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Task force sets new, lower
age for average-risk people.

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Email: custserv@aacc.org

Editorial Correspondence

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

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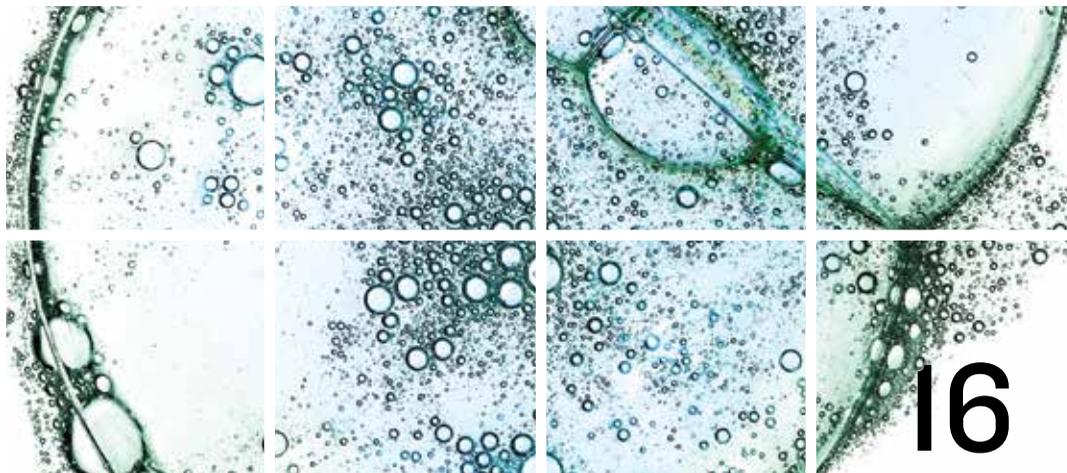
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Many mucopolysaccharidosis disorders manifest with similar clinical outcomes, and disease presentation varies from late infancy to adulthood, which renders these disorders difficult to diagnose.

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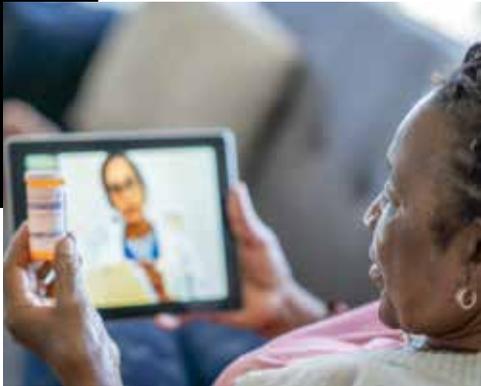
HHS Study Shows 63-Fold Increase in Telehealth Use

A report from the Department of Health and Human Services (HHS) found huge increases in the use of telehealth by Medicare beneficiaries during the COVID-19 pandemic, with specialists such as behavioral health providers seeing the highest telehealth utilization relative to other providers.

The number of telehealth visits grew from 910,490 before the pandemic (March 1, 2019 through February 29, 2020) to more than 28 million during the pandemic (March 1, 2020 through Feb 28, 2021). About 53% of Medicare users tried telehealth during that timeframe.

The types of patients who accessed care via telehealth and the types of providers they saw varied substantially. Patients in urban areas accessed telehealth services more than rural communities, and Black Medicare beneficiaries were less likely to use telehealth than White beneficiaries. Among providers, telehealth visits comprised a third of total visits to behavioral health specialists in 2020, compared to 8% of visits to primary care providers and 3% of visits to other specialists.

The Centers for Medicare and Medicaid Services (CMS) said it will use this data to design future telehealth policies. CMS significantly revised policies to pay for more telehealth during the pandemic public health emergency, and the new policies are slated to expire on December 31, 2023. Before the pandemic, CMS generally only paid for telehealth visits inside the patient's home in rural areas. While overall use of telehealth services increased and improved access to services for many beneficiaries, more research is needed to understand how it affects the quality of care and why certain beneficiaries used it less than others, CMS said.



CMS PROMOTES BIRTHING-FRIENDLY HOSPITAL DESIGNATION

The Centers for Medicare and Medicaid Services (CMS) will propose a “Birthing-Friendly” designation for certain hospitals to drive improvements in perinatal health outcomes and maternal health equity. Under the plan, this designation initially would identify hospitals that provide perinatal care, are participating in a maternity care quality improvement collaborative, and have implemented recommended patient safety practices.

Beginning with discharges on October 1, 2021, CMS adopted a new quality measure for its Hospital Inpatient Quality Reporting Program that asks hospitals to attest to whether they participate in a statewide or national maternal safety quality collaborative. They also must have implemented recommended patient safety practices or bundles to improve maternal outcomes. CMS is proposing

using these metrics to label a hospital “Birthing-Friendly”—with special designation on the agency’s Care Compare website.

According to the Centers for Disease Control and Prevention, data show that state and multistate maternal safety quality collaboratives have proven they can improve care: They’ve succeeded in reducing deliveries before 39 weeks of pregnancy without a medical reason, reducing healthcare-associated bloodstream infections in newborns, and reducing severe pregnancy complications.

PLAN FOR FREE SARS-COV-2 HOME TESTING COMING SOON

In response to the threat of the omicron variant of the SARS-CoV-2 virus, President Biden announced a series of measures intended to boost vaccine uptake and access to testing. Key to this effort is the administration’s plan to require at-home test kits to be reimbursed by private insurance.

For those not covered by private insurance, at-home tests will be distributed through community sites such as health centers and rural clinics. The U.S. is on track to quadruple the supply of rapid at-home tests compared to the summer of 2020, according to the administration.

Critics of the plan noted that paying up front and waiting for insurance reimbursement is still a barrier for some people, and it compares unfavorably to the process of some governments such as the U.K. that have offered home testing kits for free on demand. In a statement to Reuters, America’s Health Insurance Plans spokesperson Kristine Grow said the industry is still working with the administration to understand the plan. Insurers are concerned about price gouging, premiums, and the rules around implementation, she said.

Already two states, Washington and New Hampshire, have programs offering not only free SARS-CoV-2 tests, but also free home delivery.

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Validation of Point-of-Care Blood Glucose Monitoring Systems in Hospital Settings



By Nam K. Tran,
PhD, HLCD
(ABB), FAACC

Although point-of-care (POC) glucose monitoring has transformed hospital-based glycemic control programs (1), the use of POC glucose monitoring in critically ill populations has garnered much attention because research shows that some POC glucose meters are unsuitable for the hospital population.

Several investigations have highlighted the role of interfering substances causing inaccurate POC glucose meter measurements (2,3,8–11). Many of these interferences, such as anemia, presence of oxidizing/reducing substances, and high pO₂ levels, are commonly observed in hospitalized populations, especially among critically ill patients. In a study by Tang et al., low hematocrit was attributed to falsely high POC glucose measurements when compared to a plasma-based comparative method (8). The research also showed ascorbic acid leading to falsely high glucose measurements on certain devices (9). Later studies highlighted the impact of inaccurate glucose measurements causing increased risk for hypoglycemic events and glycemic variability (2,3).

POC glucose meter manufacturers evaluate their devices against known interfering substances as required by the Food and Drug Administration (FDA) (7,12–14). Unfortunately, it is difficult to evaluate all known substances. Likewise,

in vitro replication of complex in vivo physiologic variables contributing to inaccurate meter performance can be difficult. The emergence of autocorrecting POC glucose biosensors provides means to overcome these interferences (2–4). These novel sensors correct for interferences by automatically measuring hematocrit and correcting for reducing/oxidizing substances to produce more accurate glucose measurements. The clinical impact of using autocorrecting glucose meters versus noncorrecting devices has been shown to reduce hypoglycemic events and glycemic variability—representing the future direction of POC glucose monitoring technology

Validation/Verification of POC Glucose Meters in Hospital Settings

Adoption of any new hospital POC glucose meter requires institutions to

verify or validate device performance prior to implementation (15). If the POC glucose meter is used “on label” (i.e., in accordance with the FDA approved intended use of the device), a formal validation is not required and the instrument only needs to be verified to confirm accuracy, precision, and analytical measurement range, among other core elements defined under CLIA (7,14). For “off label” use, the CLIA waived status of many POC glucose meters would be negated and the device would default to high complexity classification. As a high complexity test, CLIA requires the device to undergo more rigorous validation studies, including establishing performance data for the intended use population and in the presence of expected interfering substances. Given the significance of interfering substances and high-risk nature of critically ill populations, institutions should consider the following steps as part of their implementation process:

Comparison Method Selection:

Institutions must first define a suitable comparative method. For glucose testing, the “definitive” method relies on isotope dilution mass spectrometry (IDMS); however, few healthcare facilities have access to these higher order analytical methods (16). Alternatives to IDMS include “true reference methods” or “comparative methods” which are more widely accessible. Comparative methods are perhaps more convenient and include clinical laboratory analyzers using plasma/serum, or whole blood with blood gas analyzers. Facilities must balance feasibility, accessibility, and performance when deciding on a comparison method.

Patient Population Selection: After identifying a suitable comparison method, facilities should next define appropriate patient populations to verify glucose meter performance. The Clinical Laboratory Standards Institute suggests a minimum sample size of 40 for method comparisons—with samples spanning the device’s analytical measurement range (17). If testing is to be performed in critically ill populations, laboratories also

should include samples from intensive care units and emergency departments, spanning the range of expected specimen types (e.g., arterial, venous, capillary, fingerstick). Samples ideally should include metadata to establish disease severity to classify patients as critically ill. Determining disease severity can be as simple as confirming patient diagnosis (e.g., sepsis, cancer, etc.), however, comprehensive approaches could include the use of scoring systems such as the multiple organ dysfunction, sequential organ failure assessment, and the acute physiology and chronic health evaluation scores (18–20). With the addition of autocorrecting glucose meters, it is also recommended to include populations that exhibit a range of confounding factors (e.g., hematocrit, oxidizing/reducing substances, pO₂, etc.) to challenge these devices during the verification or validation process.

Evaluation of Interfering Substances:

Healthcare facilities should identify interfering substances that are likely to be encountered by glucose meters. For example, in recent years, there has been an increased interest in high-dose ascorbic acid for a variety of diseases, including sepsis (3).

Facilities that expect patients to receive high-dose ascorbic acid therapy should conduct studies to determine if glucose meter performance is compromised and develop alternative workflows for these scenarios. Non-glucose sugars should also be evaluated if testing is to be performed in the neonatal (e.g., galactose) and peritoneal dialysis populations (e.g., icodextrin/maltose) (21). When necessary and feasible, laboratories may consider contrived samples, especially if devices are used “off label” and require method validation.

Accuracy Is Key

The implementation of POC glucose monitoring is not as simple as one would hope. Glucose monitoring is necessary to properly administer one of the most dangerous drugs in clinical use—insulin. This requires greater scrutiny and diligence when implementing new devices. Accuracy is critical to the safe administration

of insulin, especially in hospitalized patients. The role of the clinical laboratory is to not only ensure regulatory compliance, but also establish the safe application of in vitro diagnostic testing. Laboratories should rigorously evaluate POC glucose monitoring systems and be aware of limitations that could impact patient care.

See the full list of references on aacc.org/cln.

Nam K. Tran, HCLD (ABB), FAACC, is professor and senior director of clinical pathology and is director of the Pathology Biorepository and professor in the division of clinical pathology at University of California, Davis.

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The Sample

Multi-Society Task Force on Colorectal Cancer Lowers Screening Age

New colorectal cancer (CRC) screening guidelines from the United States Multi-Society Task Force (MSTF) on Colorectal Cancer (CRC) suggest screening in average-risk individuals ages 45–49 (Am J Gastroenterol 2021; doi: 10.14309/ajg.0000000000001548).

Although no literature demonstrates that CRC screening in average risk individuals younger than 50 improves health outcomes such as CRC incidence or mortality, the task force made the recommendation based on research showing increased CRC incidence and mortality in individuals under ages 50. Emerging data also indicate the prevalence of advanced colorectal neoplasia in individuals ages 45–49 approaches rates for those ages 50–59. Modeling studies show that the benefits of screening outweigh potential harms and costs, the task force said.

The task force recommendations were last issued in 2017. The 2021 update contains several recommendations that remain unchanged from 2017 guidelines. For example, the task force strongly recommends CRC screening in all individuals ages 50–75 who have not already initiated screening. For individuals ages 76–85, the decision to start or continue screening should be individualized and based on prior screening history, comorbidity, life expectancy, CRC risk, and personal preference. Additionally, screening is not recommended after age 85, according to new guidelines.

The task force says its updated guidance from the MSTF is aligned with multiple other professional societies, including the United States Preventative Services Task Force,

the National Comprehensive Cancer Network, and the American Cancer Society. Currently, insufficient evidence precludes recommending a screening method or customized screening intervals.

CRISPR SARS-COV-2 ASSAY COULD HELP MEET GLOBAL DEMAND

A high-throughput CRISPR-Cas13 SARS-CoV-2 test can identify the SARS-CoV-2 virus with high concordance to RT-qPCR, according to a recent *Clinical Chemistry* paper (2021; doi: 10.1093/clinchem/hvab238).

As the COVID-19 pandemic continues, having a high-throughput, flexible molecular method could help high-complexity laboratories increase their testing capacities quickly using simple equipment, according to the authors. This situation also would

provide some relief to pressure on lab supply chains.

The CRISPR test relies on specific high-sensitivity enzymatic reporter unlocking (SHERLOCK) for qualitative detection of SARS-CoV-2 RNA. SHERLOCK is a CRISPR-based diagnostic that enables DNA or RNA detection with single-nucleotide specificity using CAS13a from *L. wadei* combined with isothermal amplification. The test may be performed directly on swabs or saliva samples without nucleic acid extraction and provides results in an hour.

The Food and Drug Administration earlier this year granted the first

emergency use authorization for a CRISPR diagnostic test to the original SHERLOCK CRISPR SARS-Cov-2 kit. It detects the virus's nucleic acids in upper respiratory tissue. A recent report says this assay was 100% concordant to RT-PCR in detecting SARS-CoV-2 in clinical nasopharyngeal samples.

The new assay improves on the first test by allowing a simpler workflow. It enables testing up to 5,000 patient samples based on a single operator and instrument, according to the paper. For example, the new test combines two independent SARS-CoV-2 targets in a single reaction to



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ease sample preparation and uses a 384-well format with minimal liquid handling steps to increase throughput and better work with automated processes. The new test also uses an extraction method involving a simple heat and proteinase K treatment, which is enough to allow direct sample addition to a SHERLOCK reaction while maintaining high sensitivity and specificity.

The researchers evaluated their assay using 55 negative and 50 positive remnant SARS-CoV-2 specimens. When combined with magnetic bead-based extraction on 60 of these samples, the new assay was 100% concordant with the Centers for Disease Control and Prevention (CDC) RT-qPCR assay. With the direct sample addition, the new assay was also 100% concordant with the CDC RT-qPCR direct method in 45 samples. Using direct saliva samples, the negative and positive agreements were 100% and 88%, respectively, compared with results from a collaborating clinical laboratory.

BETTER LAB STEWARDSHIP OF ANEMIA TESTS MAY BE NEEDED

Overuse of laboratory screening tests for iron-deficiency anemia (IDA) and misinterpretation of iron studies in part lead to delayed diagnosis of gastrointestinal (GI) tract cancers, according to a recent paper. The authors also blamed underuse of bidirectional endoscopy for evaluation of new-onset IDA (JAMA Netw Open 2021; doi:10.1001/jamanetworkopen.2021.27827).

IDA is a classic early sign of GI tract malignant neoplasm, the study says. Up to 10% of patients with IDA may have undiagnosed GI tract cancer, so prompt evaluation is important. However, retrospective studies report common delays in diagnostic evaluation of IDA, which can lead to delayed colorectal cancer diagnosis. Meanwhile, colorectal cancer cases are rising in patients younger than the recommended age for start of screening. At least 30 different guidelines from 10 specialty societies make different recommendations for identification and evaluation of IDA.

To understand how primary care physicians handle IDA testing and evaluation, the researchers administered a survey consisting of questions about vignettes describing related clinical scenarios. In a survey of 325 primary care physicians, 76.9% of respondents said they screened at least some patients for anemia. Interpretation of iron studies was least accurate in a scenario of a borderline low ferritin level (40 ng/mL) with low transferrin saturation (2%). Just over a quarter of respondents—26.5%—incorrectly responded that this scenario did not indicate IDA, and 73.5% correctly identified this scenario as IDA. Of 312 participants, 54.5% recommended bidirectional endoscopy (upper endoscopy and colonoscopy) for new IDA for women age 65 years. Of 305 respondents, 168 (55.1%) recommended bidirectional endoscopy for men age 65 years.

The researchers say these findings suggest a need for design and use of tools to improve diagnosis of IDA and reduce risk of diagnostic errors.

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New Paths

As a new generation takes the reins of leadership, approaches to recruitment, training, and management are changing fast.

With record numbers of clinical laboratory professionals retiring or choosing to leave the profession, new laboratorians increasingly find themselves thrust into a leadership position much earlier in their careers than their predecessors. This shift is prompting a number of medical laboratory science programs to incorporate more leadership training in their curricula and leading many recent graduates to pursue additional education, either by obtaining an advanced degree or by completing additional certification programs through professional societies.

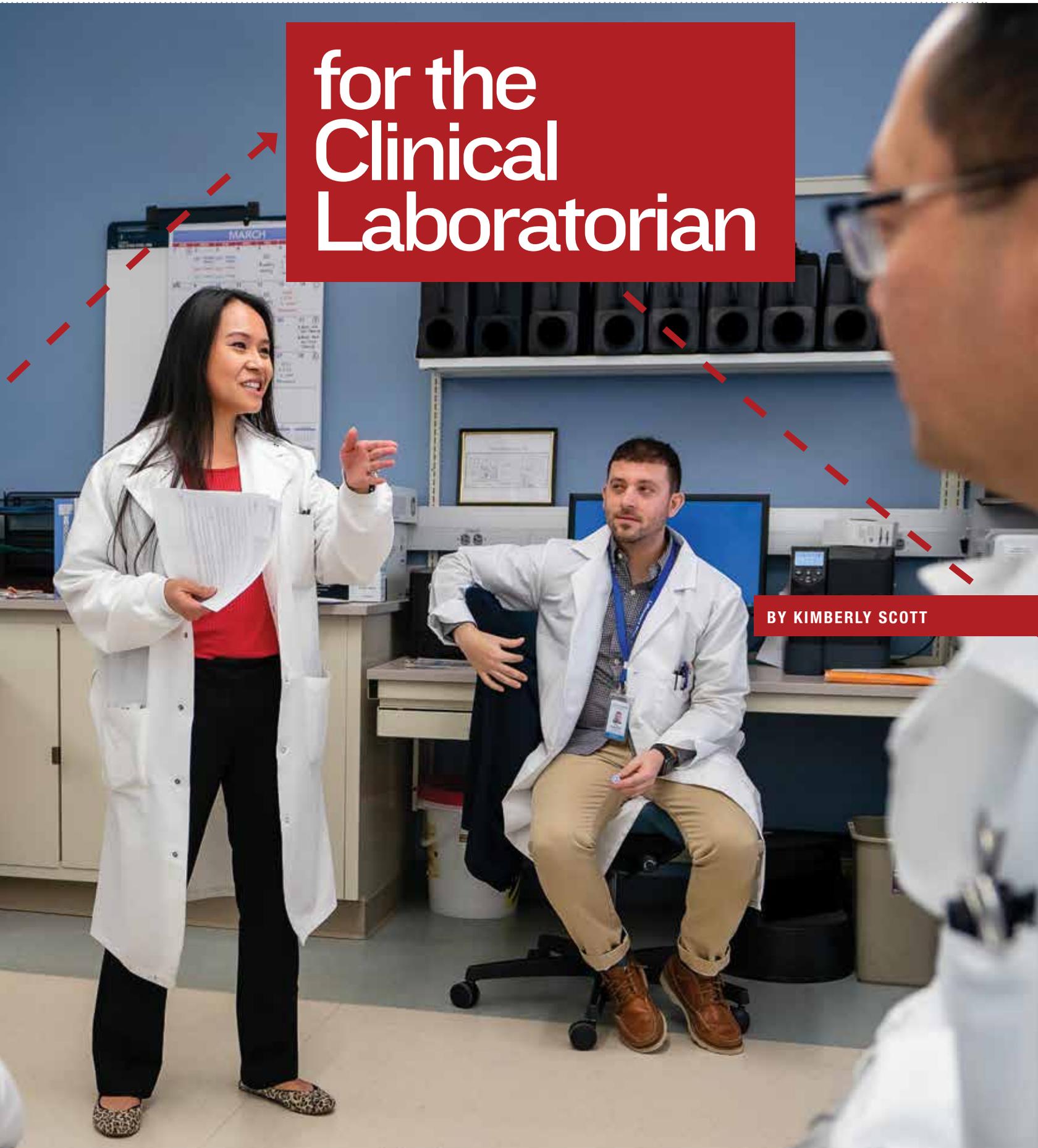
“As both a lab professional and an educator, I have seen the shift firsthand,” said Dana Baker, MBA, MS, MLS(ASCP),^{CM} assistant professor in the department of clinical laboratory sciences, School



to Leadership

for the Clinical Laboratorian

BY KIMBERLY SCOTT



of Health Professions, University of Kansas Medical Center (KUMC). “It used to take years before someone would move into a leadership position. Now, a new graduate can walk into a lab and be asked to lead in under 2 years. It is critical that they have some leadership skills and training when they walk in the door.”

Recent studies indicate that nearly one-third of managers in clinical laboratories plan to retire in the next 5 years, according to the American Society for Clinical Laboratory Science (ASCLS). For some areas, such as hematology and microbiology, that percentage is higher. As a generation of laboratory professionals leaves the workforce, younger, less experienced staff are being pressed into management positions they didn’t train for. A need exists to prepare these professionals to take on new roles.

Laboratory management is now part of the clinical laboratory

science curriculum at KUMC, Baker noted. Students are also required to participate in interprofessional activities, where they work in teams with students from other programs,

such as medicine, nursing, or physical therapy. These activities help prepare future laboratorians for professional interactions they will experience once they work in a lab, Baker said.

KUMC is one of three institutions nationally that offers a doctorate of clinical laboratory science (DCLS)—the others are Rutgers University in New Jersey and the University of Texas Medical Branch. The programs prepare certified medical laboratory scientists to become doctoral-prepared healthcare practitioners, partnering with clinical pathology to provide evidence-based consultation throughout the healthcare sectors, explained Nadine Fydryszewski, PhD, MS, MLS(ASCP), professor and interim chair of the DCLS Program at Rutgers.

“The Diagnostics Consultation Model is the framework of the Rutgers DCLS curriculum and defines activities related to quality and value improvement in clinical laboratory services delivery,” Fydryszewski said. This includes utilization review intervention, patient care intervention, diagnostic management intervention, and community intervention.

Since its inception in 2014, the Rutgers DCLS program has graduated five students. Currently, there are 18 students in the

“This teaches the students how to interact with other healthcare professionals and how to work together as a team to make decisions that produce quality and safe patient care.”

— Tera Webb



program, she notes, adding that graduates are ready to be effective leaders in many facets of the clinical laboratory science profession, particularly in consultative roles contributing to the interprofessional team. Graduates have been employed primarily in hospitals, some of which have created new positions, such as “Pathology Utilization Manager” or “Technical Specialist – Testing Formulary and Stewardship Program.”

Getting an advanced degree is one path for preparing for a leadership position in a clinical laboratory, said Tera Webb, MS, MLS(ASCP),^{CM} a professor in the clinical laboratory science program at the University of Alabama at Birmingham (UAB), a master’s program that emphasizes leadership and also incorporates interprofessional activities. In fact, the Center for Interprofessional Education and Simulation at UAB develops team training activities that involve multiple medical programs, including laboratory medicine, Webb noted.

During the training, students are split into small groups of 15 to 20, are given a hypothetical patient case, and must develop an action plan for the patient, from diagnosis to treatment to follow-up care.

“This teaches the students how to interact with other healthcare professionals and how to work together as a team to make decisions that produce quality and safe patient care,” Webb said. “This shows students the importance of sharing their expertise with one another on the healthcare team. It also gives students in other professions the opportunity to see that laboratory medicine is more than just running tests. Lab professionals are an important part of the diagnostic process on the healthcare team.”

LAB TRAINING GETS A HIGH-TECH UPGRADE

One of the challenges many medical laboratory science or technologist students face, especially in rural areas, is a dearth of internship or clinical rotation opportunities. This is due in part to the shortage of laboratory



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personnel needed to run the internship programs and provide training.

Some colleges and training programs have turned to simulation laboratories to provide a more hands-on experience before a student begins a clinical rotation. In some cases, this allows for a shorter internship, which places less of a burden on hospitals. These sim labs provide students with realistic clinical experience during which they can apply knowledge and skills in a safe environment and develop their clinical, interpersonal, inter-professional, and critical thinking skills. Typically, instructors provide feedback during a debriefing session.

“Simulation laboratories don’t replace the in-person internship, but they may be used to help meet clinical hour requirements,” Baker said. “We have students multitask as they run tests and provide reports. This is a way to demonstrate competency before the student transitions into a real clinical setting.”

GETTING THE MOST FROM PROFESSIONAL SOCIETIES

Another way of developing leadership skills is by getting involved in professional societies. Not only do

these organizations have various groups representing the interests of their constituencies, but they also offer additional continuing education and training programs, both in person and virtually.

“A person who is interested in becoming a leader needs to be connected to a professional organization, such as AACC,” said Erika Deaton-Mohney, point-of-care coordinator for Bronson Healthcare in Kalamazoo, Michigan, and a member of AACC’s Clinical Laboratory Scientists (CLS) Council. “More than that, they need to be an active member—get involved in a committee, write a paper, speak at a webinar, and look for opportunities to develop skills.”

AACC’s Society for Young Clinical Laboratorians (SYCL), for example, is a place where those new to the field of laboratory medicine can network with their peers, discuss workplace issues (such as time management or how to ask for a raise), and seek career guidance.

“The career path is much shorter than it used to be, so it’s imperative for young laboratorians to have resources available that allow them to learn and benefit from the experience of others and essentially make the learning curve a little less

steep,” said Jaime Noguez, PhD, DABCC, director of clinical chemistry at University Hospitals Cleveland Medical Center and assistant professor of pathology at Case Western Reserve. Noguez, who is a member of AACC’s SYCL Core Committee, said the group also helps young laboratorians to develop their management skills and reach academic goals such as getting published or presenting at conferences if interested. “For those early in their journey, SYCL really helps provide mentorship and resources they need to advance in their careers,” she said.

Clinical laboratorians can also pursue additional training through AACC’s Learning Lab, an online digital platform that provides more than 60 continuing education courses in myriad areas, including clinical chemistry, immunology, microbiology, general lab medicine, and hematology and coagulation. AACC now offers complimentary access for professionals in the field (www.aacc.org/education/learning-lab).

ADVANCING THE PROFESSION

As the laboratory workforce continues to age, it will be more important than ever to encourage more young people to enter the field of laboratory medicine and pursue leadership positions.

“As a profession, we can do a better job of encouraging young people to enter the field,” Webb said. “Traditionally, we have relied on booths at recruiting events, but we really need to do more in terms of connecting with middle school and high school students.”

Webb supports offering diagnostic medicine as an elective course during high school, much like business, computer science, or foreign languages. She also believes in using social media to advance the profession.

“In spite of the COVID-19 pandemic shining a spotlight on the laboratory, we are commonly not considered part of the healthcare team,” Webb said. “To address these stereotypes and improve awareness of our profession, we must become more visible.”

“Public awareness has increased somewhat due to media covering the shortage of laboratorians, but we also need to tell the story of what we do and how the diagnostic services and patient data we have is critical to quality care.”

— Nadine Fydryszewski

Deaton-Mohney notes that AACC's CLS Council, which guides the organization's activities and programs to address the professional needs of current and future members, is doing just that by reaching out on Facebook and other online communities to let prospective students know what it means to be a clinical laboratorian and the various career paths that are available.

Fydryszewski agrees on the need for outreach. "Public awareness has increased somewhat due to media covering the shortage of laboratorians, but we also need to tell the story of what we do and how the diagnostic services and patient data we have is critical to quality care," she said. "Promoting this awareness can contribute to an increasing awareness of medical laboratory science as a career path for those with an interest in science and healthcare."

Attracting young people to the field of laboratory medicine is just one challenge. Retaining them is another, Noguez emphasized. "Competitive compensation and benefits are key, as well as finding ways to show them that they are valued. The importance of promoting a positive workplace culture cannot be overlooked. It appears to me that the prioritization of work-life balance is different for this generation," she said. "Much more emphasis is placed on job flexibility and spending time with their families and pursuing other interests."

Ultimately, bringing young people into the field and into leadership roles requires a multipronged effort, experts said: attracting younger people to the field, implementing new ways of training that emphasize not only the science but also the skills and interpersonal elements required to be a leader, and engaging with professional societies, which provide unique education and mentorship opportunities for the new generation of laboratory leaders. ■

Kimberly Scott is a freelance writer who lives in Lewes, Delaware.

+EMAIL: kmscott2@verizon.net



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○ BY SARAH MICHAUD



SALIVA

IN THE SPOTLIGHT

With increasing numbers of assays for rapid SARS-CoV-2 detection, saliva could become the go-to matrix for other infectious diseases, cancers, and more.

The COVID-19 pandemic and the need for rapid, reliable testing has heightened interest in saliva as a convenient and reliable testing medium for infectious diseases. The Food and Drug Administration (FDA) has issued more than 30 emergency use authorizations (EUA) for saliva-based SARS-CoV-2 tests, recently including high throughput instruments such as Thermo Fisher Scientific's Amplitude Solution system. Recent studies also have shown that saliva is just as effective as a nasopharyngeal swab for traditional SARS-CoV-2 PCR tests and useful in at-home rapid antigen tests.

But saliva's use as a health indicator did not start with SARS-CoV-2, nor will it end with this virus. Researchers and laboratorians are investigating oral fluid's potential in detecting heart disease, human papilloma virus (HPV)-related head and neck cancers, breast cancers, lung cancers, as well as monitoring treatment efficacy, detecting disease recurrence, and stratifying patient risk. Israeli company Salignostics has even submitted a saliva-based pregnancy test for FDA approval in the U.S.

As a testing medium, saliva, unlike blood and other body fluids, is easy to collect, handle, and store. Add that to increasingly sensitive lab instruments, and it seems like there should be a lot of opportunities to exploit saliva in the clinic.

COVID-19 TESTING ON A COMMUNITY SCALE

As using saliva becomes more mainstream, in vitro diagnostic companies are showing its utility in high-throughput instruments. In October 2021, Thermo Fisher Scientific received an FDA EUA to run SARS-CoV-2 tests from saliva samples obtained with their Spectrum Solutions SpectrumDNA SDNA-1000 collection device on their Amplitude Solution system. The company rolled out the Amplitude Solution system in 2020 for SARS-CoV-2 testing of nasopharyngeal and anterior nasal swab specimens. The 2021 EUA expanded Amplitude's use with a saliva-specific workflow.

"Amplitude is a high-throughput automated molecular diagnostic testing system that can help labs quickly scale COVID-19 PCR testing to changes in demand volume and offers maximum throughput—up to 8,000 test results in 24 hours—with minimal hands-on time, equipment, and staffing," explained Manoj Gandhi, MD, PhD, senior medical director in the Genetic Testing Solutions Business at Thermo Fisher. The saliva collection system is self-contained and provides sample consistency and long-term stability while protecting the genetic material needed for accurate PCR test results.



DNA FROM HPV-RELATED HEAD AND NECK TUMORS SHEDS DIRECTLY INTO THE SALIVA AND COULD POTENTIALLY BE USED AS A BIOMARKER FOR EARLY CANCER DIAGNOSIS.



Thermo Fisher got to demonstrate such an instrument's value when it was used during the 2021 Summer Olympics in Tokyo to test athletes, officials, and staff in the Olympic Village. "About one million tests from saliva samples were performed on the Amplitude system over 50 days," Gandhi said.

With the new saliva protocol, the company hopes that Amplitude will help "provide a means to address the routine testing needed for companies, schools, universities, and communities to curb infection rates and help us return to pre-pandemic life," Gandhi said.

USING SALIVA TO SCREEN FOR HPV-RELATED CANCERS

In 2010, Chamindie Punyadeera, PhD, left a career in industry, where she was working on point-of-care saliva diagnostics to detect drugs of abuse, to start a new path in academia, where she could pursue more blue-sky research on using saliva for disease detection.

Early in her research career she worked with Johnson & Johnson to develop a companion diagnostic to their HPV vaccine Gardasil. This companion diagnostic was a saliva-based screen for persistent oral HPV infection—a condition that has been linked to increased risk for head and neck cancers. "DNA from HPV-related head and neck tumors sheds directly into the saliva and could potentially be used as a biomarker for early cancer diagnosis," said Punyadeera. "Saliva testing is a more effective way to detect lower levels of oral HPV than through a blood draw," she added, "because we are going directly to the source of the viral infection—the mouth and throat."

Punyadeera has also partnered with the lifestyle company Viome on an mRNA test to detect oral squamous cell carcinoma and oropharyngeal cancer from saliva. In April 2021, Viome received an FDA breakthrough device designation for using saliva as a liquid biopsy for mouth and throat cancers.

Now a professor at Griffith University in Brisbane, Australia, Punyadeera is championing the validation and use of saliva HPV testing as a standard clinical tool for screening and early detection of HPV-related head and neck cancers for at-risk populations. "I am persistent in pursuing support and funding to bring saliva-based HPV screening to clinical practice. These simple, non-invasive tests have the potential to save people's lives," she said.

Finding Asymptomatic Cancer With Saliva Screening

While developing the saliva-based HPV screening protocol for Johnson & Johnson, Punyadeera and her colleagues identified three individuals with persistent oral HPV infections from the 700 study participants they screened from their university lab in Brisbane, Australia. “There is a strong association between persistent HPV infection and cervical cancer, so we theorized the same could be true for persistent oral HPV infection and throat cancer,” she said. “I didn’t feel comfortable not sharing this information with these three study participants.”

Punyadeera and her clinical team obtained permission from their ethics committee to contact the three participants with high levels of HPV. Of the three, one individual appeared healthy but presented with an abnormal tonsil. Even though an MRI scan of the tonsil was clear, “this person’s salivary HPV DNA levels were sky high,” said Punyadeera. “We knew something was going on.”

The patient opted for a voluntary tonsillectomy in which a pathologist found a 2mm cancerous tumor. Per Punyadeera, this was the first time a cancer was detected with a saliva test before the patient showed symptoms of illness. Results from her study were published in *Frontiers in Oncology* (2020; doi: 10.3389/fonc.2020.00408).

USING SOUND TO SIFT FOR PATHOGENS

The quest to deliver more diagnostic information from saliva is also accelerating because of its special properties that interest researchers in both diagnostic technology and molecular biology. For example, the National Institute of Health (NIH) established the Extracellular RNA Communication Consortium to explore how extracellular RNA (exRNA) can traverse from organs and blood to saliva and other body fluids. The consortium aims to develop exRNA’s potential for diagnostic and therapeutic value. So far, the initiative has catalogued exRNA biomarkers—including categories unique to saliva—for nearly 30 diseases.

Researcher David T.W. Wong, DMD, DMSc, has been a key player in the consortium, focusing on new technologies to identify and sort different types of exRNA from saliva samples. A professor, associate dean for research, director of the University of California, Los Angeles Center for Oral/Head & Neck Oncology Research, and Felix and Mildred Yip Endowed Chair in Dentistry, Wong has been collaborating with researchers at Duke University to develop what they call an acoustofluidic chip. The small device uses sound waves to sort molecular-scale particles, including exRNA, in saliva by size and density.

This sort-of lab-on-a-chip is also tunable, allowing the same device to be used for different particles Wong said. Aside from ease of collection, one of the benefits of using saliva with the acoustofluidic chip is that the samples do not need to be processed before entering the device.

Testing for SARS-CoV-2 infection is a near-term application for the acoustofluidic chip technology. However, Wong is also enthusiastic about the chip’s downstream capabilities. “From a single droplet of saliva, we could identify in minutes an individual’s complete COVID-19 infection status—including viral load and antibody levels—simultaneously,” Wong said. “This pathogen isn’t going away. We need to employ technologies like the acoustofluidic chip that can quickly tell you if your antibodies



are low, making you vulnerable to a breakthrough infection.”

VALIDATION CONCERNS

With most assays developed specifically for blood, clinical laboratories must use caution before using tests off-label for saliva or other body fluids. “From a regulatory perspective, manufacturers will indicate testing parameters only for the body fluids that their diagnostics have been approved for,” said Darci Block, PhD, DABCC, FAACC, co-medical director of the central clinical lab at the Mayo Clinic. “And most body fluid diagnostics have not been approved for use with saliva.” Block is well-versed in body fluid testing and the issues surrounding the validation of such tests.

Proper clinical validation of alternate sample types is essential to ensure a test’s accuracy and precision. “It’s a major logistical challenge for us,” said Block. “Modifying the use of a test without validation is against the law.”

One of the main concerns clinical laboratories have in using saliva is matrix interference. “The way the assay is designed, the concentration of reagents, the amount of sample dilution that happens during testing, is optimized to the indicated testing liquid,” Block noted. “So, when you test a sample that doesn’t have the

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— DAVID T.W.
WONG

exact properties of the indicated testing liquid, you have to wonder what the test results really mean.”

With saliva, specifically, Block noted that viscosity is a potential problem. If the sample is too thick to aspirate into the testing instrument, it is imperative to find a way to increase fluidity without affecting the analytes.

Block stressed that when considering adding any new assay to a laboratory’s repertoire, laboratorians should always involve the people who order the tests in the conversation—and create a policy for how the lab handles testing fluids outside manufacturers’ parameters.

A DROOL-WORTHY FUTURE?

Subject matter experts offer many reasons to champion the future use of saliva as a testing medium, despite the important barriers to clinical integration.

“Saliva provides the opportunity for minimally invasive specimen collection and is a convenient alternative to other common respiratory samples, like nasal and nasopharyngeal swabs,” Gandhi said. “It’s readily available from most patients and can be collected with minimal discomfort or inconvenience.”

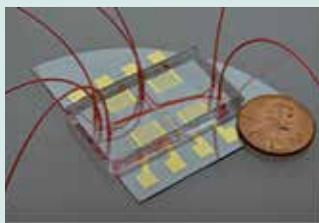
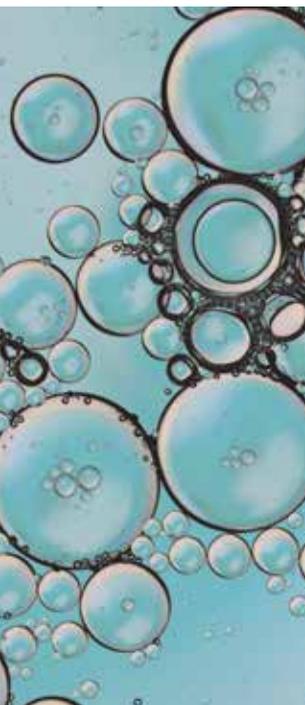
Saliva might even find a place as a matrix of choice for important new biomarkers like tau protein for Alzheimer’s disease, Wong noted. “The day will come when we can detect the tau protein in saliva instead of through a spinal tap procedure,” he said. “However, without credentialing these new methods for clinical deployment, they will remain fairytales.”

Punyadeera sees saliva diagnostics as potentially having a transformative effect on medical care by “increasing access in low resource settings, reducing healthcare costs, driving precision healthcare, and providing more equitable healthcare solutions for remote and rural communities.”

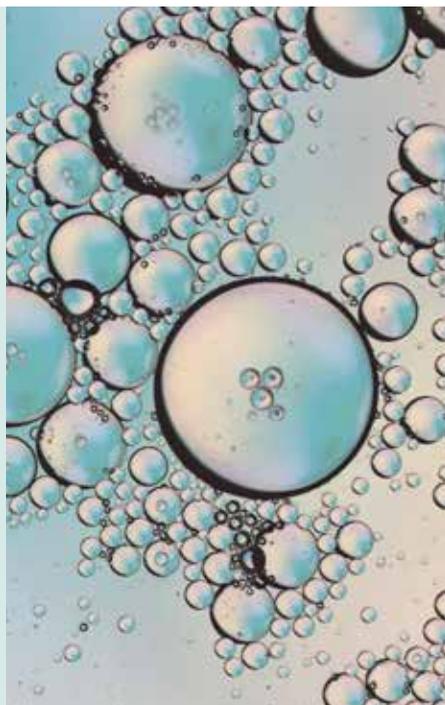
While a decade of advances has brought us closer to realizing the usefulness of saliva as a diagnostic medium, the last paragraph of the *Clinical Chemistry* paper that Punyadeera co-authored still rings true (2011; doi: 10.1373/clinchem.2010.153767): “The development of specific and standardized analytical tools, establishment of defined reference intervals, and interlaboratory tests will make saliva diagnostics a clinical reality.” ■

Sarah Michaud is a freelance writer who lives in London.

+EMAIL: michaudedits@gmail.com



David T.W. Wong, DMD, DMSc, and his colleagues at Duke University developed an acoustofluidic chip that uses sound waves generated by gold interdigital transducers to isolate molecules in saliva according to size and density. The microfluidic channel for the saliva sample is shown in red, and the coin is for scale.



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Primary Presenter

Rolando Claure-Del Granado, MD, FASN
Director, AKI/CRRT Program, Hospital Obrero, Cochabamba, Bolivia
Professor of Medicine, Universidad Mayor de San Simon, School of Medicine, Bolivia
Member at Large, International Society of Nephrology Executive Committee

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BY CHARLENE BIERL, MD

Simplifying the Test Menu to Beat Choice Overload

Ensuring patients receive the right test at the right time is a foundation of laboratory stewardship. Toward this goal, laboratories have tried many tactics to guide ordering practices and optimize the laboratory test menu. Laboratory directors can remove obsolete tests or introduce reflex algorithms that automatically trigger additional tests based upon initial laboratory findings.

While these approaches can be quite successful, what happens if the laboratory does not have ownership of the entire menu? Is the chance to guide stewardship through the menu lost?

The answer is no: The laboratory can still use the menu to influence ordering patterns through careful collaboration and organization.

The Origin of Order Menu Complexity

The modern laboratory menu resembles a network more than it does the closed system that the word menu implies. The complexity of the orderable menu within the electronic medical record (EMR) varies between health systems, and many include interfaces to external laboratories. A driving force is the incentive to reduce paper-based results, particularly with the federal government's meaningful use regulations.

In addition, there are many reasons for patients to get labs drawn outside a particular provider's system: Some insurance plans may require a different location, or patients may choose a different lab for convenience. Once a lab is interfaced to the EMR, the orders for the outside laboratory become options within the hospital's orderable menu.

To simplify finding tests, the hospital laboratory may create submenus (preference lists, order sets, or panels)

for individual providers and groups of providers. These submenus become the sources for ordering. If an order is deleted from the database, it typically does not get removed from all the downstream submenus. However, if a new order is added, it may not be visible unless it's also included on the separate menus.

While a merged menu explains duplicate or triplicate options, why might there be even more? Depending upon how the system is established, the laboratory must build a new test in the EMR in order for providers to see results. Just as an individual laboratory makes updates to its menu, the menu in the EMR needs similar changes. If inactivated tests are not regularly removed, then the menu can quickly become clogged with old and new versions of similar sounding tests. In one system, approximately 200 tests were found for drugs of abuse (1). After reviewing these and other tests in the EMR, the laboratory consolidated 859 tests to 137.

Using the Menu Structure to Manage Utilization: Three Examples

Infliximab

We recently worked with primary users to create an in-house test for infliximab, including a reflex for anti-infliximab antibodies, to avoid sending it to a reference laboratory. After adding it to the menu, we notified all providers, including focused communication to high utilizers. Yet few orders arrived.

Upon investigation, we found that the order that linked to the reference lab also linked to an external commercial laboratory and was embedded in a panel to

make it easier to find and order. We replaced the reference lab code with the in-house code for this order, so that when patients presented to the hospital laboratory for collection, the samples routed to the in-house test.

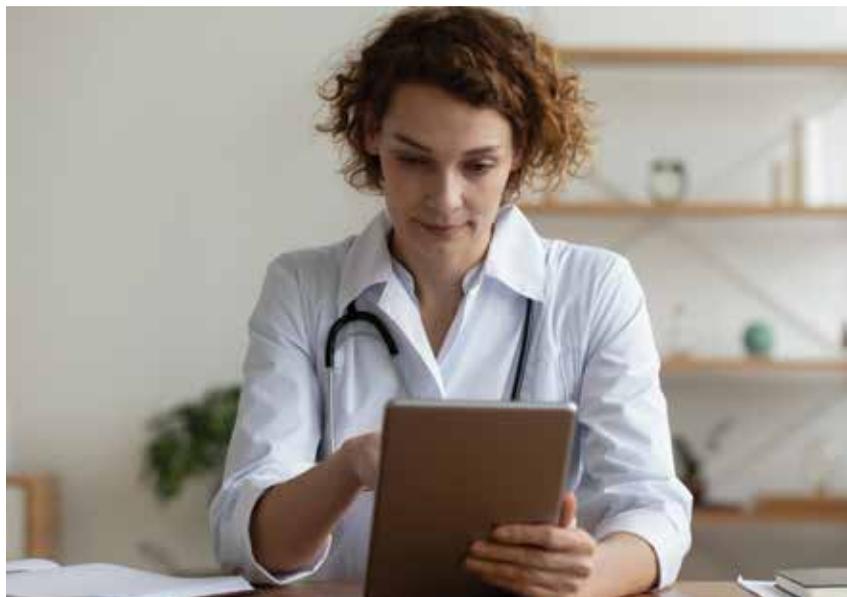
Creatine Kinase-MB (CKMB)

At a prior hospital, I worked on a utilization project to reduce the use of CKMB, given the superiority of troponin. With provider leadership agreement, we removed CKMB from the hospital menu, and orders quickly decreased as expected. However, we did not realize this order had been part of a cardiac panel that included CK. Eventually, when the laboratory reviewed CK utilization, we identified an order panel that included CK. The laboratory removed CK from the panel, and the orders decreased accordingly (2).

Antinuclear Antibodies (ANA) With Reflex

The Choosing Wisely program recommends against ordering individual serologies—such as Sjögren's syndrome-related antigen A or double-stranded DNA—if the ANA is normal. A review of one hospital menu revealed 80 options, including panels, individual markers, and different methods of analysis, reflecting three performing laboratories. An analysis showed that several tests were old versions of panels that were no longer available, while others were similar tests that could be co-mapped to one order.

Working with rheumatology and the EMR leadership, the laboratory identified a reflexive panel that started with ANA. The group found a similar panel for each interfaced



laboratory, enabling mapping to a single orderable. They took a similar approach for each of the individual tests. They reviewed preference lists and panels and placed the orders for the ANA (with and without reflex) in each, with the more specific individual tests placed on the rheumatology preference lists. The total number of options was reduced to six (1), and ordering patterns became more reflective of published recommendations (3).

How To Avoid Tension Between the Laboratory and Clinical Providers

The experiences of laboratorians who have studied the issue of choice overload demonstrate that providers appreciate changes that make their job easier and improve patient care. Except for the CKMB example above, it's notable that no tests were entirely removed from the menu. The efforts consolidated options and made it easier to identify recommended tests.

For the ANA example, providers could still individually order SSA, SSB, and other sub-serologies, as these were available in the full menu. The data showed that providers shifted to using the reflex, and the providers reported that it helped order all the needed sub-serology tests without having to place a lot of individual orders with the potential to miss one.

What Can Laboratorians Do?

As a first step, I would encourage clinical laboratorians to regularly look at the options providers see. If providers call with a question about ordering a specific test, ask if they can show you what they see as options. Understanding the organization and the options facing the providers can help highlight the barriers and opportunities to make it easier to select the recommended test.

As laboratory tests increase in number and complexity, identifying the right test for the right patient becomes more of a challenge. For any system, the laboratorians in the hospital are the local experts and are

ideally suited to review this menu for changes and updates, even if the menus extend beyond their individual laboratory. By taking on this effort, laboratorians can continue to guide utilization. ■

Charlene Bierl, MD, is director of the division of laboratory medicine in the department of pathology and laboratory medicine at the Hospital of the University of Pennsylvania, and associate professor in the Perelman School of Medicine at the University of Pennsylvania.

+EMAIL: charlene.bierl@pennmedicine.upenn.edu

References

1. Barry C, Edmonston TB, Gandhi S, et al. Implementation of laboratory review of test builds within the electronic health record reduces errors. *Arch Pathol Lab Med* 2020;144(6):742-747.
2. Behling KC, Bierl C. Cost per case mix index-adjusted hospital day as a measure of effective laboratory utilization efforts in a growing academic medical center. *Am J Clin Pathol* 2019;151(4):371-376.
3. Barry C, Kaufman S, Feinstein D, et al. Optimization of the order menu in the electronic health record facilitates test patterns consistent with recommendations in the Choosing Wisely initiative. *Am J Clin Pathol* 2020;153(1):94-98.



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BY CLAIRE WITTOWSKI

Not Just Kitting Around: Optimizing Alternate Sample Coordination for Genetic Tests

Alternate specimen collection kits for genetic testing aren't new—so-called spit kits and cheek swabs have been around for more than a decade (1). Although blood is often the preferred sample type for genetic testing due to the large amount of high-quality DNA that can be extracted from white blood cells, alternate sample types such as saliva and buccal cells can provide enough DNA to perform most genetic testing. Based on the clinical scenario, these samples may be easier to collect or preferred for testing to provide the most accurate results. For example, affected tissue may be preferred over a blood sample in a patient with a suspected mosaic condition, but a saliva or buccal sample may be preferred over blood in a patient who has had a bone marrow transplant.

Clinical laboratories require an order be matched to a physical sample that can be tracked throughout its lifecycle from collection to result (2). When a blood sample is collected for genetic testing, the clinic or laboratory will follow defined processes to get samples from the collection site to the reference laboratory. When an alternate sample, like saliva or buccal swab, is utilized for genetic testing, the patient may collect their sample remotely. With sample collection happening in a variety of locations, labs must create flexible logistics solutions for sample tracking to ensure proper handling and reporting of patient results.

Discovering Inspiration During the COVID-19 Pandemic

When the COVID-19 pandemic began, many outpatient clinics

cancelled their in-person appointments and moved to virtual visits, and our pediatric tertiary care facility was no exception. With fewer patients attending their appointments in-person, and many caregivers not wanting to risk exposure by bringing their child into the lab for a blood draw, providers shifted to offering sample collection by alternate specimen kits, when appropriate.

Because of the complexities of order logistics and institutional billing, our laboratory team created new processes to support this increase in requests for alternate sample kits. This new process has supported patient access to genetic testing during an extended pandemic, and it also has allowed patients for whom collecting blood may have been challenging to access the genetic testing they need and deserve for their healthcare (3).

Our institution serves patients in a large geographical region (the states of Washington, Alaska, Montana, Idaho, and sometimes others), so collecting a blood sample for genetic testing is not always realistic, especially during the pandemic. The alternate specimen collection kit process greatly increased access for these remote patients. In addition, in 2020 our facility retired DNA banking and restricted use of the no-cost option to hold a sample for a short period of time for one desired genetic test. The option to collect samples for genetic testing with alternate specimen collection kits has therefore eased the burden of limited sample hold options for ordering clinicians.

Implementing Alternate Sample Collection Kits

Prior to the pandemic, our outpatient clinics primarily utilized alternate sample collection kits to collect parental comparator samples for trio-based genetic tests, such as exome sequencing. As our patients and providers moved to telehealth, the utilization of alternate sample collection kits increased. In the first 6 months of data tracking (April–September 2020), our laboratory team sent out 312 kits (around 52 kits per month). In the 6 months prior to this writing (April–September 2021), our laboratory team sent out 587 kits, or nearly 98 kits per month—a 188% year-over-year increase. With the increased request volume, we needed a standardized process to reliably handle these samples.

At our institution, a team of laboratory genetic counselors and genetic counseling assistants review all preauthorization requests for genetic testing. Once the preauthorization is in place, the ordering clinician enters the test order in the electronic medical record (EMR) and a sample can be collected for either in-house or sendout testing. To comply with our institutional billing processes, the sample must be routed through our hospital lab for processing prior to sending it to the intended reference lab for testing.

To align orders for genetic testing using alternate specimen collection kits with the standard order workflow, our laboratory team sends kits directly from our sendouts department to the patient's home, instead of directly from the

intended reference lab. This allows our laboratory team to include return shipping materials to route the collected sample back through our facility, both to align with institutional billing regulations and to assure the correct requisition is sent to the reference laboratory with the sample.

Our laboratory team created a kit handoff form for clinical teams to communicate their requests for alternate specimen kits. Requests are tracked and triaged by both the laboratory genetic counseling assistants and members of the lab sendouts team (Figure 1).

Refining Our Process

As our efforts to fulfill requests for alternate specimen collection kits progressed, it became clear that not everyone understood the types of collection kits available from reference laboratories used by our institution. For example, some laboratories offer buccal swabs and saliva collection kits, while others offer only one option or the other.

Further complicating things, not all saliva collection kits are suitable for all patients. Saliva kits can include an assisted collection method, which uses small sponges to absorb the saliva in the patient's mouth. This is ideal for young pediatric patients and those with developmental differences that make spitting difficult. Other saliva kits require the patient to physically give the full sample directly into the collection tube.

To tackle this problem, our teams reviewed the indicated kit type to confirm that it was appropriate for the patient's age and abilities and an accepted sample type by the performing reference lab. Additionally, many of our patients and families speak and read a language other than English. While most of the major kit manufacturers include translations of their collection instructions on their website, our laboratory team confirmed the patient's language for care and modified our triage process to ensure that the appropriately translated instructions are included with the kit.

We also created an information page within our hospital's online test catalog. This page consolidates the various sources of information related to the alternate specimen collection kits for genetic testing. The webpage includes a link to our kit request handoff form, as well as instructions for clinicians about the ordering process and background information on the clinical utility of buccal and saliva samples for genetic testing. We also added links to translated documents and collection instructions for each specific type of collection kit used by reference labs, as well as YouTube videos of the collection instructions that clinical teams can use to walk patients and families through the sample collection process. These resources have allowed more patients to successfully collect samples and complete genetic testing.

This alternate sample coordination process is continually evolving, but it's more than just "kitting" around: Our new process for collecting and utilizing saliva samples and buccal swabs for genetic testing is truly patient-centered. We hope learning about our experience is useful for other facilities interested in implementing similar stewardship efforts to support patient access to genetic testing that is important and necessary for high quality care.

Clair Wittowski is a genetic counseling assistant at Seattle Children's Hospital in Seattle.

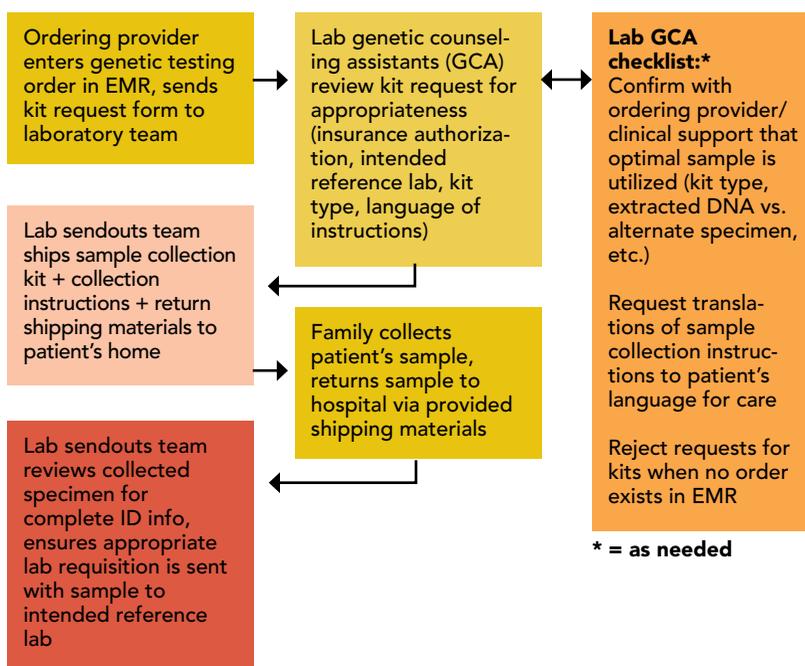
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References

1. Sun F, Reichenberger EJ. Saliva as a source of genomic DNA for genetic studies: review of current methods and applications. *Oral Health Dent Manag* 2014;13(2):217-22.
2. MacMillan D, Lewandrowski E, Lewandrowski K. An analysis of reference laboratory (send out) testing: an 8-year experience in a large academic medical center. *Clin Leadersh Manag Rev* 2004;18(4):216-9.
3. Astion ML. Moving toward patient-centered laboratory stewardship. <https://www.aacc.org/cln/articles/2021/july/moving-toward-patient-centered-laboratory-stewardship>. (Accessed November 16, 2021).

LABORATORY STEWARDSHIP FOCUS

F1 Alternate sample coordination workflow for genetic testing at Seattle Children's Hospital.



Regulatory Roundup

Labcorp Markets Home Collection Covid-19/Flu Kit

Labcorp has announced Food and Drug Administration emergency use authorization for a home collection kit that detects SARS-CoV-2 and influenza A/B simultaneously in individuals as young as 2 years old.

Called Pixel by Labcorp, the kit became available in October 2021. Samples collected with the kit are analyzed using the Roche cobas SARS-CoV-2 & influenza A/B test, which runs on the high-volume cobas 6800/8800 systems. This PCR test simultaneously identifies and differentiates SARS-CoV-2, influenza A, and influenza B—a multiplex approach that will help to increase lab efficiency and save resources, according to Labcorp. The test also has full-process negative, positive, and internal controls.

Pixel is available at no upfront cost to those who meet clinical guideline criteria, which may include experiencing symptoms of COVID-19, being exposed to someone with COVID-19, or being asked to get tested by a healthcare provider.

Adult patients can order the combined collection kit online through the Pixel by Labcorp website. Physicians also can order the kits directly from their electronic medical record systems.

Labcorp ships the home collection kit to consumers via FedEx Priority Overnight along with a prepaid return envelope. Then, once an individual returns the completed collection kit to Labcorp, test results are available on average between 1-2 days after receipt.



LBT'S MRSA ANALYSIS MODULE GETS FDA CLEARANCE

The Australian medical technology company LBT Innovations recently announced that it has received Food and Drug Administration (FDA) 510(k) clearance for its APAS Independence with associated analysis methicillin-resistant *Staphylococcus aureus* (MRSA) module, a culture plate reading technology.

LBT's MRSA analysis module automatically reads and reports the negative MRSA plates that typically account for over 95% of total MRSA

workflow. This enables users to process more tests through the APAS instrument, delivering increased efficiency and cost savings for labs, according to company officials.

A study by Johns Hopkins Hospital found the APAS Independence successfully identified all positive MRSA specimens, including five positive samples previously missed by microbiologists.

Along with the June 2019 FDA clearance for the APAS Independence with urine analysis module, there are now two analysis modules cleared for use on the APAS Independence in the United

States. Each analysis module is sold to customers as a separate software license and available to customers as a software upgrade.

HOLOGIC'S MULTIPLEX COVID-19/FLU COMMERCIALY AVAILABLE IN NORTH AMERICA AND EUROPE

Hologic's Aptima SARS-CoV-2/Flu assay has received Food and Drug Administration emergency use authorization and is now available in the United States for the simultaneous detection and differentiation of three respiratory viruses that present with overlapping

clinical symptoms. The three viruses—SARS-CoV-2, influenza A, and influenza B—typically cause fever, cough, headache, and fatigue.

The Aptima SARS-CoV-2/Flu assay uses both anterior nasal swab and nasopharyngeal samples. The test can also be used with samples from multiple collection devices, including Hologic's Direct Load collection kits, which are designed to reduce risk of viral transmission and improve laboratory efficiency. The assay runs on Hologic's fully automated Panther system, which provides initial results in approximately 3 hours and can process more than 1,000 tests in 24 hours.

Hologic said its assay will provide greater flexibility and testing options for labs and healthcare providers during the U.S. flu season.

PERKINELMER RESPIRATORY PANEL RECEIVES FDA EUA

A Food and Drug Administration emergency use authorization for PerkinElmer's PKamp Respiratory SARS-CoV-2 real-time PCR Panel 1 assay means that labs can now use it for simultaneous qualitative detection and differentiation of common respiratory viruses. Those viruses include SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus. The assay uses samples from nasopharyngeal swabs, anterior swabs, and mid-turbinate swabs.

PerkinElmer officials noted that the Centers for Disease Control and Prevention has encouraged labs to adopt a multiplex method that detects and differentiates these viruses, which cause similar symptoms. The new test will allow labs and the wider healthcare system to conserve resources by avoiding multiple tests on samples from individuals suspected to have COVID-19.

GENOMSYS VARIANT ANALYZER GETS CE MARK

GenomSys, a pioneer in the development and adoption of the ISO/IEC 23092 MPEG-G open standard for genomic data, has obtained a CE mark for and launched

its latest GenomSys Variant Analyzer. The tool enables genomic professionals to leverage the benefits of the new genomic standard MPEG-G and the most updated databases on human genetic variants. GenomSys officials noted that the National Institutes of Health predicts widespread genome sequencing by 2030, adding that their tool will help handle vast amounts of genomic data more reliably and efficiently.

The GenomSys Variant Analyzer takes full advantage of MPEG-G and user-friendly dashboard and cloud-based architecture, and is designed to allow geneticists to focus more on analysis than bioinformatics. Company officials added that the platform features an extensive range of dynamic filtering options to adapt and tailor analytical criteria, integration of Varsome-curated databases, faster data access time and storage reduction, and automated workflow for secondary and tertiary analysis.

GENETRON HEALTH'S MULTI-GENE CANCER MUTATION DETECTION KIT OBTAINS CE MARK

Genetron recently announced that its proprietary large-panel product, Onco PanScan (Mutation Detection Kit for Human Multi-Genes), has obtained the CE mark.

Genetron, a Chinese company, said that Onco PanScan is a comprehensive genomic profiling test based on hybridization capture and next-generation sequencing technology. By combining coverage of different gene mutation regions and genetic variants observed in thousands of cases with different tumor types, the detection kit covers more than 800 genes recommended by international treatment guidelines. Those guidelines were issued by groups including the World Health Organization, National Comprehensive Cancer Network, and the European Society for Medical Oncology.

Onco PanScan is suitable for targeted therapy, immunotherapy treatment guidance, and screening for susceptibility to genetic risks, the company added.

GENEMATRIX HPV29 KIT GETS CE-IVD CERTIFICATION

Genematrix, a South Korean specialist in real-time PCR diagnostics, recently announced that its NeoPlex HPV29 Detection test has received the CE mark in Europe. The test identifies 29 genotypes of human papillomavirus (HPV), which causes cervical cancer. Genematrix officials said that the product can also reduce turnaround time by more than an hour, compared to existing products on the market.



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Industry Playbook

BD Collaborates With U.S. Government for COVID-19 Combination Diagnostic Tests

Becton, Dickinson, and Company (BD) recently announced a strategic public-private partnership with the federal Biomedical Advanced Research and Development Authority (BARDA) to develop diagnostics for multiple pathogens in single samples from patients with respiratory symptoms.

Under the partnership, BARDA will award BD an initial \$24.7 million with the opportunity to increase up to \$40.3 million for development and Food and Drug Administration 510(k) clearance of five new combination tests. The tests include:

- A rapid point-of-care antigen test that detects and distinguishes between SARS-CoV-2, influenza A, and influenza B at the point of care.
- A molecular PCR test that detects and distinguishes between SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV) for hospital or other moderate-throughput labs.
- A molecular PCR test that detects and distinguishes between SARS-CoV-1, Middle East respiratory syndrome (MERS), seasonal coronaviruses, and novel or emerging coronaviruses to address future outbreaks in hospital or other moderate-throughput labs.
- A molecular PCR test that detects and distinguishes between SARS-CoV-2, influenza A, influenza B, and RSV for core, reference, or other high-throughput labs.
- A molecular PCR test that detects and distinguishes between SARS-CoV-1, MERS, seasonal coronaviruses, and novel or emerging coronaviruses in core, reference, or other high-throughput labs to address future outbreaks.



BD officials said that COVID-19 “will be with us for a long time.” The officials added that they share BARDA’s desire to ready the U.S. health-care system for diagnosis and treatment of known and emerging respiratory viruses.

TARA BIOSYSTEMS PARTNERS WITH SCIPHER MEDICINE FOR CARDIAC LAMINOPATHIES THERAPIES

TARA Biosystems and Scipher Medicine have announced a collaboration aimed at discovering and validating targets for cardiac laminopathies. TARA is a biotechnology company harnessing human biology and data to transform cardiac drug discovery. Scipher is a precision medicine company. Cardiac laminopathies, associated with mutations in the *LMNA* gene, can result in

electrical and mechanical changes in the heart. These changes can have profound clinical consequences, including cardiomyopathy, sudden cardiac death, and end-stage heart failure. Currently, there are no therapies that correct the underlying pathologies.

Scipher will leverage human molecular data analyzed by its Spectra platform, which includes data from TARA’s Biowire II *LMNA* disease models, to identify novel targets for a stratified disease population. This approach aims to detect

proteins upstream and downstream of *LMNA* signaling within the Spectra network model. The identified targets will be evaluated on the Biowire II platform, which consists of induced pluripotent stem cell-derived human cardiac tissue models, including a repertoire of healthy, gene-edited, patient-derived, and drug-induced phenotypes of human disease.

The companies say their partnership will reduce the time needed for target discovery and validation from years to months.

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I-MAB AND ROCHE DIAGNOSTICS COLLABORATION AIMED AT COMPANION DIAGNOSTICS

I-Mab has entered a strategic collaboration with Roche Diagnostics to co-develop companion diagnostics solutions for I-Mab's innovative pipeline. I-Mab is a Chinese clinical stage biopharmaceutical company committed to the discovery, development, and commercialization of novel biologics, and Roche is a global leader in the in vitro diagnostics industry. Companion diagnostics have become an important part of the innovative biologics research and development (R&D) process. They are used to detect expression levels of proteins and mutated genes, and to help identify the right candidates among patients with different types of diseases. Using companion diagnostics can help innovative biotech companies improve R&D efficiency,

ensure the effectiveness and safety of drugs, and control R&D costs.

Under the terms of the collaboration, the companies will develop companion diagnostic solutions for the innovative assets under development by I-Mab. The collaboration aims to accelerate the research and development process of innovative biologics with cutting-edge diagnosis and treatment technologies.

Roche officials said the collaboration will "bring transformative medicines to benefit cancer patients globally and in China."

AGREEMENT BETWEEN SAGA DIAGNOSTICS AND ASTRAZENECA EYES NEW CANCER TESTS

A recent agreement between SAGA Diagnostics and AstraZeneca aims to help develop unique assays for undisclosed methylated targets for analyses of tissue samples and liquid biopsies. SAGA Diagnostics is a cancer liquid biopsy and genomic testing company focused on precision oncology and noninvasive ultrasensitive monitoring of cancer patients. AstraZeneca is a global, biopharmaceutical company. AstraZeneca officials said they chose to partner with SAGA because of the ultrasensitive performance of the SAGAsafe technology and the opportunity to custom tailor highly complex digital PCR (dPCR) assays to meet AstraZeneca's desired analytical standards.

SAGAsafe is a patented improvement of dPCR that enables approximately 100-fold increased sensitivity compared with competitor methods. SAGAsafe can be used to quantify sequence variants in tissue samples as well as liquid biopsies such as blood plasma with unprecedented performance, according to SAGA.

SAGAsafe is part of a portfolio of ultrasensitive technologies, which also includes the SAGAsign technology for personalized monitoring of cancer burden and minimal residual disease using chromosomal rearrangements, as well as novel technologies in development.



ILLUMINA SUPPORTS ISRAELI NEWBORN GENETIC DIAGNOSIS PROGRAM

illumina has announced an agreement with Israel's Ministry of Health (MoH) for a pilot program that will sequence whole genomes of critically ill infants in neonatal intensive care units (NICU). The program, led by the Genetics Institute at the Tel-Aviv Sourasky Medical Center, will evaluate the use of whole genome sequencing (WGS) in routine care as an effective first-tier diagnostic tool to enable faster identification of disease-causing genetic abnormalities in infants and help in their clinical care and management.

Eighteen participating hospitals will enroll newborns admitted to a NICU with a clinically suspected genetic disorder, along with their biological parents. illumina will provide its illumina DNA PCR-Free Prep reagents for library preparation of DNA and sequencing reagents for WGS samples using the latest NovaSeq 6000 S1 v1.5 reagent kit. The 2-year pilot will lead to the creation of national reimbursement for WGS as a diagnostic tool in hospitals across Israel.

illumina officials said the program will decrease uncertainty for the infants' families and reduce need for iterative tests and time spent in the NICU.

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Ask The Expert

Testing for MPS Disease Management



EXPERT

By Stefani Thomas, PhD, DABCC, NRCC

What are mucopolysaccharidosis (MPS) disorders?

A: MPS disorders are characterized by abnormal glycosaminoglycan (GAG) accumulation resulting from deficiencies or malfunctions of enzymes involved in GAG degradation. These disorders are clinically heterogeneous and characterized by

multi-systemic manifestations, including abnormal GAG accumulation-associated skeletal abnormalities and neurological dysfunctions.

There are seven forms of MPS, some of which have multiple subtypes: I (Hurler/Scheie), II (Hunter), III-A (Sanfilippo Type A), III-B (Sanfilippo Type B), III-C (Sanfilippo Type C), III-D (Sanfilippo Type D), IV-A (Morquio Type A), IV-B (Morquio Type B), VI (Maroteaux-Lamy), VII (Sly), and IX (Natowicz).

How are MPS disorders diagnosed?

Many MPS disorders manifest with similar clinical outcomes, and disease presentation varies from late infancy to adulthood, which renders these disorders difficult to diagnose. Diagnosing an MPS disorder entails a comprehensive clinical evaluation, identifying characteristic findings (e.g., skeletal malformations, coarse facial features, and hepatosplenomegaly), and urine-based tests to detect abnormally high GAG levels. Enzymatic activity assays are also conducted to confirm the decreased levels of lysosomal enzymes associated with excessive GAG levels.

MPS I, which results from a deficiency of the α -L-iduronidase enzyme (IDUA), is currently the only MPS disorder included in the Recommended Universal Screening Panel for newborns. In the case of MPS I, the diagnostic decision-making algorithm begins with a positive newborn screening test—i.e., a dried blood spot-based fluorometric enzyme assay result that indicates low levels of IDUA enzymatic activity. A blood sample is then obtained for IDUA activity analysis in leukocytes. If this test indicates enzymatic deficiency, the patient is referred to a genetic or metabolic disease specialist for comprehensive clinical, molecular, and biochemical assessment. In some cases, identifying the specific genetic variants that cause the observed enzyme dysfunction can guide subsequent treatment.

What methods are used to measure GAG levels?

Urinary total GAG levels are commonly measured using spectrophotometric dye-based binding assays including 1,9-dimethylmethylene blue or alcian blue. However, a drawback

to these screening methods is their lack of specificity. Labs can avoid this limitation by using sensitive and specific liquid chromatography-tandem mass spectrometry (LC-MS/MS) assays to quantify individual classes of GAGs. These LC-MS/MS methods often incorporate the use of methanolysis (chemical hydrolysis) or specific enzymatic digestion to yield individual GAG-derived disaccharides followed by targeted mass spectrometric data acquisition.

Does laboratory testing have a role in MPS treatment?

Enzyme replacement therapy (ERT) using recombinant lysosomal enzymes is Food and Drug Administration-approved for the treatment of MPS I (Laronidase/Aldurazyme), II (Idursulfase/Elaprase), IV-A (Elosulfase alfa/Vimizim), and VI (Galsulfase/Naglazyme). A growing body of evidence supports the use of urinary GAG concentrations as predictive biomarkers of ERT efficacy. Urinary GAG levels are useful markers of ERT efficacy because they are measured using noninvasive procedures, respond to changes in enzyme dosing, and reflect restoration of enzyme activity in affected tissues. With ERT, urinary GAG concentrations often decrease rapidly over the first 3-6 months of administration followed by a slow continuous decline in subsequent years. However, urinary GAG levels do not precisely predict quantitative changes in specific clinical endpoints.

It is also important to note that ERT does not mitigate central nervous system abnormalities and cognitive decline due to the inability of the enzymes to cross the blood-brain barrier. For patients with severe MPS I, the gold standard treatment is therefore hematopoietic stem cell transplantation. As for MPS disorders without an approved ERT, treatment is directed toward the specific symptoms that a patient exhibits.

Stefani Thomas, PhD, DABCC, NRCC, is an assistant professor of laboratory medicine and pathology at the University of Minnesota and associate medical director of the M Health Fairview West Bank Laboratory in Minneapolis.
+EMAIL: stefanit@umn.edu

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