with those without prenatal care.

"We are trying to leverage the lab's data footprint to help close care gaps," explained VanNess. "Labs are in a unique position in America to have a positive impact on patient outcomes through their laboratory data."

Not only does the Rhodes Group help close gaps in care for pregnant women and new mothers, but VanNess hopes the insights they are able to provide can help payers meet certain Healthcare Effectiveness Data and Information Set (HEDIS) targets, which would have both clinical and financial benefits.

For example, the Rhodes Group utilizes laboratory data analytics to identify diabetes screening care gaps for Medicaid patients who are being treated for schizophrenia and/or bipolar disorder and who are taking antipsychotic medications. Under HEDIS, payers are penalized if they fail to meet target screening goals (for 2023, the goal is to screen 82.78% of these patients).

"In New Mexico, payers struggle to meet the diabetes screening target for schizophrenia," said VanNess. "Failure to meet these targets has significant cost implications to payers."

VanNess has proposed to the payers that Rhodes Group and Tricore help identify patients who need screening and connect them with the appropriate testing. The managed care companies would pay the lab a set fee for specific outcomes and for helping them meet their HEDIS targets. Ultimately, such a collaboration would be a win-win-win situation for patients, TriCore, and payers, said VanNess.

ENGAGING WITH PAYERS

Harol of Lighthouse Lab Services said that as federal payers move increasingly toward value-based care payment models where providers are paid a set fee for patient care, laboratory testing and data will become even more important than it already is. The challenge is that lab data can be difficult to put into forms that are useful.

"Showing that a test you provide now is going to help a patient a few years from now requires a lot of data collection, tracking, publishing. There's a lot of work that has to be done to package that information," he said. "It's a heavy lift. There aren't a lot of labs who are doing that."

VanNess acknowledged that many clinical laboratories don't have experience engaging with payers in this way, but he said it can be done.

"To be honest, I think a lot of labs are overwhelmed by the data," he said. "We would like to teach other labs how to do this. It does take some investment and innovative thinking, but payers need these measurements in real time, and labs are in the best position to provide this kind of information."

Fletcher agreed, noting that many laboratories are still "in the basement" and may be reluctant to approach payers or case managers to offer additional assistance in improving patient outcomes. "But some are starting to realize that maybe if I demonstrate my value to the healthcare system, I can get more allocated to the laboratory, and I can do more with the resources I have."

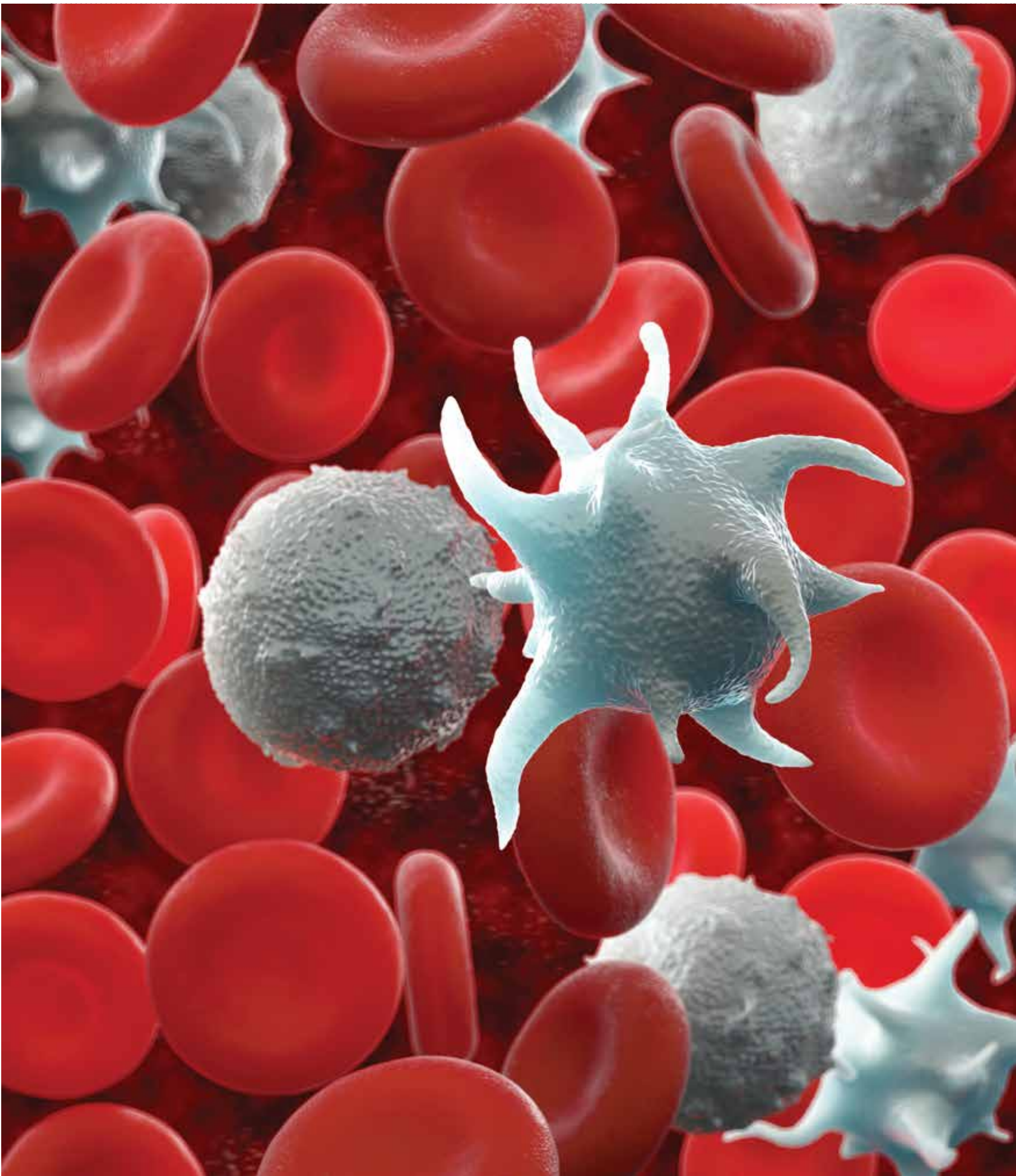
"The lab has to be a little disruptive," said VanNess. "You have to convince the payer that you deserve a seat at the table. Show them your data and what you can do for them. It's a way to prove your value and might even help you become a preferred lab in some networks."

Fletcher advises labs to approach case managers, ask about the biggest problems they are dealing with, and offer to help develop a solution.

"Explain to them that the lab isn't going to solve all their problems, but we can help contribute to the solutions," he said. "Labs can have a high-dollar impact, which in and of itself demonstrates the value of the laboratory."

Kimberly Scott is a freelance writer who lives in Lewes, Delaware.
+EMAIL: kmscott2@verizon.net

Previous page and left: Andrey Popov / iStock



Is TEG the Right Assay?

The COVID-19 pandemic accelerated the modernization of viscoelasticity testing and is bringing next-generation instruments to additional clinical settings.

BY OKSANA VOLOD, MD

Dr. Hellmut Hartert invented thromboelastography (TEG), the first viscoelastic test (VET), in Germany in 1948 (*1*). This was even before the activated partial thromboplastin time test (aPTT), which Langdell, Wagner, and Brinkhous first described in 1953 (*2*). Shortly after, rotational thromboelastometry (ROTEM) evolved from TEG. Both devices provide real-time visual assessment of clot formation and dissolution under low shear rate blood flow using so called cup and pin technology.

Clinical laboratories did not adopt VET widely until the introduction of a cell-based model of hemostasis in 1994, showing the importance of platelets and tissue factor in hemostasis. Their initial applications were limited to liver transplantation and cardiac surgeries.

Relying on conventional plasma-based coagulation testing (CCT) has proven difficult in managing trauma patients. The advent of data-driven algorithms using VET emerged as a reliable way to predict need for transfusion and to guide transfusion therapy in traumatic injury (*3*). The COVID-19 pandemic exponentially elevated the need for rapid assessment of COVID-19 patients' hemostasis and appropriate management of their coagulopathy, as many patients with COVID-19 have an abnormally increased risk for blood clotting.

MODERNIZATION OF VISCOELASTICITY TESTING

Over the past two decades, the TEG 5000 (Haemonetics Corporation) and ROTEM delta (Werfen) have been the principal VET technologies, or "legacy devices." Both technologies require personnel to pipette blood and are prone to human error. Another legacy linear motion system, Sonoclot (Sienco), is not widely used in the U.S. and will not be discussed here.

To improve precision, reduce the potential for human errors, and improve ease of performing the assay, companies recently have developed several new generations of cartridge-based automated VET that have received Food and Drug Administration (FDA) clearance for specific clinical indications. Advantages and limitations of these assays and their clinical indications are reviewed below.

Table 1.
Next-Generation Viscoelastic Systems Comparison

	TEG 6s	Quantra	ROTEM Sigma
Method	Resonance	Sonic Estimation of Elasticity via Resonance (SEER)	Cup and Pin
FDA approved sample type	3.2% citrated whole blood	3.2% citrated whole blood (arterial or venous)	3.2% citrated whole blood
Cartridges	1. Global 2. Global with lysis 3. Platelet mapping	1. Q Plus 2. Q Stat	1.ROTEM sigma complete 2. ROTEM sigma complete + hep cartridge
System operation	Open tube Unmetered pipetting	Closed tube Automated	Closed tube Automated
Cartridge refrigeration	Yes	No	No
External Quality Control	2 levels/IQCP	2 levels/IQCP	2 levels/IQCP
Connectivity	Yes	Yes	Yes
Remote view	TEG manager	Yes	Yes
Assay start time	10 min after blood draw	Immediately after draw	Immediately after draw
Time to assay completion	A patient test stops automatically when the requisite parameters for the test have finalized. Maximal run 90 minutes.	15 minutes	Can run for >= 60 minutes

IQCP, individualized quality control plan

TEG 6S

A new generation of thromboelastography, TEG 6s (Haemonetics), assesses blood viscoelastic properties by resonance technology (*4*). Alteration of resonance is measured by the light-emitting diode (LED). The collected data is converted into a graph that is identical to that used in the cup and pin method. Pneumatically controlled microfluidic cartridges improve sample handling and minimizes the effect of preanalytical variables that were affecting the original TEG device. However, it still requires specimen pipetting into the cartridge.

Currently, three TEG 6s cartridges are FDA-approved in the United States for adult patients: global hemostasis (GH) for cardiovascular surgeries, global hemostasis with lysis (GHL) for trauma coagulopathies, and platelet mapping (PM).

ROTEM SIGMA

The ROTEM sigma device (Werfen) is a completely automated cartridge-based device which eliminates specimen pipetting (*4*). A cup and pin system is still used, but it uses freeze-dried reagents.

The ROTEM sigma has two cartridges: ROTEM sigma complete and ROTEM sigma complete + hep. The ROTEM sigma complete cartridge discriminates between hyperfibrinolysis and platelet mediated clot retraction/FXIII deficiency and provides in vitro assessment of antifibrinolytic drug effect. The ROTEM sigma complete + hep detects heparin and heparin-like substances.

Recently, FDA approved ROTEM sigma use in adult patients to assess perioperative hemorrhage and/or thrombosis in cardiovascular surgery and liver transplantation.

QUANTRA

The Quantra System (HemoSonics) is a new device that assesses blood viscoelastic properties by a unique ultrasound-based technology called sonic estimation of elasticity via resonance (SEER) sonorheometry (*4*). The Quantra Analyzer is a cartridge-based, fully automated four-channel device. The cartridge is the only component of the device that is in direct contact with blood. The sample is introduced by directly attaching a standard 3.2% citrated whole blood tube to the input port of the cartridge. The sample is then automatically drawn into the cartridge to initiate testing. No sample pipetting is required.

Currently, two Quantra cartridges are FDA approved in the United States for adult patients: QPlus for use in the perioperative setting of cardiac and major orthopedic surgery (no lysis assessment) and Qstat for trauma and liver transplant surgery (allows lysis assessment).

Unlike TEG and ROTEM traces, Quantra results are displayed as dials or curves on a screen, which are more intuitive and easier to interpret.

Another important Quantra distinction from classical cup and pin technologies is that SEER sonorheometry directly measures the clot's shear modulus in rational pascal units, an objective parameter that describes the elastic properties of a solid material. In contrast, TEG and ROTEM provide a rather indirect measurement of clot stiffness: maximum amplitude in millimeters (MA, mm) in TEG, or as maximum clot firmness also in millimeters (MCF, mm) in ROTEM.

CLOTPRO

The ClotPro (enicor) is a 6-channel viscoelastic cup and pin method like the original technologies of the TEG 5000 and ROTEM delta analyzers. ClotPro uses elastic motion thrombelastography, an improved next-generation viscoelastometry technique. It also has simplified the multiple manual pipetting and reagent preparation procedures with the use of a standard pipette. The pipette contains predosed reagents that activate on contact with the blood sample.

ClotPro is used mainly in Europe and is not FDA approved in the U.S. (*3*). Table 1 provides additional comparison of the next-generation FDA-approved VETs.

Companies have developed new generations of cartridge-based, automated viscoelastic tests.

VETS AGREEMENT AND INTERCHANGEABILITY

The TEG 5000 uses a mechanical detection system (a pin suspended in a blood sample with a torsion wire that is monitored for motion). The TEG 6s measures clot viscoelasticity by using resonance technology, exposing the blood sample to a fixed vibration frequency.

Because TEG 6s and the TEG 5000 use different methods to assess similar coagulation components, there is a difference in absolute values of respective parameters of the two devices, and they are not interchangeable. Published studies in healthy donors, simple cardiac surgeries, and critically ill patients demonstrate strong correlation between the two devices especially for the reaction time (R) and MA parameters (*5*, *6*). There was poor concordance between devices for the LY 30 parameter assessing fibrinolysis with a correlation coefficient of 0.33 (*6*). TEG 5000 based algorithms may not be interchangeably used for the TEG 6s device (*6*, *7*).

The same cup and pin technology is used in the ROTEM delta and sigma devices. This allows for the use of the same algorithms that are already established for the ROTEM delta device.

In a small sample size study, the ROTEM sigma device was found to be precise and had results comparable to the ROTEM delta device (*8*). In a separate study comparing the TEG 6s with the ROTEM sigma, the authors observed strong correlations for R time, kinetic time, and alpha angle. Absolute values were substantially different between the two platforms (*9*).

Similarly, the Quantra showed a strong correlation with the ROTEM sigma for determining clot times and clot stiffness. However, these parameters were not directly interchangeable (*10*).

Whether legacy or next-generation devices, none can be used in a comparative setting. Each institution must establish its own device-specific reference ranges (*4*, *11*, *12*).

VET LIMITATIONS

Since VETs assess blood flow under low shear rate, they are not sensitive to von Willebrand disease (vWD) because activation of the vW factor requires high shear rate forces and collagen.

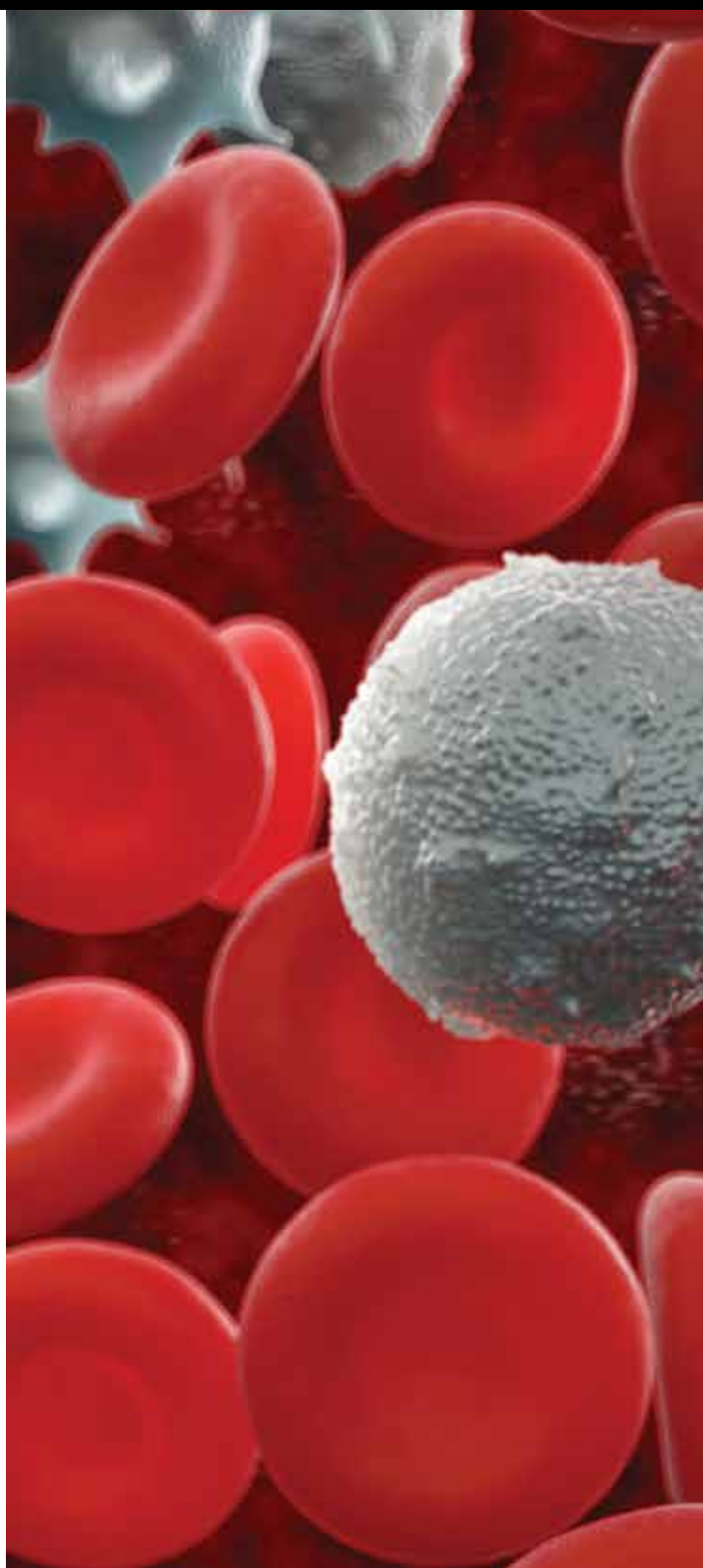
Due to the overwhelming effect of thrombin on platelets, VETs cannot detect specific platelet receptor abnormalities without the use of specialized VET assay modification known as TEG platelet mapping.

Detecting the hemostatic competence of patients treated with direct oral anticoagulants (DOACs) or warfarin also requires specialized reagents and testing. The standard TEG/ROTEM/Quantra activators activate a blood sample with a contact phase activator such as kaolin or ellagic acid. TEG 6s global and platelet mapping cartridges, Q Plus cartridges and ROTEM sigma complete + hep cartridges do not display the lysis parameter.

VETs have been widely used in pediatric patients, but they are FDA approved only for adults

VETS EXPAND ACROSS CLINICAL SETTINGS

The rapidly evolving COVID-19 pandemic has revealed a changing landscape around the acceptance of VETs in treating COVID-19 associated coagulopathy (CAC). Conventional coagulation tests (CCT) didn't reflect the complexity of hemostatic alterations and were not available for



Previous page and right: Peddalanka Ramesh Babu / iStock

Autoimmune Diagnostics

For more than 35 years, KRONUS has provided specialized immunoassay test kits to medical professionals at the world's most respected laboratory facilities. Our current product offering encompasses test kits for measurement of the following:

NEUROIMMUNOLOGY

Aquaporin-4 Autoantibody (AQP4Ab)

Acetylcholine Receptor Antibody (AChRAb):
- Binding Antibody
- Blocking Antibody

Voltage-Gated Calcium Channel Antibody: P/Q-Type

ISLET CELL AUTOIMMUNITY

Glutamic Acid Decarboxylase Antibody (GADAb)

Zinc Transporter 8 Autoantibody (ZnT8Ab)

IA-2 Autoantibody (IA-2Ab)

Insulin Autoantibody (IAA)

THYROID

TSH Receptor Antibody (TRAb)

ADRENAL AUTOIMMUNITY

21-Hydroxylase Antibody (21-OHAb)

To obtain additional information on **KRONUS'** unique line of laboratory test kits, please call us toll-free at **800 4 KRONUS** or email us at **kronus@kronus.com.**

ALSO AVAILABLE FOR RESEARCH APPLICATIONS

Acetylcholine Receptor Antibody: Ganglionic (gAChRAb)†

Voltage-Gated Calcium Channel Antibody: N-Type (N-VGCCAb)†

GAD/IA-2/ZnT8 Antibody Screen†

Titin Antibody (TitinAb)†

Voltage-Gated Potassium Channel Antibody (VGKCAb)†

† For Research Use Only.
Not For Use in Diagnostic Procedures.

KRONUS®
ISO 13485: 2016 QMS Certified

Your Source for Sensitive Autoimmune Diagnostics

800 4 KRONUS
www.kronus.com

Without a doubt, VET is becoming part of patient management protocols in a variety of clinical settings.

immediate decision-making at the point of care. Clinicians managing severe COVID-19 were interested in using tests that could help them quickly understand whether an individual patient was hypocoagulable, hypercoagulable, or had abnormal fibrinolysis.

In January 2021, FDA issued guidance allowing hospitals to use all FDA-approved VETs for COVID-19 patients. The agency indicated that using these devices in hospitals could provide real-time assessment of whole blood viscoelastic properties and aid in patient management.

In a short time, numerous case reports, as well as prospective, retrospective, and single-center observational studies, have been published using VETs to study and manage CAC (*4*). This rapid expansion of the literature on VETs and CAC led to increased adoption of next-generation VET at the bedside in a variety of other clinical settings including trauma, postpartum hemorrhage, extracorporeal mechanical oxygenation, surgical, and critical care medicine (*12*).

Without a doubt, VET is becoming part of patient management protocols in a variety of clinical settings. According to manufacturer Haemonetics, the company will continue to expand the utilization of the new TEG 6s analyzer and support all TEG 5000 users only until March 31, 2029. After this date, they do not intend to sell or service any TEG 5000 analyzers or disposables. Werfen likely will also follow Haemonetics in withdrawing ROTEM delta from the market.

Which of the next-generation VETs is more closely representative of true hemostatic alterations, including fibrinolysis, is a question that further research will need to elucidate.

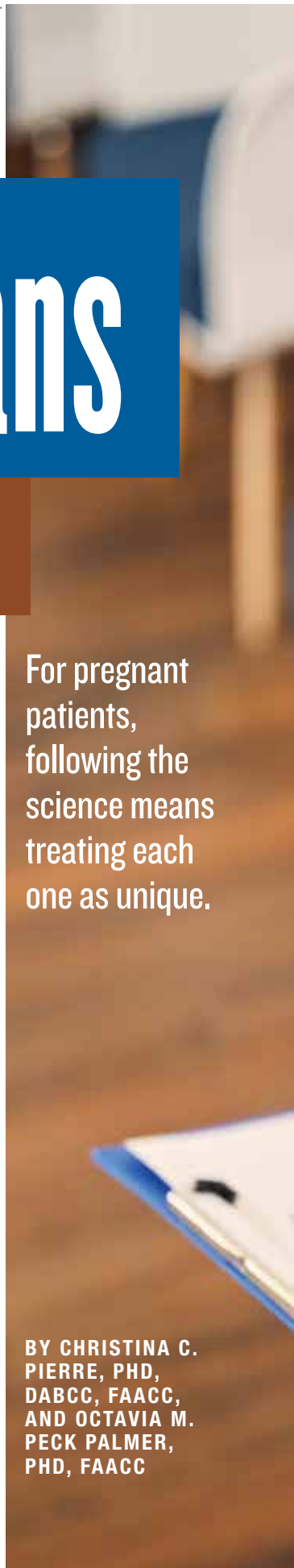
Oksana Volod, MD, is director of coagulation consultative service and professor of pathology at Cedars-Sinai Medical Center. She is also associate professor of pathology at the David Geffen School of Medicine at the University of California, Los Angeles.
+EMAIL: oksana.volod@cshs.org

REFERENCES

1. Hartert, H. Blutgerinnungsstudien mit der Thrombelastographie, einem neuen Untersuchungsverfahren. Klin Wochenschr 1948; doi: 10.1007/BF01697545
2. Langdell RD, Wagner RH, Brinkhous KM. Effect of anti-hemophilic factor on one-stage clotting tests: a presumptive test for hemophilia and a simple one-stage anti-hemophilic factor assay procedure. J Lab Clin Med 1953; doi: 10.5555/uri:pii:0022214353903126
3. Baksaas-Aasen K, Van Dieren S, Balvers K, et al. Data-driven development of ROTEM and TEG algorithms for the management of trauma hemorrhage: a prospective observational multicenter study. Ann Surg 2019; doi: 10.1097/SLA.0000000000002825
4. Volod O, Bunch CM, Zackariya N, et al. Viscoelastic hemostatic assays: a primer on legacy and new generation devices. J Clin Med 2022; doi: 10.3390/jcm11030860
5. Gurbel PA, Bliden KP, Tantry US, et al. First report of the point-of-care TEG: a technical validation study of the TEG-6S system. Platelets 2016; doi: 10.3109/09537104.2016.1153617
6. Lloyd-Donald P, Churilov L, Zia F, et al. Assessment of agreement and interchangeability between the TEG5000 and TEG6S thromboelastography haemostasis analysers: A prospective validation study. BMC Anesthesiol 2019; doi: 10.1186/s12871-019-0717-7
7. Neal MD, Moore EE, Walsh M, et al. A comparison between the TEG 6s and TEG 5000 analyzers to assess coagulation in trauma patients. J. Trauma Acute Care Surg 2020; doi: 10.1097/TA.0000000000002545.
8. Schenk B, Gorlinger K, Treml B, et al. A comparison of the new ROTEM® sigma with its predecessor, the ROTEM delta. Anaesthesia 2019; doi: 10.1111/anae.14542
9. Ziegler B, Voelckel W, Zipperle J, et al. Comparison between the new fully automated viscoelastic coagulation analyzers TEG 6s and ROTEM Sigma in trauma patients: a prospective observational study. Eur J Anaesthesiol 2019; doi: 10.1097/EJA.0000000000001032
10. Baulig W, Akbas S, Schütt PK, et al. Comparison of the resonance sonorheometry based Quantra® system with rotational thromboelastometry ROTEM® sigma in cardiac surgery –a prospective observational study. BMC Anesthesiol 2021; doi: 10.1186/s12871-021-01469-5
11. Bareille M, Lecompte T, Mullier F, et al. Are viscoelastometric assays of old generation ready for disposal? Comment on Volod et al. Viscoelastic hemostatic assays: a primer on legacy and new generation devices." J Clin Med 2023; doi: 10.3390/jcm12020477
12. Volod O, Bunch CM, Miller J, et al. Reply to Bareille et al. Are viscoelastometric assays of old generation ready for disposal? Comment on "Volod et al. Viscoelastic hemostatic assays: a primer on legacy and new generation devices." J Clin Med 2023; doi: 10.3390/jcm12020478

Peddalanka Ramesh Babu / iStock

Championing the Removal of Race-Specific Medians in Maternal Serum Screening



BY CHRISTINA C. PIERRE, PHD, DABCC, FAACC, AND OCTAVIA M. PECK PALMER, PHD, FAACC

Healthcare providers and scientists are reexamining race as an explanatory variable for genetic and biological differences. Since race is a sociopolitical construct, using it as a biological system of classification can introduce systematic differences in care and exacerbate racial and ethnic health disparities (*CLN*, March 2023).

The increased awareness in medicine about the limitations of race-based medical algorithms led to the medical community removing race coefficients from several widely used clinical calculations, including the estimated glomerular filtration rate equations and the vaginal birth after cesarean success calculator (*1*, *2*). Both race-based algorithms had the potential to compromise care for Black patients and lead to worse outcomes.

Now the clinical laboratory community is examining the potential for patient harm due to another race-based variable: maternal serum screening (MSS) biomarkers.

WHAT'S AT RISK IN MATERNAL SERUM AND CELL-FREE DNA SCREENING

MSS provides risk estimates for fetal aneuploidies including Trisomy 21 (Down syndrome), Trisomy 18 (Edwards's syndrome), and Trisomy 13 (Patau syndrome), as well as or open neural tube defects (ONTD) (*3*). Patients with increased MSS risk estimates undergo invasive amniocentesis or chorionic villus sampling (CVS) testing to provide a definitive diagnosis (*3*).

As a screening test, MSS paradigms seek to optimize sensitivity in order to maximize detection. Minimizing false positive results is also important, due to the risk of miscarriage associated with amniocentesis and CVS and the negative emotional toll that false positive results can have on the patient.

Healthcare providers perform first-trimester screening between approximately 11 and 14 weeks of gestation. They combine ultrasonographic detection of translucent fluid collection behind the fetal neck, the nuchal translucency, with maternal serum human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein A (PAPP-A) measurements. In second-trimester screening, also known as the quad screen, providers perform maternal serum hCG, alpha-fetoprotein (AFP), unconjugated estriol (uE3), and dimeric inhibin A (DIA) measurements between 15 and 21 weeks of gestation (*3*).

Clinical laboratories calculate multiples of median (MoMs) for each biomarker by dividing the patient concentration by the median concentration of the biomarker in the local population. The pattern of increase or decrease in the biomarker MoMs correlates with the risk for trisomies and ONTD. Age-specific risks are modified with likelihood ratios for the serum biomarker MoMs using Bayes' theorem, with further adjustment for demographic and clinical variables that have been shown to affect MSS biomarker concentrations, including maternal race, weight, diabetes, in vitro fertilization, multiple gestations, and smoking status.

CURRENT REQUIREMENTS FOR RACE-BASED TEST RESULTS

The College of American Pathologists (CAP) requires accredited clinical laboratories to calculate separate MSS biomarker medians for Black and White pregnant patients. Alternatively, if sufficient data is not available, labs must apply a correction factor for patients from the less common races. CAP also requires clinical laboratories to consider using median values specific to other races and ethnic groups if significant differences in biomarker concentrations exist between these groups in the screening population. Labs must document the reasoning for the inclusion or exclusion of the race adjustments (for each biomarker) and the definition the lab used to identify which patients receive the race adjustment.

Notably, the American College of Medical Genetics, in their 2019 technical bulletin on maternal serum AFP screening, also recommends race-based adjustments for AFP MoMS for the detection of ONTD.

CAP requirements for race-specific MSS biomarker medians are based on studies that have demonstrated increased concentrations of PAPP-A, AFP, and hCG and decreased DIA concentrations in Black compared to White patients. The intent of calculating MSS risk scores with race- and ethnic-specific adjustments is to improve accuracy. Indeed, researchers have reported population-level differences between racial and ethnic groups across multiple but not all studies (*1*, *4–7*).

However, the application of these adjustments is based on an inaccurate premise: that race and ethnicity describe genetically and socioeconomically homogenous groups. Further, implementing these adjustments requires patient self-identification or assignment of race by healthcare providers, although there is no gold standard for categorizing individuals by race.

Cell-free DNA (cfDNA) screening is a more sensitive and specific method for aneuploidy detection compared to MSS and does not incorporate patient race. Circulating cfDNA in the maternal serum consists of a fraction of placental DNA known as the fetal fraction (cffDNA). cfDNA in the maternal circulation is analyzed for aneuploidy, microdeletions, and large copy number changes.

Unfortunately, many patients cannot afford cfDNA prenatal screening, and insurance plans do not universally cover the testing. The Coalition for Access to Prenatal Screening only reports that several leading national commercial insurance plans cover cfDNA prenatal screening for those considered "high risk," and seven states and the District of Columbia Medicaid programs do not cover cfDNA prenatal screening at all, even for high-risk pregnancies (*8*). Furthermore, lower cffDNA has been observed in African American and South Asian individuals compared to White individuals (*9*). This suggests that MSS may remain an important prenatal screening tool for underinsured and uninsured patients.

Race-based adjustments do not account for genetic or socioeconomic heterogeneity within racial and ethnic groups.

THE LIMITATIONS OF RACE-BASED ADJUSTMENTS IN MSS

Race-based adjustments do not account for genetic or socioeconomic heterogeneity within racial and ethnic groups. To demonstrate how genetic and socioeconomic heterogeneity within racial and ethnic groups can confound MSS screening results, we can examine the results of one of the studies referenced by CAP that explored gestational age-dependent effects of maternal and pregnancy characteristics, including maternal race, on free β-hCG and PAPP-A (*4*).

The study was performed in a cohort of 27,908 singleton pregnancies from the United Kingdom (UK) and 125,461 singleton pregnancies from Denmark with normal fetal karyotypes or that resulted in the birth of a phenotypically normal neonate (*4*). The study did not describe the method the authors used to assign race to the participants. Gestational age-dependent increases in PAPP-A concentrations were statistically different in Black participants compared with White participants (~5-6% higher) in both the UK and Denmark cohorts. Gestational age-dependent increases in β-hCG concentrations were statistically higher in Black compared to White participants in the Denmark cohort (~3-4% higher), but no differences in the weekly change of β-hCG concentrations were reported in Black participants of the UK cohort compared to White participants.

In exploring possible reasons for the discrepancy in rate of change of β-hCG concentrations between the Black participants in the two different cohorts, the authors state that "maternal serum levels of PAPP-A and free β-hCG may vary according to the broad categories of racial origin and within such categories, including the exact country or, indeed, the tribe of origin." The "Afro-Caribbean racial origin" subset of the UK cohort originated from the Caribbean, in contrast to the Denmark cohort, where the majority originated from Africa.

A recent retrospective cohort study examined AFP concentrations in 27,710 pregnant patients that underwent MSS at the University of Washington in Seattle. The study found no statistically significant difference in raw maternal serum AFP concentrations, or weight- and gestational age-adjusted AFP concentrations, between Black and non-Black patients (*1*). Using a regression model to remove race adjustment, the study found no statistically significant difference between Black and non-Black patients in median raw maternal serum AFP values, nor in median maternal serum AFP MoM. The results of this study conflict with early

Previous page and left: Drazen Zigic / iStock

studies that demonstrated higher concentrations of AFP in Black individuals compared with White individuals in study cohorts in East London, the UK, and Farmington, Connecticut (*5*, *7*).

Why do racial differences in MSS biomarkers appear to be study- and population-dependent? Ancestral African populations exhibit a large degree of genetic heterogeneity. Forced and voluntary migration of people of African ancestry and subsequent admixture with individuals of other geographic ancestries has resulted in further genetic heterogeneity between people racially categorized as Black. In other words, the Black racial category describes people from multiple modern day geographic locations that are genetically diverse but treated as a single biological category when healthcare providers use race-based adjustments to generate a clinical result.

Socioeconomic differences between individuals categorized in the same racial or ethnic group between different populations may also contribute to conflicting observations between studies.

ACCOUNTING FOR SOCIAL AND STRUCTURAL FACTORS

While multiple physiologic and clinical factors reportedly impact MSS biomarker concentrations (e.g., maternal weight, smoking status, diabetes) and are incorporated into aneuploidy risk estimates, there has been limited research conducted on the impact of social and structural factors.

Systemic racism significantly contributes to the development and the continuation of racial health disparities (*10*). In the context of scientific research, Lett et al. recommend that race should not be used as a measure for biological differences, but rather as a proxy for exposure to systemic racism (*10*).

For example, systemic racism leads to racial differences in social determinants of health such as food availability, built neighborhood environment including green space, and proximity to pollutant reservoirs. Despite the availability of methods to assess how social and structural factors might interact with disease (*10*), researchers scarcely employ them to interrogate racial differences in disease biomarkers, disease incidence and prevalence, or health outcomes (*10*).

A new expert consensus report of the National Academies of Science, Engineering and Medicine urges researchers to directly evaluate the environmental factors or exposures that may affect genetic and genomic studies, rather than relying on population descriptors such as race as a proxy where possible. When the use of race as a proxy for environmental factors or exposure is unavoidable, the report recommends that researchers clearly identify how race is employed and why the use of race is relevant to the study.

Our understanding of race, genetics and social determinants of health have evolved significantly since the studies that provided the basis for the inclusion of race in MSS were performed. As such, a reappraisal of this practice is long overdue.

More in This Series

In the March 2023 issue of *CLN*, the nuances and complexities surrounding the use of race in medicine were highlighted in the article, "The Past, Present, and Future of Race in Medicine." Read more at www.aacc.org/cln

Christina C. Pierre, PhD, DABCC, FAACC, is a clinical assistant professor in the department of pathology and laboratory medicine at the Perelman School of Medicine at the University of Pennsylvania in Philadelphia, and a clinical chemist and section director of clinical chemistry and coagulation testing at Penn Medicine Lancaster General Hospital in Lancaster, Pennsylvania.
+EMAIL: christina.pierre@pennmedicine.upenn.edu

Octavia M. Peck Palmer, PhD, FAACC, is an associate professor at the University of Pittsburgh School of Medicine and division director of clinical chemistry at the University of Pittsburgh Medical Center in Pittsburgh.
+ EMAIL: palmerom@upmc.edu

REFERENCES

1. Burns NR, Kolarova T, Katz R, Ma K, Delaney S. Reconsidering race adjustment in prenatal alpha-fetoprotein screening. Obstet Gynecol 2023; doi:10.1097/AOG.0000000000005045
2. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. Am J Kidney Dis 2021; doi:10.1053/J.AJKD.2021.08.003
3. Dashe JS. Aneuploidy screening in pregnancy. Obstet Gynecol 2016; doi:10.1097/AOG.0000000000001385
4. Ball S, Ekelund C, Wright D, et al. Temporal effects of maternal and pregnancy characteristics on serum pregnancy-associated plasma protein-A and free β-human chorionic gonadotropin at 7–14 weeks' gestation. Ultrasound Obstet Gynecol 2013; doi: 10.1002/UOG.11209
5. Benn P, Clive J, Collins R. Medians for second-trimester maternal serum alpha-fetoprotein, human chorionic gonadotropin, and unconjugated estriol; differences between races or ethnic groups. Clin Chem 1997; doi: 10.1093/clinchem/43.2.333
6. Cowans NJ, Spencer K. Effect of gestational age on first trimester maternal serum prenatal screening correction factors for ethnicity and IVF conception. Prenat Diagn 2013; doi: 10.1002/pd.4010
7. Watt H, Wald N, Smith D, Kennard A, Densem J. Effect of allowing for ethnic group in prenatal screening for Down's Syndrome. Prenat Diagn 1996; doi: 10.1002/(SICI)1097-0223(199608)16:8%3C691::AID-PD946%3E3.0.CO;2-2
8. Coalition for Access to Prenatal Screening Coverage Scorecards. Accessed November 30, 2022. https://www.ptonline.com/articles/how-to-get-better-mfi-results
9. Deng C, Liu S. Factors affecting the fetal fraction in noninvasive prenatal acreening: A review. Front Pediatr 2022; doi: 10.3389/FPED.2022.812781
10. Lett E, Asabor E, Beltrán S, Cannon AM, Arah OA. Conceptualizing, contextualizing, and pperationalizing race in quantitative health sciences research. Ann Fam Med 2022; doi:10.1370/AFM.2792/-/DC1

**This article is part of a special collection on health equity, diversity, and inclusion in laboratory medicine.
Guest Editor Dina Greene, PhD, DABCC, FAACC, LetsGetChecked and University of Washington, Seattle.**

Patient Blood Management

ROTEM® sigma

Know sooner. ***Decide faster.***

Now at the point of care, ROTEM *sigma* provides real-time results in critical bleeding situations.

Introducing a simple, fully automated thromboelastometry system that supports faster decision-making at the point of care. Using proven technology, ROTEM *sigma* delivers real-time results, with A5 parameter for early clot-strength assessment. Easy-to-interpret TEMograms provide valuable clinical information to guide transfusion and other management decisions in critical bleeding situations for improved patient outcomes.

To learn more about ROTEM *sigma*, visit info.Werfen.com/ROTEM.

Results from ROTEM *sigma* should not be the sole basis for a patient diagnosis; results should be considered along with a clinical assessment of a patient's condition and other laboratory tests. Not Health Canada-licensed. Not available in all countries.

ROTsigPrintAd
NA REV 00 12.22

werfen

Regulatory Roundup

FDA Authorizes First Over-the-Counter Flu and SARS-CoV-2 Test

The Food and Drug Administration (FDA) recently issued an emergency use authorization (EUA) for the first over-the-counter at-home diagnostic test that can differentiate and detect influenza A and B and SARS-CoV-2.

The Lucira COVID-19 & Flu home test is a single-use kit that provides results in roughly 30 minutes. The test can be purchased without a prescription and performed completely at home using nasal swab samples self-collected by individuals ages 14 years or older or by an adult for individuals 2–14 years of age.

In individuals with symptoms, the Lucira COVID-19 & Flu home test correctly identifies 99.3% of negative and 90.1% of positive influenza A samples, 100% of negative and 88.3% of positive SARS-CoV-2 samples, and 99.9% of negative influenza B samples. Because of insufficient circulating influenza B cases to include in a clinical study, validation confirmed that the test can identify the virus in contrived specimens. The EUA requires Lucira to continue to collect samples to study the test's ability to detect influenza B in real-world settings.

In the wake of this authorization, FDA officials said that they recognize the benefits of home testing and that the agency will continue to use its authority to increase the number of accurate and easy-to-use at-home tests available to the public, especially tests that detect these highly contagious respiratory viruses.

HPV ASSAY GETS FDA APPROVAL FOR USE WITH PAP TESTS

BD has received Food and Drug Administration market approval for the BD Onclarity HPV assay to be used with Hologic's ThinPrep Pap test.

The BD Onclarity HPV assay detects and identifies 14 high-risk human papillomavirus (HPV) types in a single analysis. The assay reports genotypes beyond HPV types 16, 18, and 45, including types 31, 51, 52, 33/58, 35/39/68, and 56/59/66, making the test the only FDA-approved assay to individually identify and report these genotype results. The test also has approval for use in women who have received the HPV vaccine.

The ThinPrep Pap test combined with the BD Onclarity HPV assay can be used on the BD COR or BD Viper LT instrument platforms without the need to change current cytology equipment.

FDA OKS MONKEYPOX TEST

Cepheid has earned Food and Drug Administration emergency use authorization for Xpert Mpox, which runs on Cepheid's GeneXpert systems. This test for the monkeypox virus is authorized for use in settings operating under a CLIA certificate of waiver, certificate of registration, certificate of accreditation, or certificate of compliance. These include moderately complex settings and point-of-care settings.

tommaso79 / iStock

The test requires less than 1 minute of hands-on time and no specimen prep. Users obtain swab samples in viral transport medium/universal transport medium, transfer samples to a cartridge, then insert the cartridge in a GeneXpert instrument and start the test. The test then provides results in approximately 36 minutes.

RESPIRATORY TEST EARNS FDA EUA

The Food and Drug Administration has granted LumiraDx an emergency use authorization (EUA) for the LumiraDx SARS-CoV-2 & Flu A/B STAR Complete assay, which has also been validated by the U.K. Health Security Agency under the Coronavirus Test Device Approvals process. Under this EUA, high-complexity laboratories can use the test to simultaneously detect and differentiate influenza A, influenza B, and SARS-CoV-2 infections within 20 minutes or less. The assay uses qSTAR technology, which utilizes a single-step direct method for nucleic acid extraction and amplification on validated open reverse transcription PCR instruments.

SALIVA DNA COLLECTION DEVICE CLEARED

Spectrum Solutions has secured Food and Drug Administration 510(k) clearance for its SDNA Saliva Collection Device. Spectrum designed this device with the goal of solving the most common points of failure associated with detecting viral infections using whole saliva. Cleared as a microbial nucleic acid storage and stabilization device, SDNA maximizes detection of viruses at low levels and neutralizes them within 10 seconds of collection to minimize unnecessary exposure. The device also features a patented preservation media that keeps analytes stable at ambient temperatures for several weeks.

RESPIRATORY PANEL GETS FDA CLEARANCE

The Food and Drug Administration has granted bioMérieux 510(k) clearance and a CLIA waiver for its Biofire Spotfire system and its Biofire Spotfire Respiratory panel. The panel detects 15 of the most common bacteria, viruses, and viral subtypes that cause respiratory tract infections. It is intended for use in patients with symptoms of these infections, and it delivers results in approximately 15 minutes, enabling patients to get diagnoses during the course of clinician visits.

bioMérieux added that it will submit a 510(k) application for the Biofire Spotfire Respiratory Panel Mini, noting that clearance of this test will also help the company expand its syndromic testing technology beyond traditional clinical laboratories to urgent care and physician offices.

FDA EUA GRANTED FOR SARS-COV-2 TESTING DEVICES

Anavasi Diagnostics has received Food and Drug Administration emergency use authorization for its point-of-care AscencioDx COVID-19 test and AscencioDx Molecular Detector.

The AscencioDx COVID-19 test targets multiple locations on the viral genome, reducing the likelihood of missing a new strain. It also detects SARS-CoV-2 RNA in 20 minutes. It covers 99.99% of all omicron variants as well as prior variants of concern.

The AscencioDx Molecular Detector's proprietary, compact design uses reverse transcription loop-mediated isothermal amplification technology that is similar to more expensive and complex PCR testing. Unlike PCR testing, however, it neither requires sending samples to different locations nor waiting days for results.

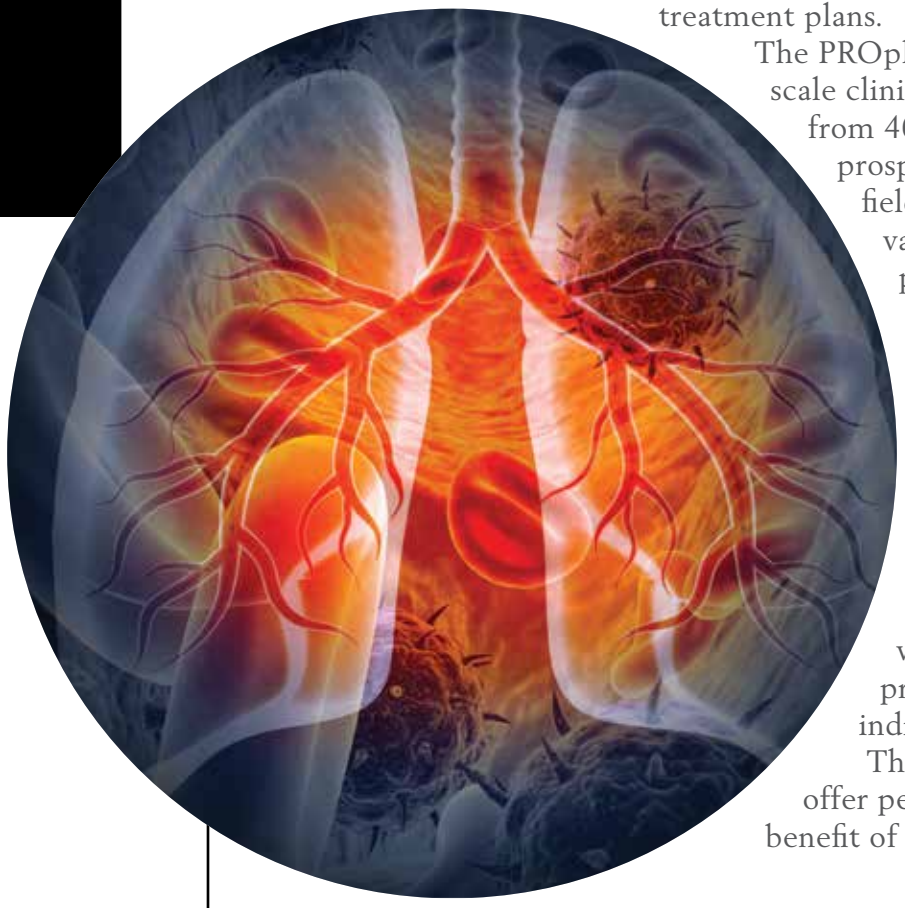
According to Anavasi, both devices create less biowaste than other molecular point-of-care tests because the detector is reusable for at least 3,000 test cycles. Batteries and electronic components need not be thrown out after a single use. The AscencioDx system also has minimal packaging and fewer disposable components than other molecular point-of-care tests.

Industry Playbook

OncoHost Launches NSCLC Cancer Test in the United States

Israel-based OncoHost recently announced the official launch of its PROphet non-small cell lung cancer (NSCLC) test in the United States.

PROphet guides first-line treatment decisions for advanced unresectable NSCLC patients. It gives clinicians actionable clinical insights into optimal first-line therapeutic choices and a better understanding of their patients' personalized cancer dynamics. In one pretreatment blood test, PROphet scans approximately 7,000 proteins in patients' plasma and delivers a report that predicts their clinical benefit from anti-programmed death 1/anti-programmed death ligand 1 (anti-PD-1/PD-L1) immunotherapy-based treatment plans.



The PROphet algorithm is trained on OncoHost's large-scale clinical trial, which has more than 1,500 patients from 40 sites worldwide, making it one of the largest prospective cohorts in the precision oncology field. The NSCLC test is supported by a blinded validation demonstrating that it accurately predicts a patient's clinical benefit and associated overall survival differences with single-agent versus combination treatment plans, the company naoted.

OncoHost officials said that although driver mutation detection is an essential factor in determining effective treatment, approximately 85% of all patients diagnosed with NSCLC do not have any detectable driver mutations. In these cases, the test, when combined with PD-L1 results, helps predict the best treatment plan for each individual patient.

The officials added that the PROphet report will offer personalized insights on the predicted clinical benefit of immunotherapy.

BIOSERO AND ALTEMISLAB COLLABORATE TO STREAMLINE AUTOMATED SAMPLE MANAGEMENT WORKFLOWS

Biosero and AltemisLab have announced a collaboration aimed at streamlining sample management automation.

The collaboration will enable scientists to integrate AltemisLab's AlteCap Swift CELL screw-cap decapper into sample management workflows controlled by Biosero's Green Button Go laboratory automation software. The rapid decapper device has interchangeable cassettes to allow for use with tubes from any manufacturer and any SBS-compliant tube format. Now the device can be controlled through Biosero's suite of laboratory automation software to enable fully automated workflows and extended laboratory productivity even in the absence of human operators.

AltemisLab officials said they are committed to developing products that work as standalone devices on the lab bench but can also be integrated into an automated work cell.

Biosero officials said the collaboration will add more capabilities for the company's users in the future.

Mohammed Haneefa Nizamudeen / iStock

FLAGSHIP BIOSCIENCES AND GENOMENON PARTNER TO ADVANCE PRECISION MEDICINE

Flagship Biosciences and Genomenon recently announced a partnership to transform the drug development paradigm with accelerated biomarker discovery and companion diagnostics development solutions.

Since acquiring Interpace Pharma Solutions, Flagship has expanded its portfolio to include proven cytogenetic, molecular pathology, and genomic profiling solutions. Partnering with Genomenon will further enrich its genomic profiling capabilities with the breadth of published clinical genomic evidence only available in the Genomenon Mastermind knowledgebase, according to Flagship.

Genomenon said its AI-driven platform delivers disease-specific genomic datasets that identify a comprehensive set of causative variants for a specific disease. These troves of genomic information—known as variant landscapes—will complement Flagship's work by accelerating its assay development, validation, and deployment services that support precision medicine drug trials, biomarker discovery, and companion diagnostic development.

As a result, this partnership will further enhance new genomic profiling services for biomarker characterization and improved patient stratification for clinical trials and treatment selection and will allow Genomenon to deliver more precise genomic profiling, insights into biomarker characterization, and better patient stratification for clinical trials and treatment selection.

HURDLE AND CLOUDLIMS PARTNERSHIP TO AUGMENT DIAGNOSTIC LAB CAPABILITIES

CloudLIMS and Hurdle have announced a strategic partnership that the companies say involves the first-ever integration between a Diagnostic-as-a-Service (DaaS) platform and a Software-as-a-Service (SaaS) laboratory information management system (LIMS) provider.

The partnership brings together Hurdle's remote diagnostic platform and CloudLIMS' secure, purpose-built Diagnostics LIMS workflow to allow labs to offer at-home tests and manage lab processes and data efficiently. As a result of this collaboration, Hurdle's partner labs, such as reference labs and clinical diagnostic labs, will now be able to seamlessly manage lab data, automate workflows, and follow regulatory compliance.

These labs also will be able to extend their services to patients present in infectious disease hotspots, remote locations, and underserved communities who are unable to travel to the lab location to get themselves tested. Additionally, labs can improve their offering to existing B2B customers by providing Hurdle's white-labeled kits.

"We experienced the importance and convenience of conducting diagnostic tests from the comfort of our homes during the COVID-19 pandemic," said Arun Apte, CEO of CloudLIMS. "Today, fortunately, the pandemic is largely behind us, but labs want to continue to offer their customers the same convenience. Our partnership with Hurdle will allow our customer labs to do exactly that."

CYTEK BIOSCIENCES TO ACQUIRE FLOW CYTOMETRY AND IMAGING BUSINESS FROM DIASORIN

DiaSorin and Cytek Biosciences have announced that Luminex Corporation, a wholly owned subsidiary of DiaSorin, has an agreement with Cytek to sell most of its assets related to the Flow Cytometry and Imaging (FCI) business unit.

The FCI business unit, acquired by Luminex in October 2018, is based on both conventional flow cytometry and image-based flow cytometry instrumentation, which provide insights into all facets of cellular phenotypes and morphology. The FCI business unit includes dedicated commercial, operations, R&D, and supporting personnel.

Cytek said that adding the Amnis imaging flow cytometers to its robust lineup of cell analysis solutions will provide researchers and scientists with tools that combine high-resolution cell images with the speed, sensitivity, and phenotyping abilities of flow cytometry. The addition of the Guava flow cytometers will expand Cytek's core instrument offerings, adding cost-effective, entry-level, and personal instrument options to broaden the market and research areas it services.

Index to Advertisers

Ask The Expert

Current Trends in Designer Drug Use

EXPERT
By Patrick Kyle, PhD, DABCC, DABFT

What are the latest significant trends in designer drug use?

A: While patterns of drug abuse vary by region and with time, a review of reliable resources indicates the following trends. Illicit fentanyl and fentanyl analogues continue to plague our society. In Q1 2023, the U.S. Drug Enforcement Agency (DEA) seized over 16 million fentanyl pills and 2,700 lbs. of fentanyl powder. Drug dealers continue to use pill presses to form counterfeit tablets that are nearly identical to pharmaceutical oxycodone tablets, alprazolam bars, and others. According to forensic laboratories, the amount of fentanyl in counterfeit tablets from the same batch may range from trace to lethal amounts.

If that is not concerning enough, in late 2022, DEA published a warning that 23% of illicit fentanyl powder seized by the agency was adulterated with xylazine. Xylazine is an alpha-2 agonist used as a veterinary tranquilizer, but is not approved for human use, nor scheduled as a controlled substance. It has been associated with many overdose deaths in the past and is making a resurgence. Xylazine is known to cause central nervous system depression, respiratory depression, hypotension, and bradycardia. Repeated injection of xylazine-adulterated drugs is associated with necrotic skin ulcerations. Routine immunoassay screens do not detect xylazine, but one company, BTNX, offers lateral flow test strips for forensic use.

The Center for Forensic Science Research & Education also reported that, in Q1 2023, bromazolam (171 cases) led the list of designer benzodiazepines, whereas pentylone (112 cases) and N,N-dimethylpentylone (166 cases) topped the list of stimulants. The synthetic cannabinoid MDMB-4en-PINACA (37 cases) was the most abundant cannabinoid, whereas more than 30 cases involving three new opioids, isotonitazene metonitazine, and N-desethyl isotonitazene, have been reported.

The National Poison Data System reported that in Q1 2023, toxic exposures from edible THC products topped the list after intentional ingestion (www.aapcc.org/national-poison-data-system). This may be due to perceived safety after the legalization of THC in many states, but other factors also contribute. The drug absorption phase from edible products is prolonged compared to other routes of administration, which may lead to overdose if an individual continues to consume the product after no psychological effect is perceived within a few minutes. Edible THC products also can be similar in appearance to gummy bears and other commercial candies, which contributes to their consumption by children. In 2021, more than 4,300 children 0-12 years of age were treated in emergency departments after consumption of THC edibles. These patients often present with ataxia, confusion, vomiting, and hallucinations.

How can labs stay abreast of these trends?

All laboratories can monitor reliable data sources such as those listed above. Laboratories can also increase their breadth of testing by incorporating a fentanyl immunoassay into their drug testing regimen. Several fentanyl immunoassays are commercially available, each with their own sensitivity and selectivity toward fentanyl analogues.

Laboratories offering comprehensive toxicology services should strive to keep their mass spectral databases updated by incorporating data from commercial standards of the most common drugs. These laboratories can use online mass spectral search tools such as those from Cayman Chemical Company (www.caymanchem.com/forensics/search/drugId) and the Scientific Working Group for the Analysis of Seized Drugs (www.swgdrug.org/ms.htm).

What else do labs need to know?

Chromatographic techniques coupled with mass spectrometry are the most reliable methods for identifying novel substances. Instruments that can perform online mass spectral matching will be most effective for identifying new designer drugs. Laboratories should also be aware that a DEA toxicology testing program will analyze biological specimens suspected to contain designer drugs (www.deadiversion.usdoj.gov/dea_tox/index.html), although the turnaround time for results may require several weeks.

Patrick Kyle, PhD, DABCC, DABFT, is director of clinical chemistry and toxicology labs and a professor of pathology at the University of Mississippi Medical Center in Jackson, Mississippi.
+EMAIL: pkyle@umc.edu

Where care begins

While each patient journey is unique, medical diagnostics plays a crucial role in delivering data and actionable insights. At QuidelOrtho, we pride ourselves in providing these critical answers early and often in the healthcare continuum.

See what's new at **QuidelOrtho.com**

QuidelOrtho™

AD10002900EN00 (12/22)

sebia
The new language of life

1705 Corporate Dr # 400 | Norcross, GA 30093 | 1.800.835.6497
info@sebia-usa.com | www.sebia-usa.com

Sebia USA SebiaUS

Scan for more information