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MEDICAL LABORATORY OBSERVER

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MLO LAB OF THE YEAR 2021

2021 LAB of the YEAR

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+ State of the Industry: Best Practices

Neutralizing SARS-CoV-2 antibodies

CE Diabetic testing levels after COVID-19

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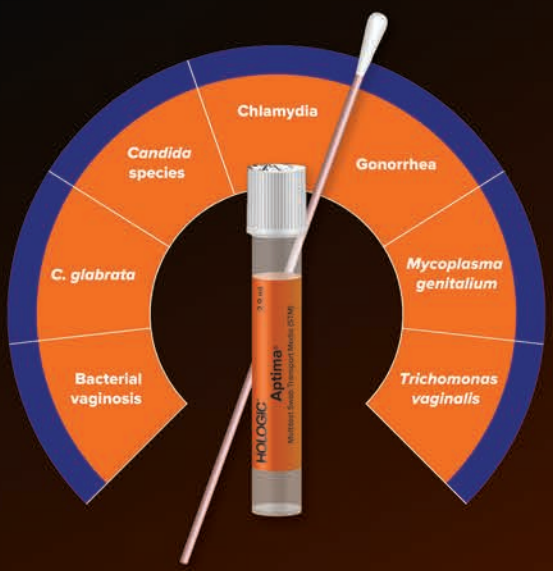

ONE SAMPLE

References: 1. Aptima Combo 2 Assay [package insert] #502446-IFU-PI_012 San Diego, CA; Hologic, Inc., 2021. **2.** Aptima Mycoplasma genitalium assay [package insert] #AW-17946_002, San Diego, CA; Hologic, Inc., 2021, **3.** Aptima CV/TV assay [package insert] #AW-18812, San Diego, CA; Hologic, Inc., 2021. **4.** Aptima BV assay [package insert] #AW-18811, San Diego, CA; Hologic, Inc., 2021.

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Reflecting on the lab's COVID-19 response

By Linda Wilson
Senior Editor

As you know, Medical Laboratory Professionals Week, which originated in 1975, occurs each year in April. In 2021, it will occur April 18-24, 2021.

The activities associated with the week-long event are coordinated each year by a committee with representatives from 17 national clinical laboratory organizations.

While it is always an opportunity to reflect on the work of clinical laboratories, this is particularly true in 2021, given the work laboratorians have done to manage diagnostic services for COVID-19 while also providing routine the testing associated with hospital stays, surgeries, chronic diseases, and health checkups.

It has been more than a year since the World Health Organization (WHO) in January 2020 first released information about a cluster of pneumonia cases in Wuhan, China, and then two months later, characterized the COVID-19 outbreak as a pandemic.

Since that time, U.S. labs have been at the center of efforts to care for COVID-19 patients and to track the spread of the virus. From the beginning of the outbreak until March 7, 2021, when it ceased reporting data, The COVID Tracking Project said the United States had processed 363,824,818 COVD-19 tests, including 28,756,184 positive results.

Rising to the challenge, laboratorians have adopted management practices that have allowed them to ramp up testing. This has included bringing new analyzers online, sourcing reagents and test kits, and purchasing personal protective equipment (PPE). They also have trained staff from other departments in the lab in molecular testing and automated processes throughout diagnostic and billing workflows.

Medical Laboratory Observer's 2021 Lab of the Year and Runner Up shared with us many examples of steps they have taken to help their patients during the pandemic.

St. Luke's University Health Network Laboratory Services – *MLO's* 2021 Lab of the Year – provided test collection kits to nine nursing homes (in addition to the three facilities that St. Luke's owns) and then processed the tests, including those for surveillance, with an average turnaround time (TAT) of 24 hours.

St. Luke's also provided analyzers, reagents, training, and ongoing supervision to five local colleges, allowing the on-campus providers to perform multiplex testing for COVID-19, flu A/B and RSV.

Meanwhile, *MLO's* Lab of the Year Runner Up – the U.S. Air Force School of Aerospace Medicine's Epidemiology Laboratory – averaged a TAT of 16 hours for SARS-CoV-2 polymerase chain reaction (PCR) tests. Up through the COVID-19 surge over the summer, the Epi Lab completed 34 percent of all COVID-19 tests at the Department of Defense (DOD).

The work at these organizations is representative of what labs across the country and have achieved in the battle against COVID-19.

But in addition to reflecting on the work of the past year, Medical Laboratory Professionals Week also presents an opportunity for the 300,000 U.S.-based practitioners of clinical laboratory science to build on consumers' new-found appreciation of the role clinical testing plays in managing both collective and individual health. I encourage you to talk to your peers in the healthcare industry, as well as your friends and family, about how important it is for the United States to invest in laboratories of all kinds – from those at hospitals and doctor's offices to those at state and local health departments.

I welcome your comments, questions, and opinions – please send them to me at lwilson@mlo-online.com

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Group Publisher/Executive Editor
Kristine Russell
krussell@mlo-online.com

Senior Editor
Linda Wilson
lwilson@mlo-online.com

Managing Editor
Marisa Williams
mwilliams@mlo-online.com

Graphic Artist
Patti Connors
pconnors@endeavorb2b.com

Audience Development/List Rentals
Laura Moulton
lmoulton@endeavorb2b.com

Ad Traffic Manager
Tiffany Coffman
tcoffman@endeavorb2b.com

eProduct Coordinator
Mary Haberstroh
mhaberstroh@endeavorb2b.com

ADVERTISING

East Coast/Midwest Sales (except IL)
Classified/Recruitment Advertising
Carol Vovcsko
(941) 321-2873
cvovcsko@mlo-online.com

South/West Coast/Illinois Sales
Lora Harrell
(941) 328-3707
lharrell@mlo-online.com

2477 Stickney Point Rd., Suite 221B Sarasota, FL 34231
Phone: (941) 388-7050 Fax: (941) 388-7490
www.mlo-online.com

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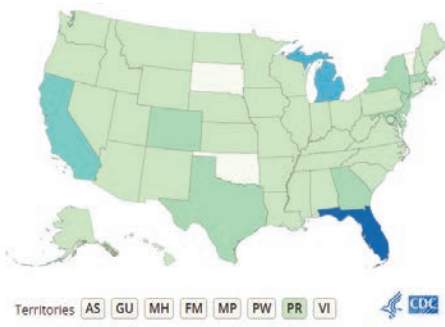


Image from the CDC

Fast Facts

Covid-19 Variants

64%

Higher death rate with UK B.1.1.7 COVID-19 variant

21%

Of Florida COVID-19 cases are from variants, and Florida has the highest number of variant cases in the U.S.

49

U.S. states now have COVID-19 cases from the UK B.1.1.7 variant

89%

Effective—Moderna and Pfizer vaccines against B.1.1.7 variant

49%

Effective—Moderna and Pfizer vaccines against B.1.351 variant

100%

Of farmed minks were destroyed in Denmark after it was discovered they transmitted Sars-CoV-2 to farmers

2

Weeks is the amount of time people are considered fully vaccinated for COVID-19 after they have received the second dose in a 2-dose series (Pfizer-BioNTech or Moderna), or received a single-dose vaccine (Johnson and Johnson [J&J]/Janssen)

Sources:
COVID Data Tracker Weekly Review 3/10/21
CDC US COVID-19 Cases Caused by Variants CDC: https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/animals.html
Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report | NEJM

Cardiovascular risks and pregnancy complications can raise risk of hypertension years after childbirth

A new study of first-time pregnant women found risk factors for heart disease, such as obesity and elevated blood sugar, can put expectant moms at higher risk for pregnancy complications and gestational diabetes, as well as lead to increased chances of high blood pressure, or hypertension, two to seven years after giving birth, according to a news release from the National Institutes of Health (NIH). The findings appeared in the *Journal of the American Heart Association*.

Researchers created the nuMoM2b Heart Health Study, supported by the NIH, to examine factors that influence pregnancy outcomes and support the cardiovascular health of new mothers. In this sub-study, researchers followed 4,471 women who had their first child at one of eight U.S. medical centers between 2011 and 2014. About one in two women were overweight or obese at the start of their pregnancy. The researchers monitored the women from the early stages of their pregnancies and stayed in touch, through self-reporting surveys, phone calls, and clinical visits, for up to seven years after the women gave birth.

The researchers found that roughly 25 percent of the study participants, 1,102 women, had a pregnancy complication or developed gestational diabetes. Women who experienced a pregnancy complication were more likely to have developed markers for heart disease before or during their first trimester, compared to those who did not experience complications. For example, women with pregnancy complications were more likely to have higher levels of blood sugar, blood pressure, and inflammation, while women who did not develop complications had normal or lower levels.

Women in the study who had a pregnancy complication or who developed gestational diabetes were also 1.6 times as likely to develop hypertension within seven years. Their risk for stage 2 hypertension, the level at which treatment is often prescribed, doubled.

The researchers suggest that screening patients for heart disease, which the American Heart Association and the American College of Cardiology recommend doing every four to six years for adults ages 20-39, could start even earlier for pregnant women or could be integrated into prenatal or obstetric care. In the study, women who exercised three hours each week had a lower risk for later hypertension.

Spinal fluid of people with Alzheimer's risk gene signals inflammation

People who have a gene variant associated with an increased risk of developing Alzheimer's disease also tend to have changes in the fluid around their brain and spinal cord that are detectable years before symptoms arise, according to new research from Duke Health as reported in a news release.

The findings, which were published online in the *Journal of Alzheimer's Disease*, provide a potential means to identify the earliest mechanisms occurring among APOE4 carriers that might contribute to Alzheimer's disease before people develop memory problems or other symptoms of dementia, Duke Health said.

Researchers analyzed data from targeted cerebrospinal fluid of Alzheimer's Disease Neuroimaging Institute research participants. Controlling for Alzheimer's disease clinical status, they identified protein level variations in the cerebrospinal fluid from people with an increasing number of APOE4 gene variant copies. They found that people with more APOE4 copies had lower CRP levels circulating in their cerebrospinal fluid.

Researchers said this is consistent with the current risk profile associated with APOE4 carriers. People with a single APOE4 variant have about a three- to four-fold increased risk of developing Alzheimer's disease, while those who carry two APOE4 variants have a greater than 10-fold risk.

Marine product off Florida's coast might help fight cancer

From cyanobacteria blooms found off the Florida coast near Fort Lauderdale, University of Florida researchers have discovered a novel marine natural product that binds to a new site of tubulin, an important target for cancer drugs, according to a news release from the university.

Tubulin is a group of proteins found in the cytoplasm of cells, outside the nucleus. They serve as building blocks of microtubules, which are involved in cellular structure and aid in cell division.

Natural products targeting tubulin have provided the basis for several anticancer drugs approved by the Food and Drug Administration, including paclitaxel and vincristine.

For decades, cancer researchers have explored new ways to modify the pro-

tein's function and dynamics by developing compounds that target one of tubulin's six binding sites. The UF researchers discovered a new chemical compound that targets a seventh binding site.

"Tubulin is among the most successfully targeted proteins related to cancer chemotherapy, and there is tremendous interest in discovering new molecules that bind to tubulin," said Hendrik Luesch, PhD, Professor and Chair of Medicinal Chemistry and the Debbie and Sylvia DeSantis Chair in Natural Products Drug Discovery and Development in the UF College of Pharmacy and a member of UF Health Cancer Center.

Identifying and fully characterizing this new tubulin-targeting compound and binding site took years of work. The compound gatorbulin-1 pays tribute in name to the UF researchers and global partners who led the way to its discovery and characterization.

In a study published in the journal *Proceedings of the National Academy of Sciences*, Luesch and his research team report on gatorbulin-1's chemical and biological development, including the isolation, structure determination and chemical synthesis of the new natural product.

Gatorbulin-1's origins in the Atlantic Ocean add to a growing list of compounds Luesch's team has discovered from marine natural products. The biodiversity present in the world's oceans offers a wealth of opportunity for exploration of new drug therapies.

Luesch previously discovered the tubulin agent dolastatin 10 from another marine cyanobacteria, which served as the basis for the development of three FDA-approved antibody-drug conjugates targeting a different tubulin binding site.

Women experience faster cognitive decline with age

A new analysis finds higher baseline cognition scores for aging women, but a more rapid drop once cognitive decline begins. Women may start middle age with stronger brain function than men, but as they get older, women's cognition declines faster, according to a news release from University of Michigan.

That's according to a new analysis from more than 26,000 Black and white men and women who had participated in one of five long-term cohort studies. The researchers found that women had significantly faster declines in overall cognition and executive function, the brain processes used in problem-solving, planning and managing your time. However, memory decline was comparable between men and women.

"We estimate that cognitive function in women declined around five years faster than their ages would suggest," says lead author Deborah Levine, MD, MPH, Associate Professor of Internal Medicine and Neurology at Michigan Medicine, and Director of its Cognitive Health Services Research Program. "Differences in biological, genetic, social and lifestyle factors between men and women might contribute to faster cognitive decline in women, and more research is needed."

AMR staph strains found to spread from pigs to people

DNA sequencing of bacteria found in pigs and humans in rural eastern North Carolina, an area with concentrated industrial-scale pig-farming, suggests that multidrug-resistant Staphylococcus aureus strains are spreading between pigs, farmworkers, their families and community residents. This represents an emerging public health threat, according to a study led by researchers at the Johns Hopkins Bloomberg School of Public Health as reported in a press release.

S. aureus is commonly found in soil and water, as well as on the skin and in the upper respiratory tract in pigs, other animals, and people. It can cause medical problems, from minor skin infections to serious surgical wound infections, pneumonia, and the often-lethal blood-infection condition known as sepsis.

The findings provide evidence that multidrug-resistant S. aureus strains are capable of spreading and possibly causing illness in and around factory farm communities in the U.S.– a scenario the authors say researchers should continue to investigate.

The study was published in *Emerging Infectious Diseases*, a journal published by the Centers for Disease Control and Prevention.

The researchers in recent years have been collecting samples of S. aureus from pigs, farmworkers, farmworkers' family members, and community residents – including children – in the top pig-producing counties in North Carolina. For the study, they sequenced the DNA from some of these samples to determine the relation of the strains found in pigs and people. They found that the strains were very closely related, providing evidence for transmission between pigs and people. Most of the strains carried genes conferring resistance to multiple antibiotics.

Epidemiologists have long suspected that S. aureus and other bacteria are transmitted from humans to pigs on factory farms, and thereafter evolve antibiotic resistance within the pigs. The animals are routinely given antibiotics to prevent outbreaks in their dense concentrations on factory farms. The drug-resistant bacterial strains may then be transmitted back to humans, becoming a potentially serious source of disease.

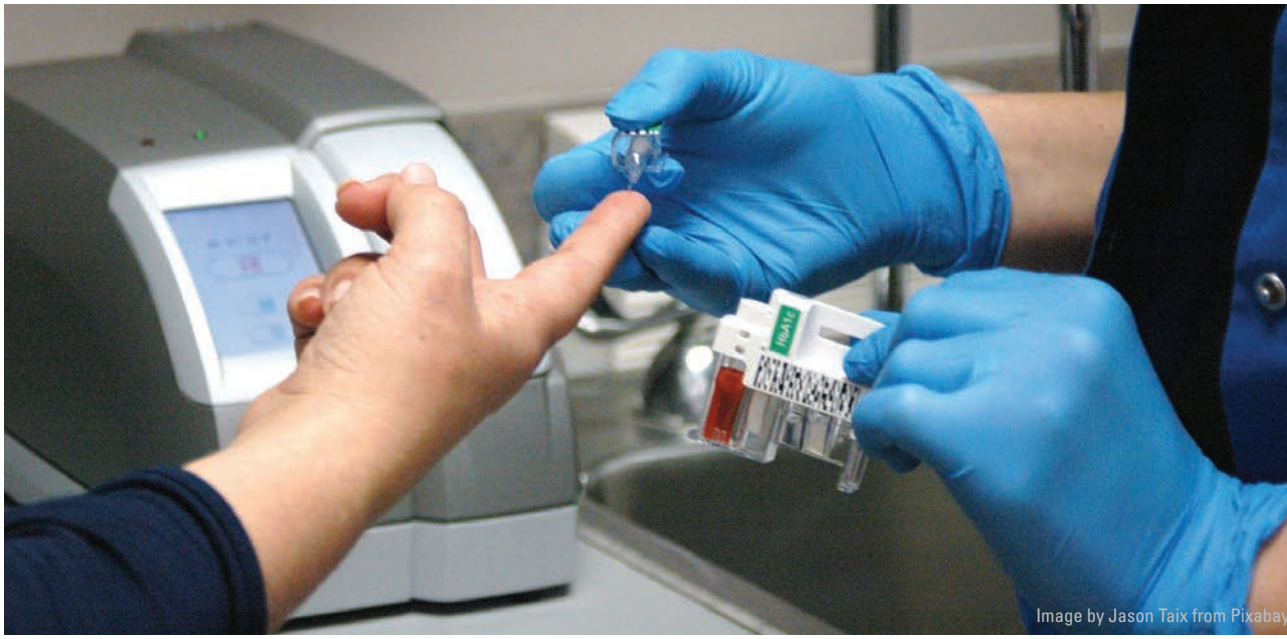
In recent years, Heaney and colleagues have been gathering S. aureus isolates from pigs and farmworkers at factory-scale pig farms in North Carolina, one of the leading pig-farming states. Their research has shown that livestock-associated strains of S. aureus, many of them antibiotic-resistant strains, can be found not only in pigs but also in farmworkers, their family members, and residents living nearby.

For the new study, they performed whole-genome sequencing on 49 of these S. aureus isolates to characterize these strains at the DNA level and get a more precise picture of their interrelatedness.

One finding was that all these isolates, whether taken from humans or pigs, belonged to a grouping of S. aureus strains known as clonal complex 9 (CC9).

The researchers also determined from their analysis that the CC9 isolates from North Carolina were closely related, in many cases implying recent transmission between pigs and people. Moreover, virtually all of the isolates that appeared to be involved in transmission between pigs and humans were multidrug resistant, suggesting that diseases these isolates cause could be hard to treat.

The scope of the study didn't include evaluating S. aureus-related disease among people in the affected communities, but one of the pig farmworkers who carried a CC9 isolate in their nose reported a recent skin infection.



The nurse is testing the patient's A1C levels.

Preparing labs for diabetic testing levels after COVID-19

By Shamiram Feinglass, MD, MPH

There is plenty of evidence that individuals with diabetes are at an increased risk of COVID-19. A retrospective observational study of 1,122 COVID-19 adult patients in 88 U.S. hospitals found that patients with diabetes and/or uncontrolled hyperglycemia had higher mortality rates and longer hospital stays than patients without these conditions.[1] A report from New Orleans claims that 97 percent of people killed by COVID-19 in Louisiana state had a pre-existing condition, and nearly 40 percent of those who died had diabetes.[2]

The coronavirus pandemic has placed an additional mental and physical burden on people with underlying health conditions, like diabetes. The pandemic has moved routine doctor visits to telemedicine and made outings to pick up medicine or get blood drawn yet another risk for exposure.[3]

Due to this, routine lab testing volumes have plummeted by approximately 60 percent as patients put off care,[4] while COVID-19 has increased lab testing demands by nearly 25 percent.[5] This trend continues in smaller regional and communal laboratories where the volume of routine laboratory testing has declined dramatically due to the closure of many doctor's offices, medical clinics, surgical centers, and other healthcare facilities.[6]

The impact of COVID-19 on people with diabetes

The pandemic has forced millions of people worldwide indoors and into isolation or quarantine, which affects both our physical and mental health.[7]

People with diabetes are more vulnerable and have a high risk of becoming seriously ill when infected with SARS-CoV-2. This can provoke anxiety and is compounded by realistic worries about the availability of diabetes medicines and technologies.[8] Stress and anxiety are known to make controlling diabetes more difficult, as they throw off the much-needed daily routines, the release of stress hormones that can increase blood pressure and heart rate, and may cause blood sugar to rise.[9] In addition, quarantining makes it challenging to perform daily physical activity, which is a critical focus for blood glucose management and overall health in individuals with diabetes and prediabetes.[10]

Not being able to get HbA1c levels tested has an adverse impact on patients with diabetes, where regular HbA1c testing is needed to control glucose levels and prevent diabetes complications. In addition, well-controlled glucose levels may prevent severe cases of COVID-19.[11]

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LEARNING OBJECTIVES

Upon completion of this article, the reader will be able to:

1. Describe the impact of COVID-19 on people with diabetes, as well as the disproportional impact on diabetic/pre-diabetic people of color and low socioeconomic populations
2. Describe the impact of lack of routine testing on diabetes management and prevention
3. Describe the challenges laboratories will face post-pandemic
4. Recall what laboratories can do to prepare for life after COVID-19

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Learning Objectives:

- Role of magnesium in disease states including heart failure, heart rhythm disorders, diabetes, hypertension, gastrointestinal and renal losses
- Why ionized magnesium is a better tool to manage magnesium status

Presenter

Prof. Dr. Klaus Kisters, MD
Med Clinic I, St. Anna Hospital, ESH Excellence Centre,
Herne, Germany

Combating COVID-19 and Building Immune Resilience: A Potential Role for Magnesium Nutrition

Several aspects of COVID-19 disease mimic metabolic events shown to occur during latent subclinical magnesium deficiency. Most notably, hypomagnesemia is a known pro-inflammatory state, and can predispose to cytokine storm, a factor in severe COVID-19 cases. A summary of experimental findings and knowledge of the biochemical role magnesium may play in the pathogenesis of COVID-19, particularly in severe cases, is presented. Frequent monitoring of ionized magnesium status with subsequent repletion, when appropriate, may be an effective strategy to influence disease contraction and progression.

Learning Objectives:

- Ionized magnesium in pro-inflammatory states
- Ionized magnesium management and repletion in COVID-19 severe illness

Presenter

Taylor Wallace, PhD
Think Healthy Group, Washington, DC, USA; Department of Nutrition and Food Studies, George Mason University, Fairfax, Virginia, USA; Center for Magnesium Education & Research, Pahoa, Hawaii, USA

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The extra burden on people of color and low-socioeconomic populations

According to the Department of Health and Human Services (HHS), African American adults are 60 percent more likely than non-Hispanic white adults to have been diagnosed with diabetes. In addition, minority populations suffer the consequences: in 2016, non-Hispanic African Americans were 3.5 times more likely to be diagnosed with end-stage renal disease as a consequence of diabetes, as compared to non-Hispanic whites; non-Hispanic African Americans were 2.3 times more likely to be hospitalized for lower limb amputations, as compared to non-Hispanic whites; and in 2017, African Americans were twice as likely as non-Hispanic whites to die from diabetes.[12]

In general, African Americans have a high risk for type 2 diabetes. Insulin resistance and obesity contribute to this risk, as do racial disparities in health, often resulting in diabetic complications because of poor glycemic control.[13] These disparities are compounded during COVID-19.

People of color, particularly African Americans, are experiencing more serious illness and death due to COVID-19 than white people. This is regardless of socioeconomic status. There are many reasons for this, including systemic racism, inconsistent access to healthcare, working in essential fields, living in crowded housing conditions, and existing chronic conditions, such as diabetes.[14]

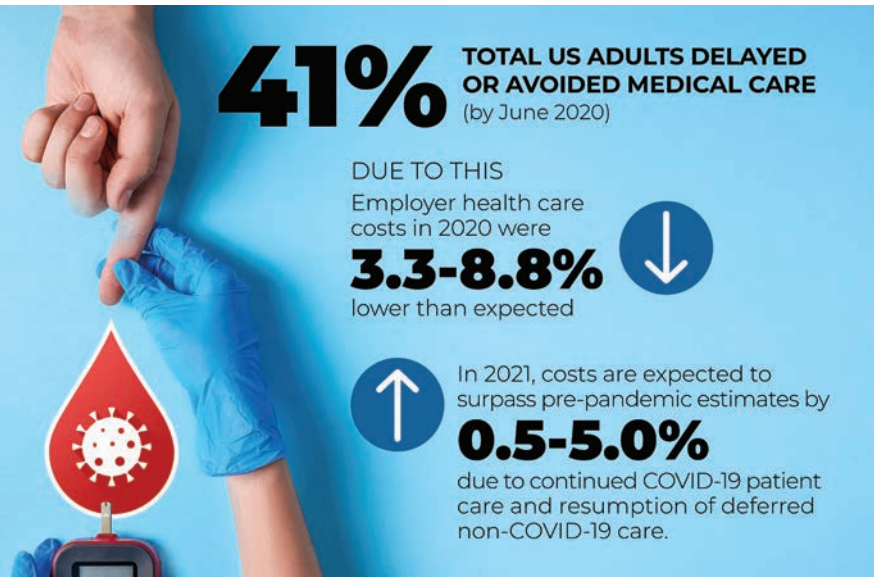

Photo courtesy of Beckman Coulter

There is also anecdotal data to suggest that people from vulnerable populations who have COVID-19 symptoms may not be referred for testing as frequently as their white counterparts. African American and Hispanic people are more likely to experience longer wait times and understaffed testing centers. As in many cities around the country, testing sites in and near predominantly African American and Hispanic neighborhoods are likely to serve far more patients than those near predominantly white areas.[15] This lack of testing can lead to further spread of infection and death – to which people with diabetes are even more susceptible.

The impact of lack of routine testing on diabetes management and prevention

According to the Centers for Disease Control and Prevention (CDC), an estimated 41 percent of U.S. adults had delayed or avoided medical care, including urgent or emergency care (12 percent) and routine care (32 percent) by the end of June 2020.[16] Avoidance of urgent or emergency care was more prevalent among unpaid caregivers for adults, persons with underlying medical conditions, African American adults, Hispanic adults, young adults, and persons with disabilities.

A delay in needed medical care likely increases morbidity and mortality associated in both acute and chronic health conditions, including prediabetic patients and those with type 2 diabetes. These individuals will benefit from HbA1c testing crucial to the assessment, diagnosis and management of diabetes.[17] Poor diabetes control has been proven to negatively affect prognosis and promote the risk of infection.[18] Lack of testing for diabetes is also detrimental for COVID-19 outcomes for patients who have diabetes. Screening of asymptomatic patients to detect prediabetes and initiate lifestyle changes has the added benefit of reducing the risk of adverse events if a person contracts COVID-19.[19]

Having untreated or unmonitored diabetes can pose a serious health risk, and unfortunately, one in five adults don't even know they have diabetes.[20] The consequences of delaying treatment in type 2 diabetes can impact long-term outcomes. A study evaluated a cohort of 600,000 hypothetical patients with type 2 diabetes, based on real-world data, found that mean HbA1c at one year was 6.8 percent for patients undergoing treatment intensification (No Delay group), compared with 8.2 percent for those where treatment was delayed (Delay group). The risk for major adverse cardiac events (MACE) – myocardial infarction, stroke, and death from coronary heart disease – was lower among patients in the group who received treatment without delay. Patients in the No Delay group also had a lower five-year incidence of other complications compared to those in the Delay group, with the greatest difference observed for myocardial infarction, followed by heart failure and stroke.[21]

We know from literature that the first year after diagnosis is crucial for patients with type 2 diabetes, and new research shows that better control during that first year can reduce the future risk for complications, including kidney disease, eye disease, stroke, heart failure, and poor circulation to the limbs,[22] making it even more important to get tested regularly and early.

Pre-pandemic challenges compound the COVID-19-related delays in testing. A study found that the median delay in diagnosis from onset of diabetes mellitus was 2.4 years, and nearly 7 percent of incident cases remained undiagnosed for at least 7.5 years after onset of the disease.[23] When left unmanaged, diabetes, we know, can trigger a cascade of symptoms, ranging from mood changes to organ damage.[24]

Post pandemic challenges for laboratories

The introduction of vaccines is a welcome relief. Still, many industry players suggest it will not impact SARS-CoV-2 testing volumes in the near term, and the demand for COVID-19-related testing will continue through 2021 and potentially into 2022.[25] This means that the pressure on healthcare utilization will continue. New challenges of operating in a COVID-19 environment limit hospital efficiency and capacity, perhaps contributing further to a future backlog. Many hospitals do not believe they will be able to return to historical procedural throughput levels, even if demand increased to previous levels or higher.[26]

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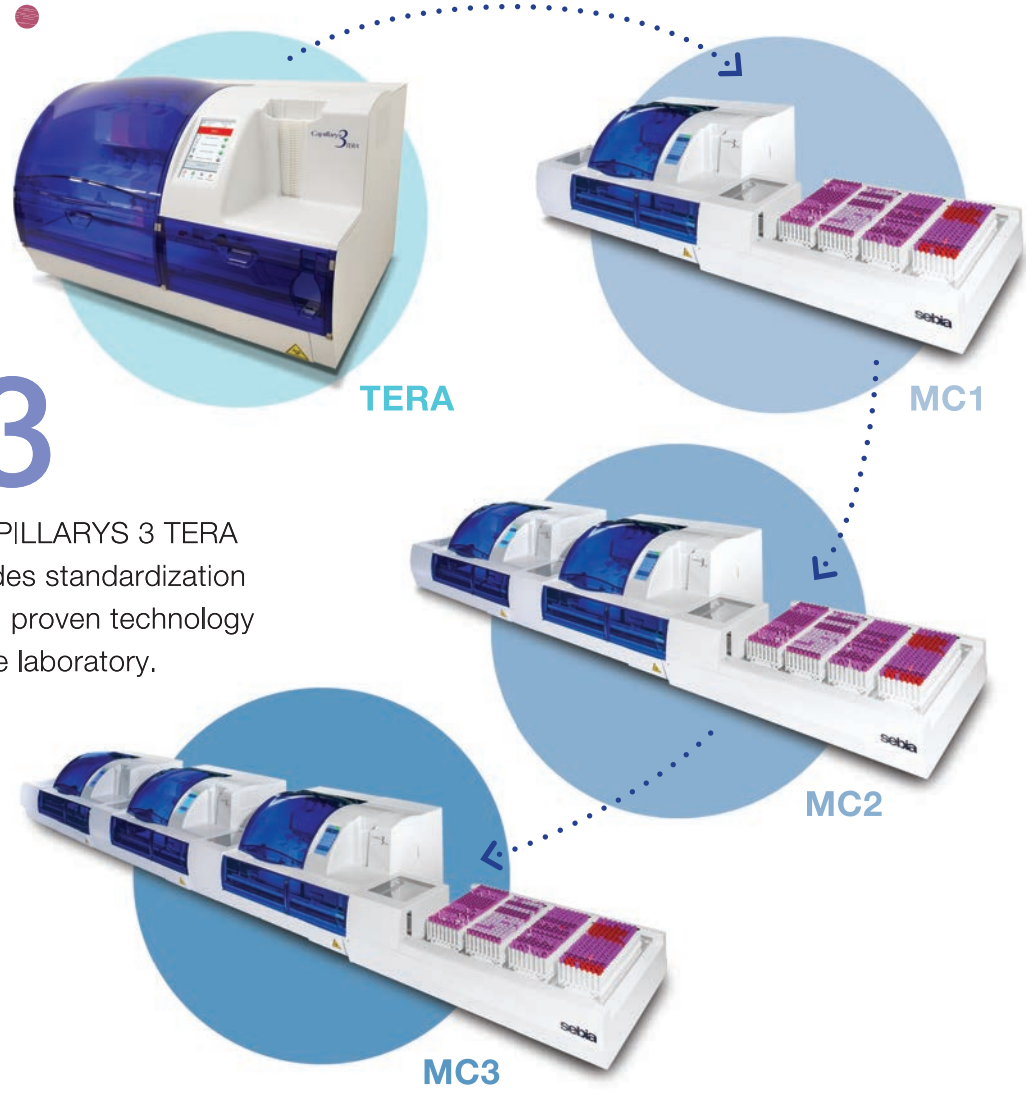

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It was estimated that employer healthcare costs in 2020 were 3.3-8.8 percent lower than originally expected due to the pandemic, as system capacity shifts and a fear of contracting the virus in medical settings continued to depress volumes. However, in 2021, costs are expected to rise by 0.5-5.0 percent above pre-pandemic projections, due to continued care for COVID-19 patients and delivery of previously deferred non-COVID-19 care.[27] Doctors predict a surge of new cancer cases post-pandemic due to delay in screenings forced by the pandemic;[28] this will posit true for diabetes patients and others who have chronic conditions.

Post-pandemic, an influx of testing will add pressure on laboratories, as those who put off annual checkups will need testing. Due to delays in preventive testing, conditions like prediabetes, that could have been managed if diagnosed early on, would turn into diabetes, and require even more frequent testing – an added burden on laboratories and caregivers.

As people get tested, diagnosed, and treated, a backlog in both the laboratories and doctor's offices is expected. A case study that looked at a backlog of patients waiting for surgery following the COVID-19 pandemic in the United Kingdom found that even if surgical capacity is doubled after a month of resuming normal service, it will still take more than six months to clear the backlog. This case study shows that every healthcare system around the world is going to have to make difficult decisions post-pandemic for balancing workforce and capital resources against the needs of the patients.[29]

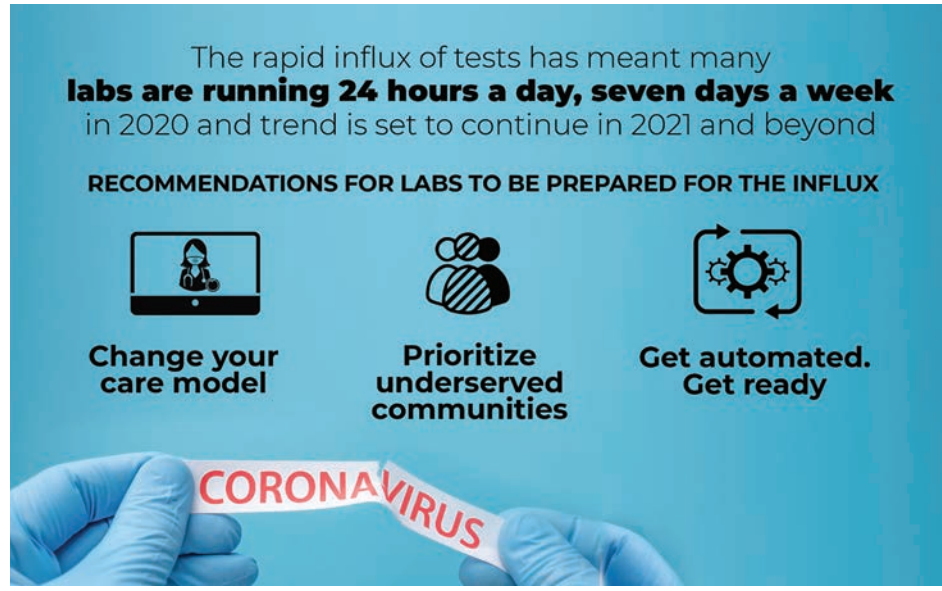

Photo courtesy of Beckman Coulter

Three ways labs can labs be strong enough

Nearly 216 million COVID-19 tests have been performed in the United States since the beginning of the pandemic.[30] The rapid influx of tests has meant many labs are running 24 hours a day, seven days a week, with the increased demand often leading to employee burnout.[31] This trend is set to continue in 2021 and beyond, due to COVID-19 as well as routine testing.

Laboratories are on the frontline of protecting everyone's health – during and after the pandemic. So, how can labs prepare for what's coming? Here are three recommendations:

- Change our care model. COVID-19 is forcing and will continue to force caregivers to look at new models of care, especially for chronic conditions. With an unprecedented and rapid transition to telehealth services across the country, many healthcare organizations have had to change how they approach prediabetes care. For Vidant Health in Greenville, NC, that has meant quickly shifting patients from an in-person National Diabetes Prevention Program (DPP) lifestyle-change program to a new virtual format – also known as distance learning, which is offered through the internet and telephonic conference – while adapting classes to meet changing priorities.[32] However, this new format does not change the need for laboratory testing. This is why laboratories must adhere to the CDC Laboratory Safety Guidelines to create an environment where people with diabetes and other high-risk conditions are comfortable getting tested – not putting off testing.
- Prioritize underserved communities. The impact of diabetes and COVID-19 is even more dire for African American, indigenous and people of color.[33] While vaccination campaigns begin globally, continued outreach is one of the best ways to educate at-risk populations. Laboratories can help their healthcare organizations leverage predictive and prescriptive analytics across their population to identify those with hidden and rising risk for diabetes and/or pre-diabetes for outreach. By assessing risk progression in the diabetes population, it is possible to get ahead of issues, before they become critical and costlier in the future.[34]
- Get automated. Get ready. As the pandemic rages and testing volumes increase, laboratories have an opportunity to deliver high-quality results more cost-effectively and efficiently with automation, which can help to address staff shortages, while enabling resources to focus on high value, clinical tasks. There is strong evidence that an efficient total lab automation model can successfully lower laboratory diagnostics costs, while decreasing congestion in laboratories and improving efficiency[35] – which is exactly what labs of all sizes will need after the pandemic to deal with the increase in testing volumes. In a laboratory, TAT is queen, and instrument downtime is the villain. Laboratories need to dust off the instruments and the backup instruments that may not have been in use during the pandemic, and ensure that they are in mint condition – with completed validation and quality control.

Conclusion

COVID-19 is forcing, and will continue to force, caregivers to look at new models of care, especially for chronic conditions, such as diabetes. Early on, healthcare utilization dropped substantially, but telemedicine use increased. In more recent months, in-person care has mostly rebounded; although, that trend could now reverse as the pandemic worsens across the country.[36] With this in mind, laboratories have an opportunity to overcome testing volume challenges and help people with diabetes by streamlining workflow, ensuring impactful outreach by identifying populations at risk and enabling a safe testing environment to sustain employees' and communities' wellness.

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Shamiram Feinglass, MD, MPH, is the Vice President, Global Government and Medical Affairs at **Beckman Coulter**. In this position, she leads Global Medical, Government, Reimbursement, and Clinical Affairs for Life Sciences and Diagnostics and drives talent diversity in every environment in which she works or leads. Feinglass was formerly the Vice President for Global Medical and Regulatory Affairs at Zimmer.

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TEST QUESTIONS

Circles must be filled in, or test will not be graded. Shade circles like this: ● Not like this: Ⓧ

1. **What percent of people killed by COVID-19 in Louisiana had a pre-existing condition?**
   - A. 40 percent
   - B. 25 percent
   - C. 60 percent
   - D. 97 percent

2. **Patients with diabetes and/or _____ had higher mortality rates and longer hospital stays.**
   - A. hypoglycemia
   - B. hyperglycemia
   - C. dementia
   - D. hypotension

3. **The New Orleans report revealed what percent of people who died from COVID-19 had diabetes?**
   - A. 40 percent
   - B. 25 percent
   - C. 60 percent
   - D. 97 percent

4. **COVID-19 has increased lab testing by nearly _____.**
   - A. double
   - B. 10 percent
   - C. 25 percent
   - D. 60 percent

5. **Release of stress hormones can cause _____ and _____ to increase.**
   - A. blood pressure, oxygen rate
   - B. blood pressure, blood sugar
   - C. blood sugar, oxygen rate
   - D. blood sugar, WBC rate

6. **_____ and _____ are known to make controlling diabetes more difficult.**
   - A. Fear of needles, anxiety
   - B. Sugar cravings, anxiety
   - C. Stress, sugar cravings
   - D. Stress, anxiety

7. **African American adults are _____ more likely than non-Hispanic white adults to have been diagnosed with diabetes.**
   - A. 60 percent
   - B. not
   - C. 25 percent
   - D. 39 percent

8. **Regular _____ testing is needed to control glucose levels and prevent diabetes complications.**
   - A. CBC
   - B. ferratin
   - C. ACE2
   - D. HbA1c

9. **Compared to non-Hispanic whites, African Americans were _____ as likely to die.**
   - A. not
   - B. twice
   - C. three times
   - D. half

10. **Racial disparities, _____ and _____ contribute to the risk of diabetes in the African American community.**
    - A. stress, malnutrition
    - B. lack of supplies, stress
    - C. insulin resistance, obesity
    - D. none of the above

11. **Due to systemic racism, inconsistent access to healthcare, working in essential fields, living in crowded housing and having existing chronic conditions, _____ are experiencing more serious illness from COVID-19.**
    - A. people of color
    - B. Caucasians
    - C. Asians
    - D. Hawaiians

12. **Poor diabetes control has been proven to negatively affect ____.**
    - A. mood
    - B. prognosis
    - C. blood pressure
    - D. stress

13. **African American and Hispanic people are more likely to experience _____.**
    - A. longer wait times
    - B. understaffed testing centers
    - C. lack of testing
    - D. all of the above

14. **Myocardial infarction, stroke and death from coronary heart disease are _____.**
    - A. not very common
    - B. called major adverse cardiac events (MACE)
    - C. impossible to predict
    - D. increasing the risk of hyperglycemia in COVID-19 patients

15. **By the end of June 2020, an estimated _____ of U.S. adults had delayed or avoided medical care.**
    - A. quarter
    - B. 41 percent
    - C. half
    - D. 63 percent

16. **Nearly 7.5 percent of cases remained undiagnosed for at least _____ after the onset of diabetes mellitus.**
    - A. 3.5 years
    - B. 7.5 years
    - C. 5.2 years
    - D. 6.1 years

17. **When left unmanaged, diabetes can trigger symptoms like _____ and _____.**
    - A. cancer, skin lesions
    - B. low blood pressure, asthma
    - C. mood changes, organ damage
    - D. none of the above

18. **Distance learning through _____ and _____ can help meet changing priorities.**
    - A. telephone, fax
    - B. internet, telephone
    - C. mail, telephone
    - D. fax, mail

19. **Laboratories can overcome testing volumes and help people by_____.**
    - A. streamlining workflow
    - B. enabling a safe testing environment
    - C. ensuring impactful outreach to at risk populations
    - D. all of the above

20. **Lab automation_____.**
    - A. is never going to happen
    - B. is expensive but worth it
    - C. lowers costs and congestion in labs
    - D. increases costs and congestion in labs

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St. Luke's University Health Network Laboratory Services – dedicated to patients

By Linda Wilson

The laboratory staff at St. Luke's University Health Network Laboratory Services

Judging the entries for M*edical Laboratory Observer's* Lab of the Year award is always a daunting job. This was particularly true this year, given the central role clinical labs have played in managing the COVID-19 pandemic.

As *MLO's* staff and judges reviewed every entry, we read many inspiring stories about how laboratorians worked diligently and courageously to ramp up COVID-19 testing while continuing to provide other diagnostic services.

But in the end, a winner emerged. *MLO's* 2021 Lab of the Year is St. Luke's University Health Network Laboratory Services.

Located in Bethlehem, PA, the 12-hospital system treats patients in 11 counties in Eastern Pennsylvania, including Allentown and Easton, and across the border in Warren County, NJ. With more than 16,000 employees, 270 outpatient locations and three nursing homes, the network is expanding, with plans to open an 80-bed hospital in Carbon County, PA, in 2021.

That expansion follows on the heels of another new hospital. In 2019, St. Luke's opened a 130,000-square-foot, three-story hospital in Orwigsburg, PA, in conjunction with Geisinger Health in Danville, PA. In a news release, the two organizations said that it was the first time in Pennsylvania's history that two health systems had come together to co-own and co-build a hospital.

At St. Luke's, Network Laboratory Services is an integral part of the health system's continued growth. Its 469 employees perform more than 5 million tests per year through 10 rapid response labs (which serve inpatient units and emergency departments), one core lab and one specialty lab. Patient specimens are collected at 50 patient service centers and a mobile phlebotomy program. In addition, 14 pathologists – with specialties including dermatopathology and neuropathology – analyze more than 60,000 specimens annually.

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Devonna Punter, Lab Aide

"We strive to provide results in an efficient and timely manner to every patient and provider accurately the first time, every time, through teamwork, professionalism, and a caring attitude," Jennifer Burrell, BS, Senior Network Director, Clinical and Ancillary Operations at St. Luke's, wrote in the nomination submission.

Customer service

That effort starts with customer service.

One example is a profitable mobile phlebotomy program, which the lab network staffs with 4.5 full-time equivalent (FTE) employees who draw blood samples in the comfort of patients' homes. Although it was launched in 2017, the program took off in May 2020, after lab directors removed a $25 service fee, allowing the number of patient accounts to grow by 2,600. The average number of visits increased from 3.2 visits per day to 18 visits per day. The payment per visit varied, depending on whether the account was self pay, commercial insurance or government program.

Jennifer Burrell, BS, Senior Network Director, Clinical and Ancillary Operations

After the outbreak of COVID-19, the lab assigned one phlebotomist to draw blood samples from patients who were COVID-19 positive or awaiting SARS-CoV-2 test results. This provided ease of access for patients dealing with COVID-19, as the lab did not want to "make someone who is sick travel," Burrell explained in an interview, pointing out that these patients might need tests to monitor chronic conditions or manage COVID-19 symptoms.

Another initiative – a central call center – is targeted at both patients and providers.

The network call center is staffed with 10 FTEs, which includes a supervisor, customer service representatives and technical support specialists. In 2020, the call center handled 55,427 incoming calls and placed 19,461 calls to patients and providers. The average time on hold was 19 seconds. More than 90 percent of the calls were answered without a delay (within 4 rings).

In addition to assisting customers, the call center also helps to monitor a lab-outreach quality-assurance program, and it is responsible for notifying the state and local health departments of test results related to mandatory reporting.

The key to the program's success is lab managers' commitment to training staff on how to answer callers' questions accurately and succinctly. "The clinical staff caring for the patient doesn't always have time for long, drawn out responses," Burrell explained in the nomination submission.

Call Center Supervisor Mary Ellen Burker, MLT, said that the call center staff has access to paper scripts and an electronic procedure catalog, which provides information on topics such as specimen collection, tube types, and fasting requirements. In addition, "We have two med techs available to help all team members with real-time answers to difficult clinical questions that may arise," she said.

Mary Ellen Burker, MLT (ASCP), Call Center Supervisor

In response to the pandemic, customer service in 2020 also included outreach to local colleges and nursing homes – both of which needed help with SARS-CoV-2 testing.

St. Luke's provided test collection kits to nine nursing homes (in addition to the three facilities that St. Luke's owns) and processed their tests, including those for surveillance, with an average turnaround time (TAT) of 24 hours.

St. Luke's also provided analyzers and reagents to five local colleges. Two of St. Luke's employees taught the on-campus clinic staff members how to perform multiplex testing for COVID-19, flu A/B and RSV. The health system's employees also provided ongoing management and oversight of the testing programs.

Productivity

As is the case in labs throughout the country, St. Luke's strives to improve productivity.

One project – the practice of alerting providers about critical values on lab tests – improved both customer service and productivity. "As you know, this can be an extremely time-consuming process for staff, but also extremely frustrating and dangerous when the ordering provider cannot be contacted," Burrell wrote in the nomination letter.

Lab managers worked with a team of physicians, nurses, information technology staff members, and telemedicine employees to craft a solution. They leveraged a HIPPA-compliant texting product, which allows the lab to notify providers of critical values through secure text messages. Once a provider acknowledges

Kelsey Elliott, Lab Aide

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Richard Matthews, CT (ASCP), MBA, Network Director of AP and the Specialty Lab

a text, the texting software interfaces with the electronic medical-records system to record the time stamp. "One campus is already using this model comfortably, and we intend to transition the rest of the labs this year," Burrell wrote.

Anatomical pathology (AP) also improved productivity in 2020. St. Luke's goal is for the AP staff and pathologists to prepare, read, and finalize 90 percent of specimens within 72 hours. By that definition, TAT was 14 percent in December 2019.

To improve productivity, the managers with input from pathologists used fishbone diagrams to analyze the histology process. They realized that the task of embedding samples, or hardening them in a fixative, was a bottleneck in the process. This happened, because staff was handling embedding in addition to other duties. "No one was actually assigned to the embedding stations for an entire shift," Burrell explained.

> "The laboratory was so short staffed in January that we were sending out a substantial amount of pathology work to be processed by a local reference laboratory in order to maintain TAT," —Richard Matthews

Other pieces of histology operations – accessioning, grossing and microtomy – showed similar issues.

The bottom line: Not enough staff to meet TAT goals. "The laboratory was so short staffed in January that we were sending out a substantial amount of pathology work to be processed by a local reference laboratory in order to maintain TAT," explained Richard Matthews, CT (ASCP), MBA, Network Director of AP and the specialty lab.

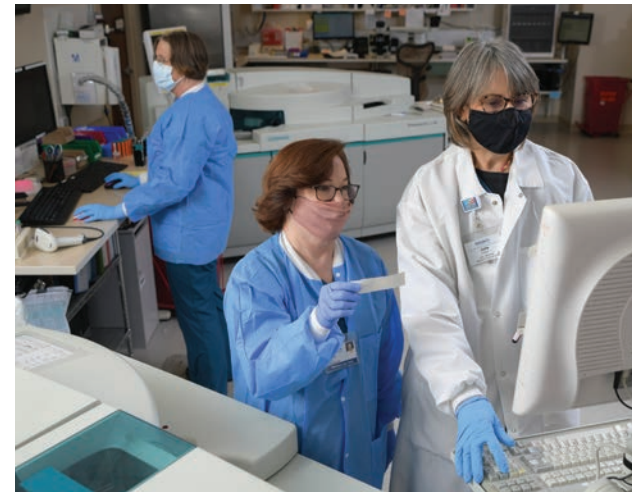
To solve the problem, St. Luke's added additional staff to each area, growing the FTE count from 43 in January 2020 to 56.75 in December 2020.

As a result of these efforts, St. Luke's was able to meet TAT expectations 94.3 percent of the time by October 2020. The TAT improvement occurred despite increases in surgical volume, which rose from 5,236 cases in January 2020 to 5,802 cases in October 2020.

The blood bank also logged productivity improvements. It implemented a test to detect bacterial contamination in platelets, extending expiration dates on units of platelets. With the implementation of Verax testing in 2018, the number of wasted platelet units dropped by 35 percent to under 5 percent, averaging 2.5 percent in FY19 and 2.9 percent in FY20. The lab also saved $110,000 by wasting fewer platelet units between 2018 and 2020.

Teamwork

Teamwork at St. Luke's was tested in 2020, as the lab staff worked to manage the workload, despite job-sharing arrangements and the ever-present national shortage of medical technologists.



Julia Kester, MT, Judy Stern, MLT and Dani Roy, Technical Coordinator

"We have had to rely on out-of-the-box thinking to staff our departments, and the team has pulled together to, not only cover their own departments, but help cover other campuses," Burrell said. There are many anecdotal examples, such as:

- A microbiology technical coordinator with previous experience in histology who put in extra time to prepare quality control slides.
- A histology supervisor who spent weeks embedding specimens, so her team could focus on microtomy.
- Lab managers who supervised multiple rapid-response labs, because St. Luke's was not able to hire enough qualified managers.
- POCT coordinators who filled in as medical technologists working at lab-testing stations.

Education and training

St. Luke's is combatting national shortages in lab personnel by developing education programs internally.

For example, the lab outreach team is designing a new phlebotomy training program. "During this past year, we have found it more and more difficult to recruit good phlebotomists. We decided that training our own is a better solution than

Deborah Samuels, MLT

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using a staffing agency," Burrell said in the nomination submission.

The goal is to launch an accredited phlebotomy training program that is standalone; meaning, it is not connected to a college or technical school, in the second half of 2021.

Lucille Hough, MT (ASCP), MHA, Network Director of Clinical Pathology

The idea was modeled after a similar approach in histology; although, St. Luke's works with an accredited college in that case. "We help lab aides or other hospital employees gain valuable knowledge and expertise in histology," Burrell said, noting that the lab network has hired six employees from this program over the last three years.

In 2020, the lab network launched two paid-internship programs: one for microbiology and a second for medical laboratory science. For microbiology, the internship is generally offered to a lab aide with a college degree who expresses interest in the field. Meanwhile, anyone with a college degree in one of the life sciences and who meets CLIA requirements, can apply for an internship in medical laboratory science.

Cathy Janny, MT

Laboratory Inspections

Over the last several years, St. Luke's has developed a quality team comprised of project managers and medical technologists who perform scheduled mock inspections and audit compliance with policies and procedures. The lab also has standardized document control. Based on the results of this work, the lab develops performance improvement initiatives to address identified deficiencies. In addition, each inspection outcome is debriefed during manager-level meetings, so recommendations for improvement can be implemented throughout all labs in the network.

St. Luke's Network Laboratory Services has a combination of both CAP and Joint Commission accreditation. In 2018 and 2019, all of St. Luke's laboratories had been inspected. St. Luke's now is working with the accrediting agencies on planning and scheduling inspections.

"This has been challenging since restrictions still exist. Depending on the inspection team, we will be having a combination of virtual and on-site inspections," Lucille Hough, MT (ASCP), MHA, Network Director of Clinical Pathology, said.

Strategic Outlook

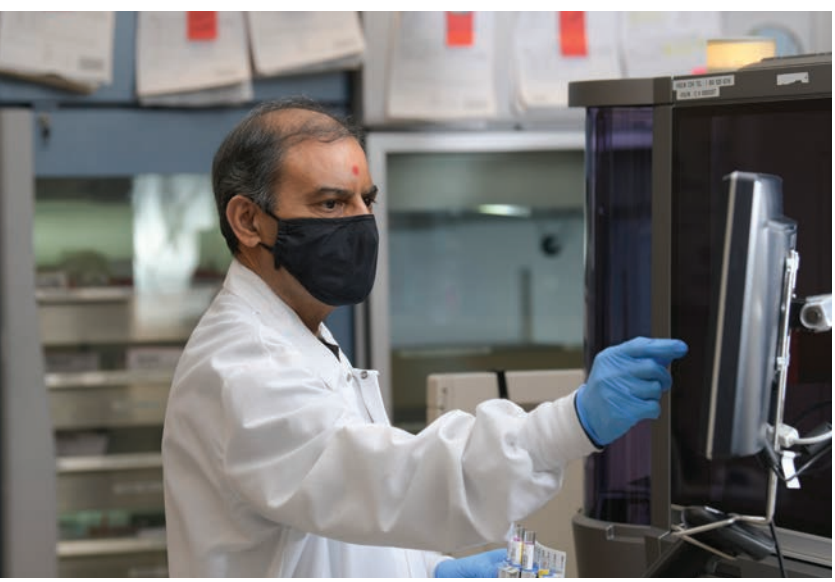
The lab network also develops strategic plans, allowing it to continue improving the work it does.

The core laboratory has seen a major increase in outpatient testing volumes, and this has had an impact on TAT for inpatient specimens at St. Luke's University campus. To improve productivity, the health system plans to move the core lab to the same location as the specialty and AP labs. This would allow the couriers to make fewer stops, saving time. The lab network also plans to create its own courier system that it will not share with other departments at the health system.

In addition, the network lab plans to standardize equipment in its rapid response labs. This includes new chemistry equipment and additional analyzers for procalcitonin. In the specialty lab, St. Luke's also plans to bring in house flow cytometry and direct immunofluorescence – services that are now sent to reference labs.

In addition to improving existing services, the lab managers also plan new services. For example, they plan to launch a direct-to-consumer testing program; although, a definitive date has not been set yet. The service would allow consumers to order and pay out-of-pocket for a test online, then go to a patient service center to have their specimens drawn. They would not need to see a provider for a lab order because a medical director will oversee this program, which will include about 30 different panels, ranging from sports performance to women's health.

"Our network is all about patient access. Anything we can do to get patients to invest in their health we will do," Burrell said. "Life is so busy, so it so important to offer convenience."



Dilip Sheth, MT

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2021 Lab of the Year Runner Up: U.S. Air Force School of Aerospace Medicine's Epidemiology Laboratory

By Linda Wilson

Located at Wright Patterson Air Force Base, OH, the U.S. Air Force School of Aerospace Medicine's (USAFSAM) Epidemiology Laboratory (Epi Lab) is the sole reference lab for the U.S. Air Force.

That means the lab's staff does a lot of testing: 2 million tests per year through a menu of 130 assays. In addition to reference lab duties, the Epi Lab also provides infectious disease testing, which includes both SARS-CoV-2 and HIV testing.

Customer service

The laboratory's customer service endeavors in 2020 often focused on the pandemic, completing 13 percent of the Department of Defense's (DOD) SARS-CoV-2 polymerase chain reaction (PCR) tests. Up through the COVID-19 surge over the summer, Epi Lab completed 34 percent of the department's tests.

To meet that demand, the lab's turnaround time (TAT) for SARS-CoV-2 PCR tests averaged 16 hours, which far exceeded its initial goal of 48 hours. The only exception occurred during a single week in July, when a surge in demand corresponded with supply shortages.

Epi Lab took many steps to achieve that TAT. For example, it validated 11 different viral/universal transport media and seven specimen types. The lab also acquired bulk quantities of standardized phosphate buffered saline (PBS) and transport tubes. Using those supplies, the lab's staff made more than 30,000 aliquots of PBS and shipped them throughout the DOD's healthcare system.

Productivity

To keep up with testing demand for SARS-CoV-2 and all other diagnostic assays, Epi Lab has a vast array of analyzers, which it is continually upgrading to increase productivity. For example, the instruments used for immunodiagnostic testing were upgraded, allowing the lab to return results to providers 66 percent faster.

Teamwork

The pandemic taxed Epi Lab's ability to maintain its non-COVID-19 testing services, and it put 25 percent of the test menu (lower volume tests) on hold from the end of May until September.

To resume all testing services, the lab hired staff, growing from 90 employees working on two shifts to 126 employees working on three shifts. The lab also shifted to a 24/7 operation, with active-duty staff covering evenings and nights on 12-hour shifts.

Epi Lab not only added staff, but also trained 15 techs from microbiology and immunology in molecular processes.

As a result of the efforts in teamwork, productivity and other areas, the staff won many awards. The lab was named the U.S. Air Force School of Aerospace Medicine's Collaboration Team of the Second Quarter, the Public Health Collaboration Team of the Year, and the Biomedical Services Team of the Year for the 711th Human Performance Wing. In addition, 47 team members were awarded the Air Force Achievement Medal and 62 were awarded the Armed Forces Service Medal.

Education and training

To keep up with continuing education, Epi Lab's managers hosted 26 webinars in conference rooms where staff could practice social distancing. If available, electronic links were also sent out, so staff members could sign in using a computer or mobile device.

Strategic outlook

One focus of Epi Lab's strategic planning process involves bringing tests routinely sent to civilian reference labs back in to the military system.

In 2021, Epi Lab plans to add carbohydrate deficiency transferase (CDT) testing to its in-house roster, saving a projected $9 million dollars annually on 629,000 samples. In addition, Epi Lab plans to shift HbA1c testing from an immunoassay to an electrophoretic assay. This change will allow Epi Lab to provide information about hemoglobin variants to providers and patients.

A second focus of Epi Lab's strategic planning is to move from manual to automated testing processes. For example, the lab plans to update Lyme disease testing a using a two-tier testing algorithm from the CDC. The updated algorithm utilizes an enzyme immunoassay in place of the western immunoblot assay. The lab has also ordered a new analyzer to automate the 11,000 thousand rapid plasmin reagin (RPR) tests it performs each year.

Lab inspections

The laboratory is accredited by the College of American Pathologists and the Clinical Laboratory Improvement Program (CLIP is the Military equivalent of CLIA). To prepare for its next inspection in 2021, the lab completed 135 proficiency testing surveys in 2020, maintaining a 99 percent average.

In 2019, CAP inspected the lab, and only noted one deficiency. "This is an amazing accomplishment for the lab, considering the large turnover in military staff that takes place," said Peter Wasik, Maj., USAF, BSC, Branch Chief for Microbiology at Epi Lab.

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GROW ON PANTHER

The role of intestinal inflammation in *Clostridioides difficile* disease

David M. Lyerly, PhD, Chief Science Officer, TECHLAB, and Jodie Y. Lee, MS, MBA, Marketing Manager, TECHLAB

In 2019, there were more than 250,000 cases of *Clostridioides difficile* infection (CDI) in the United States, possibly as many as 500,000, resulting in the death of up to 30,000 patients. Healthcare costs were well in excess of a billion dollars. Figures in Europe were staggering as well, and the numbers of cases of CDI reported elsewhere around the world increased. CDI leapfrogged over Methicillin-resistant (MRSA) infections years ago as the most common hospital-acquired infection (HAI) in the United States.

C. difficile is a prototypical opportunistic pathogen

C. difficile is very opportunistic. It is capable of taking advantage of a weakened intestinal microbiota, and it forms very hardy endospores. Consequently, CDI's continuing presence at the top of the HAI list is no surprise. A single CDI patient sheds millions of endospores daily. Endospores are spread in healthcare facilities even when mitigation efforts are in place. Unfortunately, the endospores are often shed where there is a highly susceptible population, such as hospitalized patients who have a weakened microbiota, because they are receiving antibiotics. Endospores enter patients via the fecal-oral route, survive stomach acid, and arrive in the anaerobic environment of the colon where they germinate. In the absence of a diverse healthy microbiota, *C. difficile* can grow to high numbers. Under these conditions, this pathogenic anaerobe produces deadly toxins A and B that damage the gut mucosa and trigger inflammation.

Our healthy microbiota does an amazing job keeping this pathogen in check, making it difficult to detect *C. difficile* in healthy adults. Infants, however, are a different story. More than 50 percent of infants carry *C. difficile* as part of their normal flora, until their "adult" flora develops between 1 and 2 years of age. Why infants have this protection remains a mystery; although, the lack of suitable cellular toxin receptors may be part of the reason. Many patients become carriers of *C. difficile*, probably because they are exposed to high numbers of endospores while hospitalized and immunocompromised. Carriers in hospitals tend to outnumber true cases of CDI. As a result, it can be difficult to distinguish *C. difficile* carriers from patients with CDI. Algorithms (e.g., GDH plus toxin, NAAT plus toxin) improve diagnostic accuracy and reduce inappropriate treatment of carriers.

In some patients, CDI is mild, and the disease resolves when an inciting antibiotic is discontinued. Occasionally, patients may have a norovirus or Campylobacter infection, with *C. difficile* simply being a bystander organism. Infectious diseases are also not the only cause of diarrhea, particularly in hospital settings. In these situations, *C. difficile* may be blamed for diarrhea with an entirely different etiology. Although efforts should be made to minimize inappropriate treatment of carriers, at the same time, it is critical that patients be accurately diagnosed and treated, because CDI can rapidly progress to colitis and become life-threatening. Up to 25 percent of CDI patients will relapse with recurrent CDI, because the endospores are not killed by the antibiotics used to treat CDI and will linger in the patient. Recurrence can occur multiple times weeks or months apart, each time causing further deterioration of the patient's health.

Inflammation is a hallmark of CDI

Higher levels of inflammation in CDI are associated with increasingly severe disease. Pseudomembranous colitis (PMC), the severe stage of CDI, is an acute inflammation of the colon with pseudomembranes comprised of necrotic debris and inflammatory cells. Pseudomembranes in the large intestine are clinically diagnostic. Fortunately, with today's improved laboratory tests and increased awareness of CDI, most patients do not progress to this stage. Peripheral white blood cells (WBC) counts have been used for many years to monitor severity. Counts >15,000 per mm^3 signal severe CDI.[1] Elevated white cell counts are included as an indicator in the Hines VA Severity Score, an often-used assessment based on fever, ileus, hypotension, white blood cell count, and thickening/dilation of the colonic wall.[2]

More recently, fecal lactoferrin, an 80 kDA glycoprotein released from secondary granules during degranulation and lysis of fecal leukocytes, has been used to assess inflammation and severity. Fecal lactoferrin is highly stable in feces, can be measured qualitatively and quantitatively, and serves as an accurate biomarker for direct assessment of intestinal inflammation.

Numerous studies have evaluated fecal lactoferrin, peripheral WBC counts, and stool toxin as biomarkers in patients with CDI, and all continue to illustrate the important role of inflammation in CDI. In one study, the correlation of these biomarkers with clinical assessment of severe CDI was examined in patients infected with ribotype 027.[3] Ribotype 027 is notorious for causing severe disease. It is a fluoroquinolone-resistant 027 variant that appeared in the early 2000s, causing severe outbreaks in Europe, Canada, and the United States. In some outbreaks, the mortality rates more than doubled in patients with 027-associated CDI. Fortunately, the incidence of 027 infections is decreasing in the United States and in Europe, and this ribotype is not prevalent in Asia. Treatment for an 027 infection is not different from non-027 CDI.

In the 027-based study above, fecal lactoferrin levels >900 µg/g feces were observed in 027-infected patients, highly elevated above the lactoferrin baseline of 7 µg/g. Peripheral WBC counts in this group of patients approached 19,000 per mm^3. Patients with moderate CDI had mean fecal lactoferrin levels of 292 µg/g, with mean WBC counts of 13,000 per mm^3. Patients with mild CDI had mean fecal lactoferrin levels of 73 µg/g and normal WBC counts of about 9,000 per mm^3.

Another study also assessed 027-infected patients; in this case, patients were admitted to hospitals from long-term care facilities.[4] The study similarly showed that 027-infected patients had higher fecal lactoferrin and peripheral WBC counts than non-027-infected patients, and that higher responses with either fecal lactoferrin or peripheral counts correlated with higher mortality rates. Although not focused on ribotype 027, additional studies have demonstrated the correlation of toxin levels with elevated fecal lactoferrin, elevated peripheral WBC counts, and inflammation.[5,6]

There is supporting evidence that inflammation, determined by elevated fecal lactoferrin or peripheral WBC counts, rather than fecal bacterial burden, correlates with severity.[7] This is noteworthy, because it suggests that sustained host inflammatory

responses are involved in patients who suffer from prolonged CDI. Further, there is the possibility that prolonged inflammation may be predictive of patients at-risk for relapsing CDI.

Inflammasomes and cytokines play a role in CDI

Inflammasomes are complexes comprised of multiple proteins that become activated and undergo oligomerization. They are associated with inflammatory responses in chronic diseases (e.g., diabetes or inflammatory bowel disease) and infectious diseases (e.g., respiratory diseases, such as COVID, and intestinal infections). There are different types of inflammasomes, depending on which proteins are activated to start the process towards complex oligomerization. In CDI, inflammasome formation appears to be triggered following toxin-mediated cellular damage. The formation of inflammasomes results in activation of caspase 1, with subsequent activation of pro-inflammatory cytokines, such as IL-1β, according to results seen in mouse models of CDI. There possibly are other mechanisms of inflammation, one being pyroptotic cell death defined by cellular death via an inflammatory pathway.

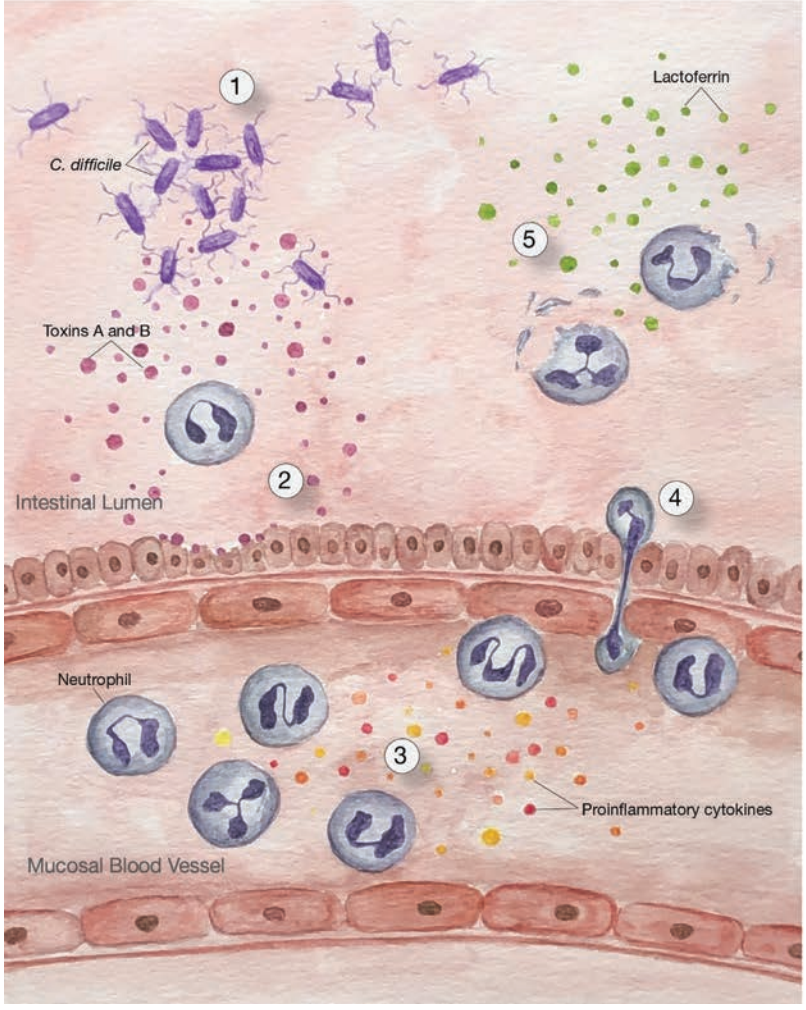
The involvement of inflammasomes in CDI likely serves as an initiating step, based on studies showing that proinflammatory cytokines activated through inflammasomes are upregulated in patients with CDI.[8-10] Higher levels of innate host response interleukins in CDI patients are associated with poor prognosis, another signal for inflammation involvement.[9] Because inflammasomes are an innate host defense mechanism, cellular signaling appears to be instrumental in determining which interleukins participate in this defense mechanism.

Toxins A and B are key to disease. They not only directly cause tissue damage; they are inflammatory triggers. Both toxins are glucosyltransferases, and this unusual enzymatic activity inactivates G proteins, leading to cell death. When their glucosyltransferase activity is shut down, upregulation of pro-inflammatory cytokines does not occur, strongly supporting the important role of toxin-initiated events. Additional evidence for toxin involvement is provided by *in vitro* results, showing that treatment of peripheral blood mononuclear cells with toxin leads to responses that are characteristic of inflammasome formation and stimulation of cytokine expression.

Understanding the roles of different cytokines that become activated through this series of events is challenging, but inflammasome-activated secretion of IL-1 seems to be an important first step. The production of IL-1 results in the subsequent production of IL-23, an inflammatory cytokine that signals the involvement of other cytokines.[11] Mouse models show that when IL-23 is controlled, CDI is less severe. Looking at the results to-date collectively, this very complex signaling of the inflammatory cascade is instrumental in the upregulation of multiple pro-inflammatory cytokines.

Inflammation plays an important role in CDI

The onset of inflammation in CDI is illustrated in **Figure 1**. When inflammation is elevated, as determined by clinical assessment,



Inflammation during CDI

1. Infection with toxigenic *C. difficile* and release of toxins A and B.
2. Toxins damage mucosal cells, triggering an influx of neutrophils. Toxins are chemotactic, bringing in more neutrophils that activate inflammasomes.
3. Activated neutrophils express increased levels of granule proteins such as lactoferrin. Proinflammatory cytokines are released.
4. Cells undergo diapedesis and enter intestinal lumen.
5. Neutrophils lyse in and release lactoferrin and other granule proteins.

Artwork by Lily Zhu

peripheral WBC counts, fecal lactoferrin, or a combination of these, CDI becomes more severe, and the patient's condition worsens. One episode of CDI is bad enough, but when complicated by multiple relapses exacerbated by inflammation, the patient's health deteriorates rapidly. Progress is being made in understanding the role of inflammation in CDI and how this process might provide competitive advantages for the organism. For example, inflammation may increase the availability of nutrients to *C. difficile,* while suppressing the competing microbiota.[12]

New findings will lead to a more complete understanding of how inflammation is triggered in CDI. Inflammasomes and pro-inflammatory cytokines are involved following complex cellular signaling, indicating that inflammatory cascades are key to this understanding. Hopefully, controlling the inflammation will reduce severity, lower rates of recurrent episodes, and lead to new strategies to treat this disease.

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David M. Lyerly, PhD, is a Co-Founder and serves as Chief Science Officer for **TECHLAB**, Blacksburg, VA, which manufactures a variety of in vitro diagnostic tests for enteric diseases.

Jodie Y. Lee, MS, MBA, serves as Marketing Manager for **TECHLAB**. She has spent 16 years in the life science and diagnostic industries.

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Best practices in proficiency testing documentation

By Mike Argall, MT (ASCP), BS

Passing a laboratory inspection is no easy feat. In preparing for a laboratory inspection, documentation is key. Documentation practices are often the backbone to an effective quality assurance (QA) plan. Laboratories often have standard operating procedures categorized in special document-control software to track the life cycle of the document, including reviewing, updating, printing, and eventually archiving. The same level of detail should also be used to document the proficiency testing (PT) process for the laboratory.

Proficiency testing, as defined by ISO 17043, is an evaluation of a participant's performance against pre-established criteria by means of inter-laboratory comparisons.[1]

Documentation of proficiency testing results is often overlooked. With a little investment, a well thought out and controlled process can create great efficiency and help you and your team pass your next laboratory inspection. This documentation doesn't just start and end with a signature on a final evaluation report. If we consider the PT process to be a cycle of events consisting of an enrollment, shipment, analysis, submission, report, review, and follow-up, a simple set of tools can be created to accurately document the entire process. Developing such tools includes having a clearly documented set of workflows, procedures, and checklists to help keep everyone in the lab equally informed and empowered throughout the enrollment, pre-analytic and post-analytic components of the proficiency testing process.

A simple set of tools can be created to accurately document the entire proficiency testing process

Enrollment

When preparing documentation for the enrollment component of proficiency testing, start by reviewing CLIA policy, as provided below:

CLIA 493.801(a) A laboratory must notify HHS of the approved program or programs in which it chooses to participate to meet proficiency testing requirements of this subpart, and the laboratory must designate a program to be used for each specialty, subspecialty, and analyte.[2]

This requirement can become especially complex, because there are some analytes that can appear in multiple programs with just one provider. This becomes infinitely more complex when you consider the number of providers available. Your workflow should include an identification of the analytes currently on your test menu, along with the designated proficiency testing provider and program name.

If there is more than one provider or program, make sure these are designated on a document for this workflow. All providers and programs with which your facility participates should be available and transparent to every individual performing the testing. Proficiency testing samples do not come with labels designating where they should be tested, so it becomes increasingly easy to assay and report the samples on the wrong instrument, leading to a potential failure. Save any confirmation documents from the proficiency testing provider, as laboratories may need to provide proof of enrollment if an accrediting agency has any question about your test menu. More importantly, review your menu every year as part of the enrollment process. The regulatory process can become very complicated if a lab manager realizes they failed to submit the enrollment form.

Most PT providers will include a list of scheduled dates for each shipment. Make a note as part of your workflow. A posted calendar in the lab with the dates outlined is one way to do this. Another idea is to create a PT checklist that shows everyone what date materials should arrive.

Pre-analytic

Once you have completed the enrollment process, shift your workflow to the actual events. A workflow should be designed with an eye toward the report review process. Try creating a checklist by working through an example scenario in which a failure appeared on a report. Then, determine what you would want to know in this simulated case. Think of the questions that would need to be answered at that time. When was the sample received? What was the condition of the sample at the time of receipt? How was it stored? Who performed the testing? Consider including a spot on the checklist for when the last time maintenance (scheduled or unscheduled) was performed on the instrument.

Incorporate information on the PT provider in the workflow and encourage staff to follow up with the provider if there are any package, sample, or analysis issues. Including the account

information and the phone numbers for the PT providers involved in the testing gives staff members the information they need to facilitate the replacement of samples or get answers to questions as they arise during the event. This could save time for the lab and potential non-participation failures.

Have a spot in the workflow document to indicate if the sample required any special pre-treatment prior to analysis that was beyond what would be done for a patient.

Post-analytic

Create a post-analytical part of your workflow and document any information required for submitting results, including fax numbers or web portals necessary to complete data submission. Build in time for a review of all submitted data to ensure every analyte includes a result. Include steps for the attestation signatures by the analyst and director or director designee. Take time to analyze the results, comments, and narratives that the PT provider includes with the report. Check that your instrument, method, reagent, and reporting units match what the PT provider has currently listed on your account. Be sure to include copies of the instrument printouts with the documentation. Highlight failures and ungraded results, and investigate each situation using a standard QA process. Consider adding failed PT events to an adverse event follow-up process. The workflow document should end with the evaluation report review process.

Using a checklist that includes multiple components to promote review by all staff will make the PT process more transparent to everyone in the laboratory. In turn, a more transparent process will facilitate a smooth on-site inspection, allow a laboratory to track participation, and create a standard way of reviewing the evaluation reports. If you use a checklist, add the titles of all the people who need to review and sign the report prior to filing. If a failure includes follow-up at a staff meeting, consider saving the meeting minutes as part of the documentation.

Include a step to review patient data from the same day and add the PT sample analysis to serve as part of the corrective action in the workflow document. Have the checklist follow the samples, results, and eventually, the evaluation report. Build in pre-analytic, analytic, post-analytic, and report follow-up sections. Cover just the basics to make the checklist is quick and easy to follow. Use "yes/no" answers for each checklist item. Detailed quality-assurance information should be assessed only after the evaluation report has been reviewed, as the return on this investment of time becomes minimal if the report has no failures or ungraded results. Incorporate this checklist into your document control system and include references to any applicable proficiency testing procedures your lab might have.

Building a robust documentation process is an important way to prepare for laboratory inspections. When staff members have developed a system to document and communicate practices and procedures, labs are better equipped to handle an inspection at any time of the year. The proficiency testing process can be a very stressful experience generally for technical supervisors, bench staff, and managers. Having clearly understood workflows, procedures, and checklists can help alleviate some of this stress. Creating a transparent documentation procedure allows all members of your team to become involved in the proficiency testing process and creates a series of checks and balances. Furthermore, having staff equally informed and engaged in the documentation procedure helps keep everyone in the lab equally empowered throughout the enrollment, pre-analytic and post-analytic components of the PT process. Empowering lab staff means that lab managers are giving their staff members everything they need to have a successful inspection.

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Mike Argall, MT (ASCP), BS, serves as Technical Supervisor for WSLH Proficiency Testing, a provider of proficiency testing programs and continuing education courses. He has worked in clinical laboratory science for 20 years, including 14 years in proficiency testing.

STATE OF THE INDUSTRY

Best practices while surviving COVID-19 chaos in the lab

by Marisa L. Williams

In our second "State of the Industry" survey topic for 2021, *Medical Laboratory Observer* (MLO) chose to refocus on questions about Best Practices in the clinical lab. With the COVID-19 pandemic influencing the industry, we questioned whether those practices had changed after one year into the pandemic.

Laboratory professionals have had to adjust their best practices to keep up with the changing needs of the pandemic by implementing new workflows and policies, adding new equipment and training to keep quality control in check and revenue flowing. We asked labs how they were dealing with hurdles caused by the pandemic, comparing that data to our Best Practices State of the Industry report from April of 2020, which was sent out in March, just as the pandemic was creeping in, slowing enveloping the world's laboratories.

How lab directors best maneuver through the unforeseen, while keeping up with the latest products on the market, implementing new training, and all the unexpected challenges of a worldwide crisis is not easy, but here's insight to keep the lab running optimally. This may include launching a tracking program, opening a new lab, or policy changes, all while keeping up with quality care issues and trying to stay within a reasonable budget.

RUNNING OUT OF ESSENTIALS

Supply chain issues plagued many labs during the pandemic, and some responded differently than others, with 64% using multiple testing platforms, 57% working with state public health officials to gain access to needed testing supplies, and 45% implementing standing orders for crucial supplies.

Survey responders indicated that 24% of their facilities switched to reusable types of personal protective equipment (PPE), and 20% revamped their product evaluation process, with some paying extreme prices to secure products, using multiple suppliers, doing daily inventory updates system-wide, and using additional areas to store supplies to prevent running out. Others switched brands of products or vendors used, sent specimens out to multiple reference laboratories, and started the ordering process sooner on all items to give an additional couple weeks of lead time.

With supply shortages across the globe, labs had to take extra steps to improve inventory control and supply costs. Nearly 70% evaluated inventory levels for basic supplies, with 45% working with supply chain management for group purchasing organization contracts that offer savings (down from a whopping 73% last year), and 32% used supply tracking and record keeping. Only 9% implemented lease agreements that do

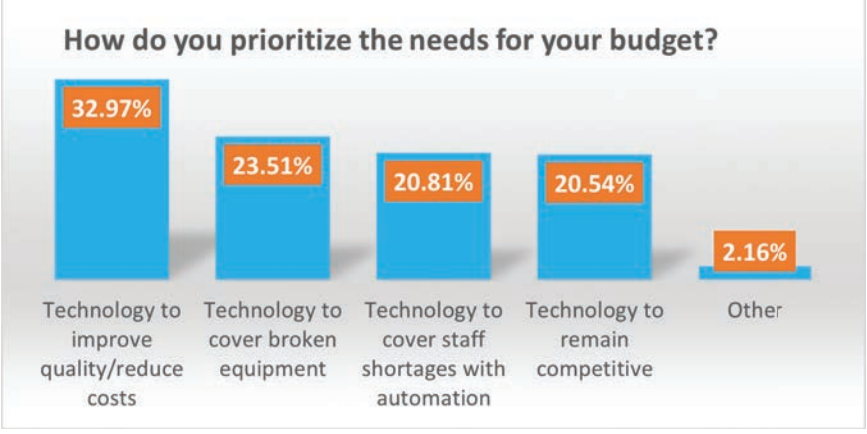

Table 1 displays technology needs and how labs have prioritized their budget.

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501Y.V2	South Africa (Oct 2020)	**B.1.351**
501Y.V3	Brazil (Dec 2020)	**P.1**
484K.V3	Multiple (Dec 2020)	**B.1.525**
452R.V1	USA (Nov 2020)	**B.1.429**

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not include volume commitments, down from 21% last year, while 10% got access to electronic inventory tracking from materials management, 13% did vendor-managed ordering, and 22% developed an ongoing review, comparing supply reports to invoices.

Last year, lab professionals also streamlined their contracting processes, as 52% said they developed good relationships with supplier support personnel, so they have access to training and product optimization suggestions. Another 51% adopted ongoing reviews of reference lab costs and contracts.

Walter Valliere, ScD, of Vizient Advisory Solutions, works in analytical labs in biotech, biopharma, research, and those labs serving healthcare, both hospital-based and independent. He analyzed things he could routinely make versus buy and stopped reagent rental agreements to help with supply chain issues; additionally, he implemented new rules to improve efficiency at his facility: no physician-specific test profiles, no standing orders, and no exceptions.

IMPROVING QUALITY

Striving to continually improve both quality and customer experience, lab workers have taken steps to improve the quality and efficiency of testing, as 65% of survey respondents standardized their test ordering procedures and formularies, 31% programmed hard stops or other functionality in their electronic health records, 23% implemented a pre-approval program for send-out tests, 21% automated manual processes in the pre-analytic phase of testing, but only 7% purchased additional centrifuges to reduce bottlenecks in testing workflows.

To improve the quality of testing last year, 72% said they had standardized ordering procedures to ensure that physicians and other providers order tests correctly, while 23.7% implemented a preapproval program for tests that are sent out, and 27.1% developed evidenced-based test ordering practices.

"Quality is also about the smart use of technology. In recent years, health systems and hospitals have implemented 'test utilization' programs to identify patterns in lab ordering," explained Lee Hilborne, MD, MPH, Senior Corporate Medical Director, Quest Diagnostics. "However, many hospitals use time-consuming manual uploads of data or platforms that cannot pull from disparate enterprise systems."

Quest introduced a lab stewardship service in 2019 that uses behind-the-scenes technology layered over a health system's existing LIS and other technologies. The data is shared with doctors and healthcare leaders, so they may compare their practice with medical guidelines, discouraging the use of lower-value or less-proven tests.

"Fundamentally, this helps physicians order the right test for the right patient at the right time. It provides practice feedback regarding situations where tests are inappropriately repeated and improves transparency, providing better patient care. By improving technology and data management, our laboratory pathologists and other laboratory professionals can more easily anticipate needs and help their medical colleagues deliver better care," said Hilborne.

ADDING TESTING CAPACITY

Last year's top budget priority was technology to remain competitive at 33%, compared with 21% this year. A close second last year, at 32%, was technology to cover broken equipment, which also dropped this year to 24%.

Having so many new analyzers, and software tools, 66% of labs have analyzed workflow processes for proper space planning, which was 70% last year; 54% say they are involving IT early in the process of getting new automation tools, last year was 49%; and 30% have designated a project manager to coordinate planning and implementation with the vendor in getting these new products, with last year being 25%.

"As the pandemic spread, we realized we would need to expand our testing capacity to meet the needs of our patients and clinicians, but also to ensure we would have the capacity due to supply chain challenges," shared Steven R. McLaren, DO, Assistant Regional Medical Director for the Lab Care Delivery System of Southern California Kaiser Permanente Medical System. Within 70 days, Kaiser Permanente created a COVID-19 lab for all its markets, housing eight Amplitude systems, each capable of 5,000 tests a day, from Thermo Fisher Scientific. They installed a Roche 8800 and 3 Hologic Panthers.

"We also opened up our specimen types to include saliva as well as swab samples. The learning curve with the Amplitudes was steep, and our TAT suffered because of it. It was complicated by the fact we also introduced a

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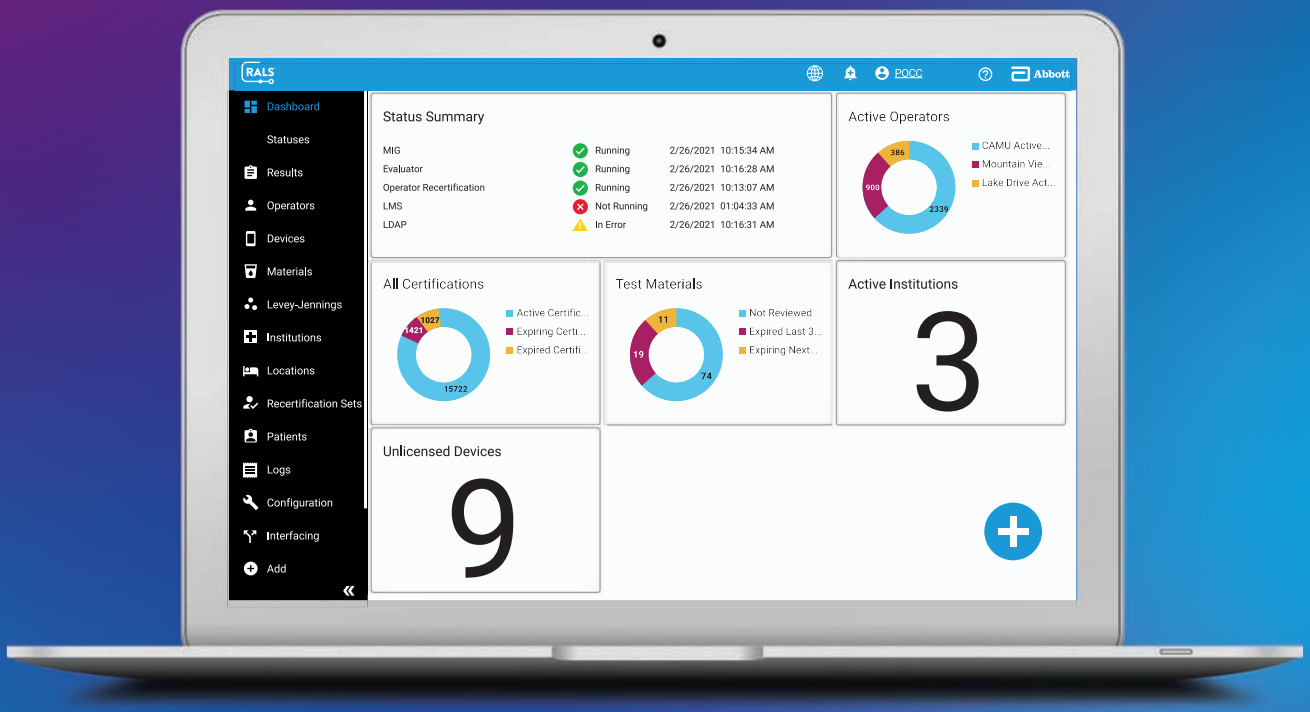

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new specimen type, which has its own issues requiring attention," said McLaren. "To round out our services, we have introduced serology testing using the Abbott IgG anti-nucleocapsid assay, and we are assessing the possibility of bringing on-line an anti-spike assay in anticipation of the need for assessing immune status following vaccination."

TESTING AND PANDEMIC CHALLENGES

The pandemic pushed labs to testing limits. The volumes of tests were incredible, with 23% saying they performed 1-2 million tests, 21% performed more than 2 million, another 21% did 100,001-500,000 tests, and 16% did 500,001 – 1 million tests. Only 2% did less than 25,000 tests.

"Where I am working, we commenced testing only after obtaining national accreditation. Additional manpower has been recruited as a temporary measure, which functions for 14 hours a day," said (Col) Mahendra N Mishra, MBBS, MD (Pathology), ESHI Diploma, of Baptist Christian Hospital in Tezpur, India.

Problems were prevalent during the pandemic, even on the other side of the globe, as Mishra faced a high rate of COVID-19 positivity amongst the staff. "It was the supply of other reagents that impacted us minimally as the workload had declined, and we had to contend with reagents from other vendors who had not supplied us in the past. The hospital has purchased two GenXpert-like (pieces of) equipment for performing cartridge-based testing, and we have a capability of up to 40 tests per day in addition to rapid antigen detection tests."

With frustrations running high, 77% say they have implemented IT efforts to reduce human error when trying to get reimbursed for testing of non-SARS tests, and nearly 57% have implemented efforts for SARS testing.

"The COVID-19 pandemic has put a tremendous amount of pressure on the already challenged laboratory. It now is more critical than ever for laboratories of all sizes to leverage automation," said Anthony Barresi, Senior Manager, Beckman Coulter Workflow and IT Solutions.

"For large laboratories that run about 20,000 tests a day, total lab automation is already a reality. However, for medium-volume labs that process fewer than 4,000 tests per day, available solutions are neither total or wholly automated. This is why innovative automation solutions are needed for labs of all sizes - to enable every lab to manage increasing volumes and STAT requests by reducing manual steps, decreasing pre-analytical errors and minimizing turnaround time."

Table 2 illustrates additional steps labs have taken to ensure their costs were reimbursed, with most respondents, 86%, adopting processes to review savings opportunities on a regular basis for non-SARS testing, which was not as readily prevalent for SARS at 38%, likely due to the massive influx of new products designed for COVID-19 on the market at once.

New standard lab processes and staff education materials for SARS were created by 63%, as new education and policies were put into place in response to the pandemic, which may have spilled over into the 79% creating processes and education for non-SARS.

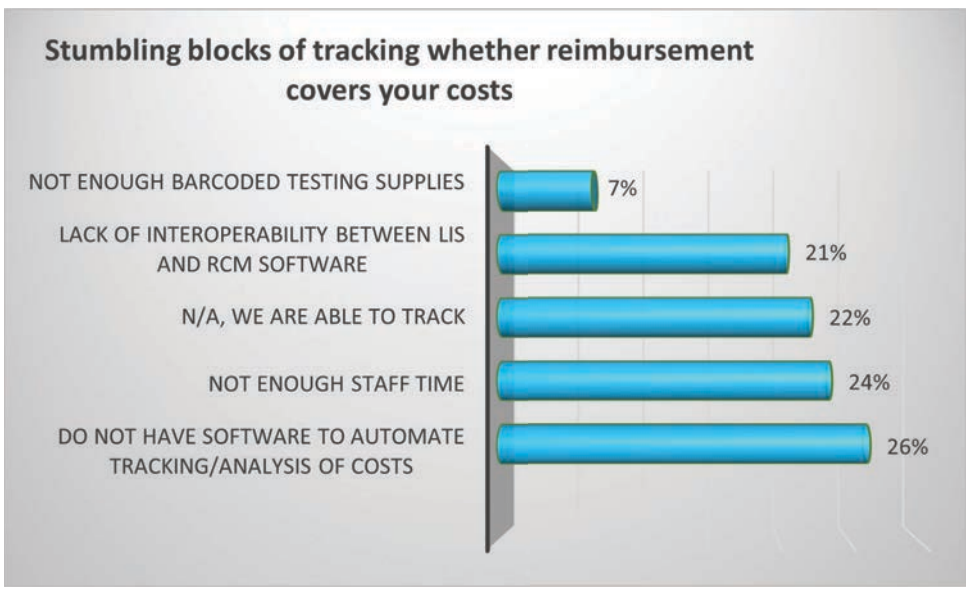


Table 2 reveals the biggest reimbursement stumbling blocks when trying to cover costs this year.

TRAINING LAB STAFF

With new automation comes new training, and when it comes to training the staff on the new software, 60% have created standard workflows for all lab employees, last year was 53%; while 56% created a train-the-trainer model, down from 64% last year. Survey results showed 18% have pulled in the

IT department to lead mandatory training for the products, down from 25% in 2020; with 11% doing lunch-and-learn training sessions, way down from last year's 21%. While 10% of labs have sent a lab person to LIS school to develop an in-house expert for all the new software, which was about half ot last year's 22%.

Last year, half of the respondents created standard lab processes and staff education materials to help testing run efficiently, and 48% said they adopted analyzers with walk-away testing. Even when things run smoothly, there can be hiccups along the way.

STAFFING CHALLENGES DURING A PANDEMIC

Costs were not the only hurdle to leap over, as staffing issues became prevalent during the pandemic. Not only did people get sick and get shuffled around to new positions, but staff had to learn new equipment and processes to handle the pandemic, while dealing with supply shortages and other challenges.

A Blood Bank Supervisor and Lab Quality Assurance Coordinator, who asked to remain anonymous, confessed that she ran into chaos during the COVID-19 pandemic. "We ran out of nasopharyngeal swabs, and suppliers could barely keep up with the demand. The manufacturers of our SARS/COVID tests also allowed nasal and throat swabs, so that helped." She was grateful that her hospital nurses would help collect swabs during day shift.

The facility also faced staffing challenges during the pandemic. When it came to staffing, she explained, "our staff was spread very thin, and several quality assurance items were put on hold nearly the whole year (March to February). No additional staff and no additional pay." The biggest struggle was scrambling when four lab employees were infected.

Though no new equipment was purchased, they overcame the challenges. "Whenever there were shortages of supplies, our procedures and processes changed, or because of what CDC or the State Health Department recommended that week. There were times when there were new sets of workflow on a daily basis. It got to a point where when we clocked in to work, we had to ask, 'How are we handling it today?'"

Respondents experienced similar challenges. Hiring freezes were put in place at 38% of labs, while an additional 38% said they saw fear or anxiety among job candidates about working in a lab during the pandemic.

"In early March, as the pandemic was hitting California, the leadership within SCPMG and Kaiser Health Plan, created a Regional Command Center group made up of healthcare providers across multiple disciplines, administrators and ancillary staff. Daily calls were held, which included laboratory leadership," explained McLaren.

"Out of this support, we were able to stand up internal testing rapidly, which then quickly expanded. Our ability to be at the table with this group of leaders, early in the pandemic, was crucial to our success. The next step was for our lab care delivery system to reach out to the medical center labs to offer support in any way possible. We created a Microsoft Teams chat line, and every other day, we would touch base in group calls with the medical center lab directors that included the lab medical directors. These calls facilitated sharing of best practices, as well as provided an avenue to

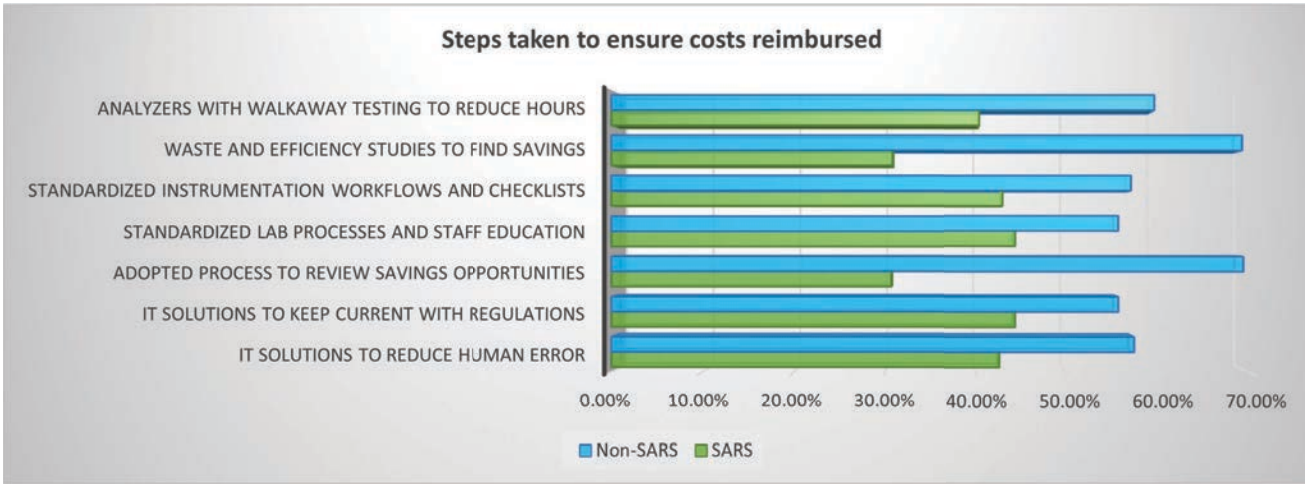
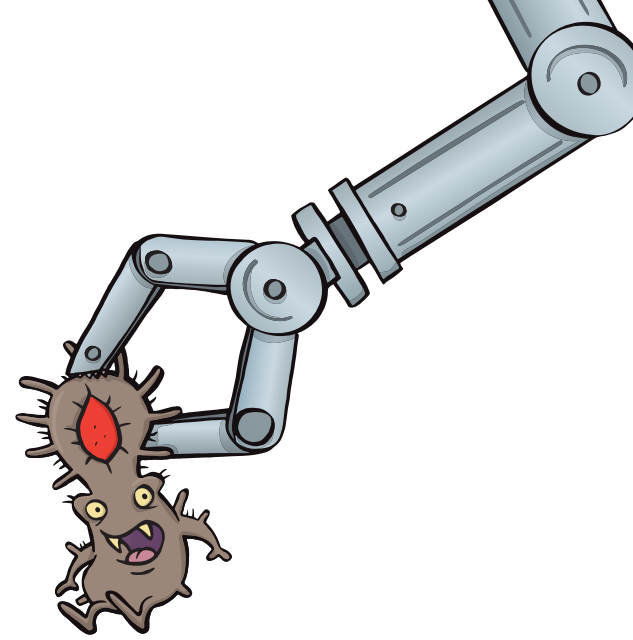


Table 3 illustrates additional steps labs have taken to ensure their costs were reimbursed.



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reach out for help or advice. As the pandemic progressed, the calls did not need to be as frequent and are now held once a week."

Of course, keeping the budget in mind is important. "We look at test volumes and costs, and if we can internalize a test by maintaining or improving on quality, while at the same time decrease our overall costs, we will internalize it. When a test is internalized, it is often done in conjunction with the clinicians or specialty groups to ensure we are going to meet their needs. Often times, we are approached by these same groups who ask for a test to be internalized, because they are experiencing issues with quality or turnaround times."

Kaiser was not the only company leaping through hoops because of the demands of the pandemic.

"When the pandemic began, we made sure that protecting the health and safety of these employees was our number one priority," Hilborne said. "We implemented many processes and procedures to foster safe work environments and held special safety training while implementing other key health and safety measures, such as expanded PPE. Many of our employees continue to work long hours to provide 24/7 testing for our patients."

Staffing challenges hit labs hard during the pandemic. Multiple staff members out sick with COVID-19 at the same time plagued 60% of the labs, while 41% dealt with budget cuts from lost revenue from elective procedures and tests, causing temporary staff furloughs. Making turnaround times difficult to meet, 38% had fewer staff in non-SARS-Cov-2 areas, and 38% had more staff than usual assigned to the pre-analytical area to keep up with SARS-CoV-2 tests.

Policies for social distancing and limiting outsiders in facilities impacted the numbers of internships offered, as there were drops from last year's best practices survey statistics, as well as staff benefits, such as having an available gym to use as an employee perk.

To retain and recruit, 38% provided continuing education (last year, 60% provided continuing education), 47% offered shift changes or scheduling flexibility, 45% addressed safety concerns, 43% partnered with local colleges and tech schools for internships in their labs, and 42% offered financial incentives, such as sign-on and retention bonuses, up from 36% last year.

Clinical ladders, a structure that encourages professional development from novice to expert, were offered by 34% of lab respondents. Another 33% had daily huddles with peer recognition to boost morale, down from 40% last year, and 21% had a succession-planning process by offering additional responsibilities to their top performers and measuring results, similar to last year's 21%. Up from last year, 17% lured employees with perks like free parking, reimbursing public transportation costs, an onsite gym or daycare. Perks like these were offered to employees by 16% of labs last year, revealing an uptick in benefits offered to laboratory employees.

"Overall, the pandemic revealed that private and public sector collaboration is critical to addressing any major, rapidly evolving heath crisis. None of us can address major challenges like COVID-19 alone, and none of us can assume that COVID-19 will be the last major pandemic in our lifetimes," said Hilborne. "This includes the recognition of the value of laboratory professionals to assure the quality of healthcare and the need to assure that our laboratories have sufficiently trained and competent professionals in the decades to come."

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Molecular genetic analysis of primary lactose and hereditary fructose intolerances

Aya Elhage, PharmD, MBA; Ilana Heckler, PhD; Iswariya Venkataraman, PhD

Abdominal cramps, nausea, bloating, and diarrhea are often symptoms observed in patients with gastrointestinal (GI) issues. Even though such complaints are common, they are difficult to diagnose accurately.[1] Most patients with such symptoms are frequently misdiagnosed, such as with irritable bowel syndrome (IBS).[1] However, such issues could be also due to genetic deficiencies in digestive enzymes, as seen in primary lactose intolerance or hereditary fructose intolerance. Lactose and fructose are two types of sugar that are naturally occurring in milk and fruit, respectively. Both lactose and fructose comprise a significant amount of daily intake, and the human body can sometimes metabolize and digest them. However, many individuals are intolerant to these sugars, exhibiting signs and symptoms that lead to poor health and well-being. It is imperative to analyze the causes of these enzyme deficits to aid in differential diagnosis and appropriate treatment, resulting in efficient management of these conditions.

Lactose intolerance

Primary lactose intolerance is the most common form throughout the world.[2] Primary lactose intolerance arises from an inherited defect of lactase, an intestinal enzyme responsible for breaking lactose into glucose and galactose.[2] Primary lactose intolerance is common among mammals due to a decrease in lactase activity upon weaning.[2] This usually occurs after the age of 2, with symptoms being most prominent in adulthood.[2] In lactose intolerant individuals, undigested lactose is fermented in the ileum and large intestine, producing byproducts that cause nausea, diarrhea, and abdominal pain.[2] Other secondary symptoms, such as chronic tiredness, fatigue, and depression, have been attributed to vitamin deficiencies.[2]

In addition to the primary genetic form, there is also a secondary acquired form of lactose intolerance. This form develops as a result of damage to the small intestine, which may lead to a decrease in lactase production.[3] Although the symptoms of both primary and secondary lactose intolerance may be similar, accurate diagnosis is essential for appropriate treatment and management regimens. Improper management of lactose intolerance may predispose individuals to reduced bone health, fragility fractures and osteoporosis.[4]

Fructose intolerance

Fructose is a simple ketonic monosaccharide found in certain foods including fruits, vegetables, and honey. The inability to digest fructose is referred to as fructose intolerance. GI manifestations of fructose intolerance include nausea, bloating, vomiting, sweating, abdominal pain, and growth retardation.[5] Fructose intolerance results from either a genetic deficiency in a key enzyme in the fructose metabolism pathway or is more commonly due to a defect in fructose absorption by the intestine.[6,7]

Fructose malabsorption is caused by a deficit in the transport of fructose into absorptive intestinal cells called enterocytes.[8] While the exact molecular mechanism for fructose malabsorption is not known, it is believed to involve the main fructose transporter GLUT5.[8] Further, studies have shown a link between fructose malabsorption and IBS, and have demonstrated that patients with IBS benefit from a fructose-restricted diet.[9]

Hereditary fructose intolerance (HFI) is a rare metabolic disorder caused by specific mutations of the aldolase B enzyme.[10] Aldolase B is responsible for the breakdown of fructose-1 phosphate (F-1-P) into dihydroxyacetone phosphate, and glyceraldehyde. Aldolase deficiency results in the buildup of toxic F-1-P in the body and subsequent gastrointestinal symptoms. In addition to gastrointestinal disorders, fructose ingestion by patients with HFI may lead to severe hypoglycemia.[10] Early diagnosis of HFI is critical to avoid permanent damage to the liver, kidney, and small intestine.

Prevalence

A 2017 study estimated that the overall frequency of lactose intolerance was around two-thirds of the world's population with large variations between countries and regions.[11] In the United States, the prevalence rate was 36 percent.[11] Higher frequencies of lactase persistence are observed in European populations, due to longstanding traditions of dairy farming and livestock raising.[12] On the other hand, more than 90 percent of East Asian groups are lactose intolerant, due to their predominantly non-pastoralist population.[12]

Due to the rarity of the disease, less is known about HFI. Fructose malabsorption is much more common than HFI, occurring in approximately 40 percent of individuals in the western hemisphere.[5] The incidence of HFI is estimated to be 1 in 20,000 to 60,000 individuals each year worldwide.[5,13]

Genetic polymorphisms

The two most common mutations associated with primary lactose intolerance are $13910_{C/T}$ and $22018\text{-}_{G/A}$ located at the promoter region of the lactase gene (LCT).[14] Symptoms of lactose intolerance are generally seen with homozygous genotypes 13910_{CC} and 22018_{GG}.[15,16] On the other hand, humans with heterozygous genotypes $13910_{C/T}$ and $22018_{G/A}$ may only express symptoms during GI infections or stress.[15,16] Individuals who are considered to be lactase persistent often present with the genotype 13910_{TT} and 22018_{AA}.[15,16]

In HFI, the most frequent single-point amino-acid mutations associated with HFI are A149P, A174D, N334K, and a deletion variant, del4E4, in the aldolase B gene.[17] For a person to exhibit symptoms of HFI, both alleles of the individual's DNA must contain the mutation.

Diagnosis

It is important for physicians to diagnose whether an individual presents with primary or secondary lactose intolerance to rule out Crohn's disease, celiac disease, and other gastrointestinal disorders.[12] This ensures appropriate treatment options are provided to patients with primary lactose intolerance. These individuals must indefinitely adhere to a lactose-free or low-lactose diet or take lactase supplements.

To detect lactose intolerance, intestinal function is challenged by the lactose intolerance test, where a lactose solution is consumed at specific intervals to understand the variability and severity of symptoms.[3] Another test is the hydrogen breath test (H2 test), which detects hydrogen in the breath formed as a result of the fermentation of undigested lactose into

hydrogen, methane and other short-chain fatty acids.[18,19] In addition, a blood glucose test may also be done to determine if lactose can be digested normally. If lactose can be digested, blood glucose levels would rise.[19] However, due to invasive and frequent blood draws, this approach is not commonly used. These tests have lower specificity and sensitivity because of external influences, such as GI flora, motility, and internal pH levels. Therefore, the clinical value in guiding clinical decisions for patients with bowel disorder is limited with hydrogen breath tests.[20,21]

Fructose malabsorption is also similarly diagnosed using a H2 test. The scientific basis for this test is that undigested fructose is fermented in the ilium by intestinal bacteria, producing hydrogen as a by-product. In a H2 test, following ingestion of a defined amount of fructose, the amount of hydrogen in a patient's exhaled air is measured at various time intervals. An increase in hydrogen above baseline levels is an indication of fructose malabsorption. While a hydrogen breath test is a safe procedure for the diagnosis of fructose malabsorption, this test is not recommended for diagnosing HFI, due to the high risk of triggering symptoms in lactose intolerant individuals, especially a newborn child. A liver biopsy test, which determines aldolase B activity, is a conclusive test for the diagnosis of HFI. However, this is an invasive test, which requires minor surgery. The need to distinguish between fructose malabsorption and HFI is due to differences in the dietary requirements of patients, which are needed to prevent long term organ damage.[6]

Both lactose intolerance and HFI require a more reliable and accurate test method to support accurate diagnosis of these conditions.

Parallel testing of lactose intolerance and HFI

Molecular genetic testing can aid in confirming or excluding primary lactose intolerance with a high probability. Additionally, it can also assist differentiation between primary and secondary forms and does not pose the risk of triggering symptoms in lactose intolerant individuals. Molecular genetic testing for the diagnosis of fructose intolerance is used for the detection of the HFI-associated mutations A149P, A174D, N334K, and del4E4, in human genomic DNA. Furthermore, molecular testing can be used as a reliable non-invasive supplement test in addition to traditional H2 tests or blood glucose tests.[22]

Perspectives

A conclusive and specific diagnosis of GI disorders is critical to ensure proper treatment and management of patients. If undiagnosed, the patients can experience long-term organ or bone damage. Molecular genetic testing enables verification or exclusion of primary lactose intolerance or HFI to be the cause of a patient's GI complaints with high accuracy. The ability to simultaneously test for both lactose and fructose intolerance facilitates a prompt diagnosis, which allows patients to readily adapt their diets to alleviate symptoms.

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Aya Elhage, PharmD, MBA, is currently the Scientific Affairs Manager at **EUROIMMUN US**. Elhage supports the team with commercial activities including scientific collaborations, scientific marketing, and business development of diagnostics.

Ilana Heckler, PhD. As the Scientific Affairs Associate at **EUROIMMUN US**, Heckler supports scientific collaborations and assists in the validation of diagnostic assays for autoimmunity and infectious diseases.

Iswariya Venkataraman, PhD, serves as Scientific Affairs Lead, **EUROIMMUN US**. She's currently a member of the Alzheimer's Disease Neuroimaging Initiative (ADNI) Private Partner Scientific Board (PPSB), an independent, pre-competitive forum for study-related scientific exchange in the field of neurodegeneration. During her doctoral studies in neuroscience, she identified novel auto antigens in autoimmune hyper-excitability disorders.

Why neutralizing antibodies remain vital in SARS-CoV-2 variants and vaccines

Katherine Soreng, PhD, and Kalen Olson, PhD

SARS-CoV-2 is the RNA coronavirus responsible for the COVID-19 global pandemic. Just when newly approved vaccines (and many more in development) offered the prospect of a return to normalcy, the emergence of highly circulating variants has raised significant concerns about vaccine efficacy.[1-3] The term "viral variant" can be confusing and is often (and incorrectly) used interchangeably with other terms, such as mutations, strains, and lineages.[1] **Figure 1** describes formal definitions and distinctions. Mutations are normal, abundant, and expected, especially with an RNA virus. When a mutation or group of mutations confers an advantage, a new variant can emerge. If the altered phenotype allows it to outcompete existing virus (for example, if it is more infectious or more capable of evading immune pressure), it may become the dominant strain.

Variants have been with us since the beginning

As confirmed by the recent joint investigation by the World Health Organization (WHO) and Chinese scientific teams, variants have been with us since the dawn of the pandemic.[4] It was a presumed variant that produced one or more strains highly capable of infecting humans (likely from a yet-to-be-identified zoonotic progenitor that may trace back to bats), principally through changes in the spike protein that increased viral affinity for the human ACE2 receptor. The original "Wuhan" strain was subsequently displaced outside China by a variant with a single amino acid change at position 614 in the S1 region of spike protein that changed an aspartic acid to a glycine (D614G).[5-7] Starting in April of 2020, D614G spread rapidly to become the dominant global strain. Data indicates the D614G variant has increased infectiousness, but fortunately, it remains susceptible to current vaccines based on the original Wuhan strain.

New "variants of concern"

Despite the rapid spread of D614G as the dominant strain, until recently, much of the public remained unaware of variants. The identification of "variants of concern" (VOC) in several parts of the world (including those first identified in the United Kingdom, South Africa, Brazil, and the United States, but now detected in multiple countries) has elevated recognition and prompted investigation.[1-3] More variants continue to be identified globally, as countries initiate enhanced sequence surveillance programs, with the greatest focus on mutations in the spike protein. Concerns include impairment of some diagnostic tests, including a small subset of molecular tests where the mutation impacts primer annealing, or the possibility of changes that enhance pathogenesis or transmission.

The United States has recently identified a commonly emerging variant with a mutation in S2 (Q677P) that may enhance fusion of virus with the host cell.[8] An additional variant spreading rapidly in California has a mutation in spike at position 452 (L452R) that has also sparked concerns of potential increased transmission and possible resistance to a neutralizing antibody.[9] The variant first identified in the United Kingdom (B.1.1.7) shares a mutation with the variants first noted in Brazil and South Africa at position 501 (N501Y) that may increase transmission. B.1.1.7 is present in the United States, and some predict it will become a dominant variant, as it appears to be spreading rapidly.[10] Though not yet determined, worries also exist on increased pathogenicity with B.1.1.7. Of significant concern with any spike/RBD mutants is the potential for resistance to, or escape from, neutralizing antibodies from recovered infection or, more relevantly, vaccination.

Vaccines target the spike protein

All currently approved vaccines (and most in development) target the viral spike protein, which contains the receptor-binding domain (RBD) that recognizes and binds the virus to the ACE2 receptor on the host cell.[11] Therefore, a spike or RBD-based assay must be used if assessing a vaccine antibody response if the nucleoprotein is not a part of the construct. Abundant data show the RBD is the primary target of neutralizing antibodies.[12-14] Since neutralizing antibodies can interfere with viral binding and so limit infection, they are especially appealing as a mechanism of inducing protection.

Vaccine study data using whole spike show highly correlated detection of binding and neutralizing antibodies using either spike or RBD-based assays (unsurprising, as the RBD is contained in the spike).[15-17] "Neutralizing" antibodies are defined by their ability to inhibit infection in-vitro, which often translates to protection in-vivo. Vaccine-related data generated with animal models has clearly established the importance of spike/RBD antibodies for protection from SARS-CoV-2 challenge.[18,19] Thus, changes in the RBD are of particular concern, though mutations in the S1-NTD and S2 may also present a potential immune escape adaptation.

Role for neutralizing antibodies

While data indicate that elements of both the cellular (T-cell) and humoral (B-cells producing antibody) adaptive immune response contribute to protection from (re) infection, neutralizing antibody alone has been shown to be highly significant.[19-21] Therapies based on neutralizing antibodies are utilized and include both monoclonal-based and convalescent plasma (CP).

Importantly, the level of neutralizing antibodies may be essential for vaccine efficacy and therapeutic CP. Vaccines requiring a two-dose regimen resulted from observations that a single dose failed to achieve sufficient seroconversion and titer of neutralizing antibody. While vaccine-induced antibody responses may generally be higher compared to many recovered infections, levels vary between subjects. The current unknown is if individual susceptibility for infection (including variants) is associated with variable neutralizing antibody levels in vaccine recipients. Infusion of highly neutralizing polyclonal serum in animal models subsequently challenged with live virus indicate a protective threshold exists and may be important for protection.[19]

RBD mutations and immune escape

To better understand worries for variants able to evade/resist neutralizing antibody, an understanding of the current mutations of concern is required. **Figure 2** shows some of the the mutations of concern in spike protien.[22] Mutations can include an amino acid coding change, a deletion, or an insertion. Most mutations are either

silent or eliminated as deleterious, but a subset may improve viral fitness. Mutations occur throughout the viral genome but not with equal frequency. "Hotspots" exist and include the spike protein.[23] While some RBD variants have shown the ability to resist/evade some neutralizing antibody, other mutations in spike may also contribute to evasion. These include deletions in the S1 N-terminal domain and mutations in S2 also found in these variants.[8,24,25]

Selective pressure and immune escape variants

One significant potential source of environmental selective pressure is the presence of neutralizing antibodies. In tissue culture, SARS-CoV-2 rapidly mutates with passage in the presence of neutralizing antibody, developing resistance that necessitates higher titers of antibody to neutralize.[26] The variable resistance observed for variants and individual CP samples may result from the types of neutralizing antibodies arising from the polyclonal response or high versus lower antibody levels.[27,28]

Vaccines may be in a race with variants, as lack of widespread protection may promote increased pressure for selection of resistance. Variants better able to evade antibody neutralization may exploit this vulnerability and become the dominant strain (especially if also more transmissible), potentially challenging successful vaccination efforts.[29]

The need to modify current vaccines and variants

It will be essential to understand if escape variants translate to increased susceptivity in vaccinated populations. Despite a reduction in neutralization in-vitro, relevant protection in a vaccinated individual may remain, especially if neutralizing antibodies are high or if elements of T-cell immunity are able to compensate. Alternatively, "variant specific" vaccine boosts may be important. Vaccine trial data from regions of high variant transmission do indicate a reduction (but not elimination) in current vaccine efficacy with variants (though primarily limited to analysis showing symptomatic clinical infection). For example, preliminary vaccine trial results for a recombinant spike protein-based vaccine showed 89 percent efficacy in the United Kingdom (including B.1.1.7 infections), but a reduced efficacy of 49 percent in South Africa, where the B.1.351 (also called 501Y.V2) variant with three RBD mutations predominates.[30]

Early data (requiring additional confirmation) from a chimp adenoviral-based vaccine trial, also conducted in South Africa, showed essentially no difference in rates of mild to moderate infection in the vaccinated population.[31] However, data for the same vaccine in the United Kingdom indicates it is effective at limiting infection and that a higher efficacy was observed even with the B1.1.7 variant, including significant protection from a single dose.[32] The ability to reduce severe disease or hospitalization may be an important parameter, even with impaired efficacy, as shown in data from a similar vaccine using a human adenoviral vector also encoding the spike protein.[33]

While the format of the vaccine (e.g., mRNA, adenoviral, recombinant protein etc.) may be a factor impacting efficacy, it will be necessary functionally to understand the role levels of neutralizing antibodies and cellular immune components play following vaccination. Data points to the level of neutralizing antibody, much of it targeted to the RBD, as a major component of protection.[12-14,19] Quantitative testing for antibody targeted to known neutralizing regions like RBD or whole-spike assays is likely salient for assessment of protection, including with variants.

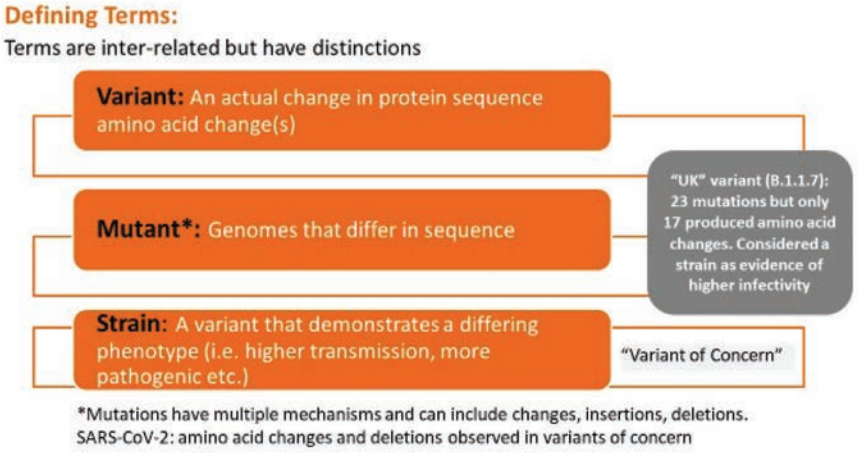
The same variant can arise independently

Some mutations or groups of mutations are shared between distinct variants, so they likely confer an advantage. Parallel evolution in independently arising variants is almost certain and supported by genome analysis.[9,23,24] Therefore, the finding of the "UK" variant in multiple countries may trace back to imported cases or arose from local mutagenesis. With enhanced surveillance, a better understanding of variant emergence and frequency will evolve. Consistent findings of recurrent mutations indicate lockdowns on international travel may be insufficient to control variant spread.

A mutation at position 501 (N501Y) in the RBD is shared by the three highly reported strains and has been linked to potentially higher receptor affinity and increased infectiousness.[22] Two additional mutated positions in the RBD are shared by the South Africa (B.1.351) and Brazil (P.1) strains (K417T, E484K). The E484K mutation alone has been linked with both reinfection and reductions in neutralization from both CP and some vaccine sera.[28,34,35]

However, encouraging in-vitro data has been published for vaccine sera from recipients of the currently approved mRNA vaccines. Comparatively small reductions in neutralization were observed with sera from individuals who'd received both doses of the BNT162b2 vaccine when tested with several spike mutations found in the three highly circulating variants.[36] In similar data, sera from recipients receiving both doses of mRNA-1273 vaccine showed generally modest reductions in neutralization; although, constructs with the three RBD mutations alone or for all mutations identified in B.1.351 did reveal notable reductions in, but not elimination, of neutralization.[37]

The N501Y mutation (shared by the 3 common variants and the only RBD mutation found in B1.1.7) appears to remain largely susceptible to vaccine-induced neutralizing antibodies. Importantly, studies thus far examining these various mutations have used primarily pseudoviral constructs representing either a subset or the constellation of mutations associated with a given variant. While this data is highly useful, testing with live



Lauring and Hardcroft, *JAMA* Published Online: January 6, 2021. doi:10.1001/jama.2020.27124

Figure 1.

virus variants will be necessary to confirm findings.[38]

(Semi)quantitative testing for spike or RBD antibody following vaccination

As variants emerge and spread, it will be essential to understand if there is a continued role for the level or titer of neutralizing antibody induced against a prior strain (such as the Wuhan strain spike sequence used by several vaccines) and protection from a new variant.[14,28,39] Studies with CP and variants suggest that the level of neutralizing antibody may indeed matter, as CP with high levels of neutralizing antibody appears to offer greater protection against mutated strains.[28] Data indicating continued if diminshed protection from some spike mutations in vaccinated individuals is encouraging, but also suggests the level of neutralizing antibody may be a significant factor if higher levels are required to maintain protection.[40]

What is essential to know is if (semi) quantitative tests might show a significant reduction in reported value with antibodies associated with spike variants. While levels of spike/RBD antibodies are most salient to neutralization, testing for seroprevalence or evidence of infection can utilize either spike or nucleocapsid antibodies. Since mutations can impact both the nucleocapsid and spike proteins, all assays are potentially susceptible based on the antigenic regions they target.

At least some manufacturers are working to determine this with their respective assays, although initial limitations in variant-infection sample access present a challenge. While the polyclonal nature of the response would suggest continued detection (as assays detect antibody to multiple epitopes), the possibility of a reduced signal or need for a "variant specific" threshold exists. Further investigation is needed to elucidate this.

Aiding the simplified assessment for the level of antibody (versus titer) is the increasing availability of quantitative SARS-CoV-2 antibody assays (technically semi-quantitative in the United States, due to the current lack of an accepted international reference standard). Moreover, some manufacturers have published correlation data to specific neutralization titers determined by plaque reduction neutralization assay (PRNT), which uses live virus in the presence of differing levels of antibody to assess for percent inhibition of viral infection in cell culture and is considered the gold standard neutralization method. Such assays could support studies with dominant viral variant infections to assess for any altered "variant threshold" that may be associated with protection relative to the prior strain. Thresholds could have clinical implications as to protection/vulnerability and inform decisions of need to boost or prioritize for variant-specific vaccines should they become available.

Are "variant-specific" vaccines required immediately?

It is clear from the vaccine trial data to date that sterilizing immunity is unlikely to be achieved with vaccination. Vaccinations may be more aligned with preventing severe disease or hospitalizations. The limited data to date with approved vaccines indicates a level of protection may persist with the variants, albeit at reduced levels.[35-38] This likely reflects the polyclonal nature of the neutralizing antibody, elements of cellular immunity, and variability in individual vaccine responses.

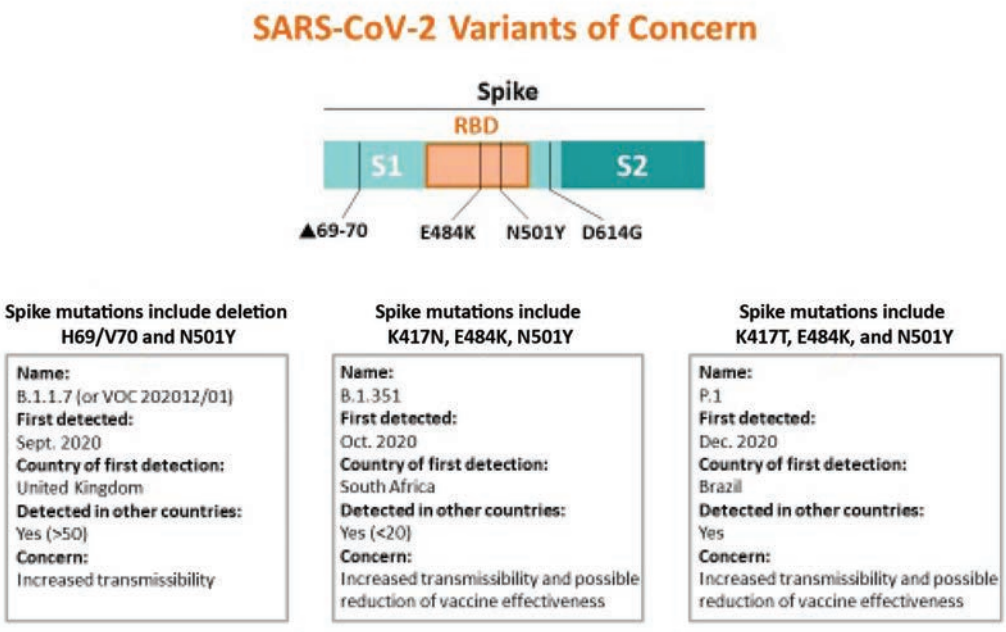
There is intriguing data using sera from patients recovered from COVID-19 and given a single dose of an approved mRNA vaccine, showing an almost thousand-fold increase in the ability to neutralize the highly-mutated B.1.351 variant, which supports continued utility with at least some available vaccines.[40] The authors determined that antibodies to the RBD were a primary source of neutralization (with some contribution from antibodies in S2) and that increased vaccine-induced levels may be essential for effective neutralization. Therefore, immediate modification of existing vaccines may not be exigent (though may be important for optimal protection overall), at least in individuals with high levels of spike/RBD antibodies.

The FDA and "high-titer" CP: immunoassay values correlate

The recent emergency use authorization (EUA) issuance from the U.S. Food and Drug Administration (FDA) of validated assay-specific cut-points for SARS-CoV-2 screening of "high-titer" CP further indicates a role for neutralizing antibody level.[41] If given early, high-titer CP appears therapeutic and may mitigate disease, presumably by interfering with the ability of the virus to bind to or fuse with the host cell. Since wide variability is seen for neutralizing antibodies with CP, it is critical to identify high titer for use as a therapeutic, as low-titer plasma does not perform well. This FDA issuance of correlated values vastly simplifies the identification of acceptable CP donations and supports the value of (semi)quantitative antibody testing.

Conclusion

Variants of concern will continue to emerge, and enhanced surveillance will support earlier identification. Currently, data indicates that at least with most available vaccines, protection is maintained, albeit at a reduced



Xie X, et al. doi: 10.1038/s41591-021-01270-4. (see reference 36.)
https://www.astrazeneca.com/what-science-can-do/topics/disease-understanding/the-natural-evolution-of-sars-cov-2.html

Figure 2.

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a reduced level in some. It is unknown if new viable variants with additional spike mutations will emerge, or what further impact they might have on vaccination. Spike/RDB-based semi-quantitative antibody tests could prove highly useful, especially if levels of antibody post-vaccination are confirmed as a relevent correlate of protection for circulating virus, including variants.

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Katherine Soreng, PhD, is the Global Director of Clinical Education for Laboratory Diagnostics at **Siemens Healthineers**. She writes and educates on a variety of clinical diagnostic disease states, including infectious disease, liver fibrosis, and cardiology.

Kalen N. Olson, PhD, serves as Head of Medical Affairs and Medical Officer for Laboratory Diagnostics at **Siemens Healthineers.** Before joining Siemens, she was the Clinical Laboratory Director at a large healthcare system in the Minneapolis/St. Paul metropolitan area.

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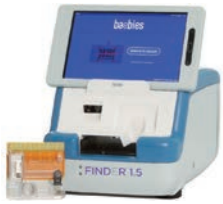
Since SARS-CoV-2 began spreading around the world in 2020, companies have developed a range of products to address large-scale diagnostic- and surveillance-testing needs.

Rapid RT PCR test



The rapid RT-PCR test for SARS-CoV-2 features a disposable cartridge with all reagents included, providing results in 17 minutes or less. The test runs on the FINDER 1.5, which is a toaster-sized instrument powered by digital microfluidics, without pumps, tubing, or valves.

Baebies

Run Controls

The SARS-CoV-2, Flu, RSV Positive and Negative Run Controls are unassayed external controls used to monitor the presence or absence of SARS-CoV-2, Influenza A, Influenza B and RSV (A). The products are formulated in a synthetic matrix and contain human genomic DNA.

Bio-Rad Laboratories

Molecular diagnostics

The Aptima SARS-CoV-2 assay is a molecular diagnostic test that utilizes proprietary TMA (Transcription-Mediated Amplification) technology to detect RNA from SARS-CoV-2. Meanwhile, the Panther Fusion SARS-CoV-2 real-time PCR assay also detects RNA from SARS-CoV-2. Both tests process 1,000 tests in 24 hours and deliver results in 3.5 hours or less.

Hologic

Quality tool

AccuPlex SARS-CoV-2 in synthetic oral fluid is a research tool for developers creating saliva-based SARS-CoV-2 assays, as well as a complete quality solution for clinical laboratories employing such tests. The product includes positive vials containing the full SARS-CoV-2 viral genome, and human RNase P sequences to monitor sample collection.

SeraCare

RT-PCR test

The QIAstat-Dx Analyzer, combined with QIAstat-Dx assay cartridges, uses real-time RT-PCR to detect multiple respiratory pathogens in about an hour. The QIAstat-Dx Analyzer and cartridges are designed as a closed system that contains on board all necessary reagents, enabling an easy-to-use workflow.

Qiagen

Third party control

The Acusera SARS-CoV-2 Antibody Control comprises both reactive and non-reactive controls for Anti SARS-CoV-2, supporting assay validation and routine performance monitoring of serological assays for COVID-19. The control, which is CE marked, is supplied in a liquid format with a 30-day open vial stability.

Randox

Variant detection

The high-throughput Allplex 2019-nCoV Assay (FDA EUA) detects 3 different target genes (E, RdRP, and N) of SARS-CoV-2 and covers multiple variants in a single reaction tube. The test provides results within 1 hour and 50 minutes. It is designed for maximum throughput to accommodate high volume testing.

Seegene Technologies

Incubator

The Heratherm Advanced Protocol Security Microbiological Incubator enables reliable heat virus inactivation to protect medical laboratory personnel from infection and allow safe sample handling. It offers temperature uniformity, continuous operation, and a sterile environment for sample protection and reliable results.

Thermo Fisher Scientific

Foam swab

The specialty swab includes an applicator tipped with 100ppi medical grade polyurethane foam with high particle collection capacity and sturdy handle for control. Used widely for COVID-19 testing, the swab also can be used for various medical, diagnostic, and DNA testing applications.

Puritan Medical Products

Automated PCR test

The cobas SARS-CoV-2 Test is intended for the qualitative detection of SARS-CoV-2 in nasal, nasopharyngeal and oropharyngeal swab samples from patients with suspected COVID-19 infection. Laboratories can run the PCR test on the automated, high-throughput cobas 6800/8800 systems, which provide results in about three hours.

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Instrumentation Laboratory

Covid-19 proficiency testing available

American Proficiency Institute

API is offering non-infectious PT samples for the detection of SARS-CoV-2. Samples are whole genome and are available in a swab or liquid format, ensuring compatibility with all molecular methods. PT samples serve as a full process check; allowing labs to test their entire workflow, including extraction, amplification and detection.

American Proficiency Institute

KRONUS® 21-Hydroxylase Autoantibody (21-OHAb) ELISA

The KRONUS® 21-Hydroxylase Autoantibody ELISA Kit is for the qualitative determination of antibodies to steroid 21-OH in human serum, the measurement of which is useful as an aid in the diagnosis of autoimmune adrenal disease. *Manufactured Under Assigned Patents and Licenses*

KRONUS

InteliQ: the Intelligent QC Choice for all Labs

Bio-Rad recently announced new enhanced features for the InteliQ load-and-go Quality Control product line. The new features support off-board, open-vial refrigerator storage for all platforms, and on-board storage for the fully automated Siemens Atellica platform.

Bio-Rad

Discover the Randox RX imola

The RX imola is a cost-effective, random access, small footprint, benchtop clinical chemistry analyzer delivering consistent high-quality results. Capable of performing 560 tests per hour boosting intuitive software, STAT capabilities and extensive testing menu.

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Sebia, Inc.

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Sysmex

Seegene's COVID assay with variant detection

Seegene's high-throughput Allplex™ 2019-nCoV Assay (FDA EUA) detects 3 different target genes (E, RdRP, N) of SARS-CoV-2 and covers multiple variants*.

*As demonstrated by in silico and wet analysis. Data on file.

Seegene

Proficiency Testing

WSLH Proficiency Testing offers a variety of SAR-CoV-2 proficiency testing programs, including molecular, serology and antigen products. WSLH PT also offers the SARS-CoV-2 analyte for our Respiratory Multiplex product. Reliable, affordable, and easy-to-use proficiency testing products from a national public health lab.

WSLH Proficiency Testing

Vitamin D testing during COVID-19 pandemic

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LABORATORY INNOVATOR

Fostering education, patient safety and collaboration

By Linda Wilson

Deborah Ann Sesok-Pizzini, MD, MBA, joined **Labcorp Diagnostics** as Chief Medical Officer on January 11, 2021. Prior to joining Labcorp, Sesok-Pizzini held multiple appointments with the Children's Hospital of Philadelphia, including Departmental Patient Safety Officer, Chief of the Division of Transfusion Medicine, and Vice-Chief of Pathology and Laboratory Medicine.

Why did you choose a career pathology, transfusion medicine, and lab mangement?

I was always intrigued by what happens "behind the scenes" during the diagnosis of a patient and determining the best lab test to perform to help arrive at the right diagnosis. At the same time, I really enjoyed interacting with patients, and I had great experiences with early mentors in transfusion medicine. Transfusion medicine enabled me to further pursue an education in clinical pathology, while allowing me to continue to see outpatients and hospitalized patients for chronic and acute care needs on the apheresis service. My interest in lab management came from a desire and need to learn about compliance and regulation and to lead teams and manage operations.

What new developments do you expect to see in transfusion medicine in the next three to five years?

I see transfusion medicine continuing to expand in the areas of cellular therapies, molecular matching, and advancements in pathogen inactivation. I also hope to see continual efforts in donor recruitment to help sustain a reliable and diverse blood supply for our patients. We found that this was particularly important during the COVID-19 pandemic, as we were challenged to find best-matched donor blood for our sickle cell patients needing monthly red cell exchanges.

What factors led to your decision to move from Vice Chief of Pathology and Laboratory Medicine at Children's Hospital of Philadelphia to Chief Medical Officer at Labcorp Diagnostics?

As CMO at a large commercial laboratory, I am still able to practice my specialty of clinical pathology, but I can also explore new ways to help patients and physician colleagues across the United States and around the world. We saw with the COVID-19 pandemic the importance of laboratories working together to provide testing to our patients, and I am now excited to be part of a larger vision that brought those teams together in the interest of patient care. I hope that collaborative partnerships continue in the future.

You have decided to continue teaching at the University of Pennsylvania Perelman School of Medicine. Why did you make this decision?

I firmly believe in mentoring and training the next generation of pathologists, and I am very invested in continuing to be involved in that mission. I co-direct the leadership course for our pathology residents and fellows at the Perelman School of Medicine. I now bring a new and different perspective to my lectures, with my experience in the corporate world. My goal is to formalize a rotation for pathology residents at Labcorp, to introduce our trainees to the inner workings of a large, commercial laboratory. I also plan to continue to be an official mentor to our junior faculty, both at Penn and Labcorp, to ensure success early in their careers.

What steps should labs take to manage quality and patient safety while juggling both SARS-CoV-2 testing and other work of the lab, such as testing for chronic diseases or before surgical procedures?

I am glad you asked this question. Most recently, I served in a pediatric hospital, and during the pandemic, we needed to be able to take care of our patients – the majority of whom did not have COVID-19 – during a time of crisis and uncertainty. Everyone worked really hard to make certain that patients were safe and received the necessary laboratory tests and procedures. The same applies to changes we had to make with our blood donor drives to safely manage the collection of blood. I am proud of my colleagues, both in reference and hospital-based laboratories, who quickly pivoted to develop testing strategies that were needed for SARS-CoV-2, and at the same time, focused on the core laboratory tests needed to manage patients with other health concerns.

Thinking about both providers and patients, what initiatives or approaches do you recommend labs implement to improve customer service?

The patient experience begins at the point of blood draw to ensure that the right patient is getting the right amount of specimen collected and placed in the right tubes, so there aren't any issues with insufficient quantity that might require a patient recall or delayed test results. That is a seemingly small but vitally important step. One of my big focuses is on patient safety and patient identification, ensuring that the blood collected from the patient is correctly labeled. Another critical part of the patient experience is having physicians and scientists in pathology available for consultation and to guide test use and interpretation. Consumer-initiated testing continues to increase in popularity, and it is extremely important to provide sufficient educational material, so patients understand their testing results and when to seek further care.

We have many opportunities now, with more sophisticated analytics, to bring test results and interpretation to a new level to help provide better patient care. I'm excited to be on that journey with my colleagues and to see how it will provide added value for both our physicians and patients.

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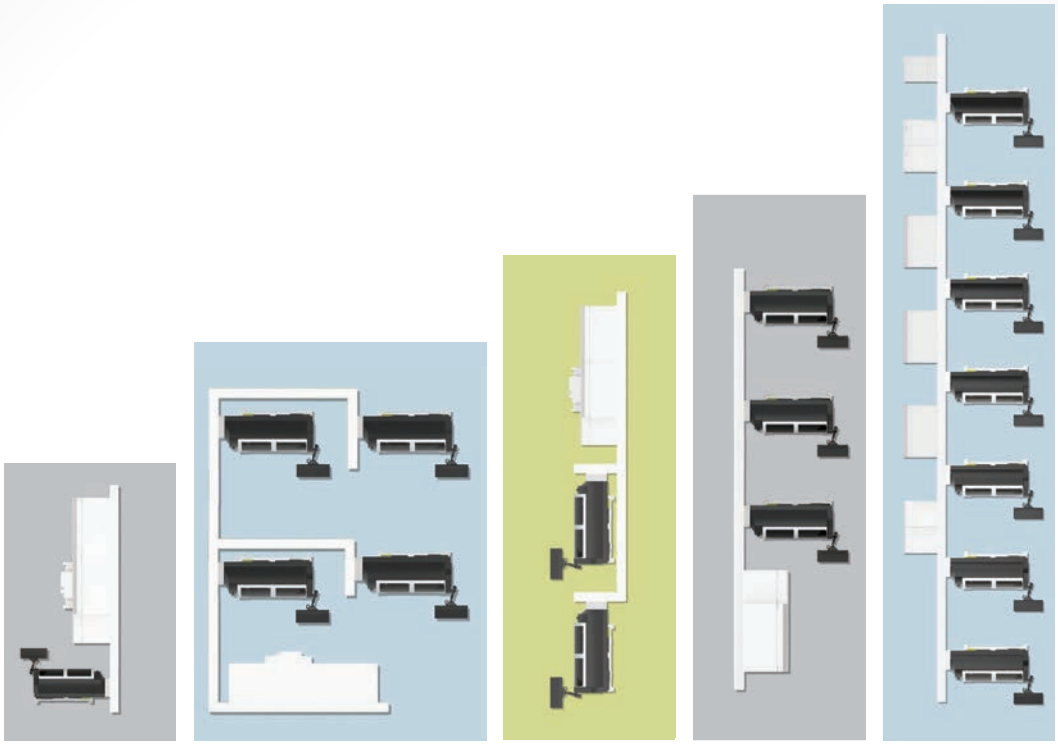

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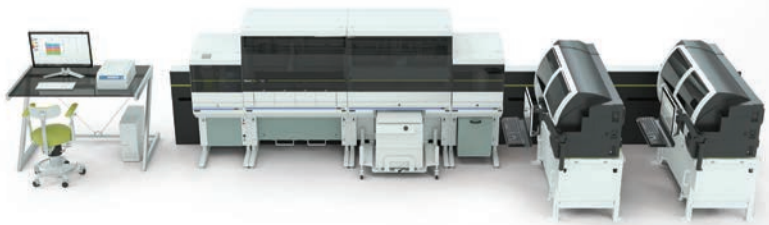

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Reference: 1. Compared with other high-throughput, fully automated systems. U.S. Food and Drug Administration. SARS-CoV-2 Reference Panel Comparative Data. Last reviewed December 07, 2020. Accessed February 23, 2021. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data