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CE SARS-CoV-2 sequencing for public health impact around the world

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STIs and the COVID-19 impact

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LAB INNOVATOR

Dr Ghazala Nathu
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References: 1. Taylor-Robinson D, et al. Mycoplasma genitalium: from Chrysalis to Multicolored Butterfly. Clin Microbiol Rev. 2011;24(3):498-514. doi:10.1128/CMR.00006-11. **2.** Workowski, et al. Sexually Transmitted Infections Treatment Guidelines 2021. MMWR RecommRep 2021;70. **3.** Le Roy C, et al. French prospective clinical evaluation of the Aptima Mycoplasma genitalium CE-IVD assay and macrolide resistance detection using three distinct assays. J Clin Microbiol. 2017;55(11):3194-3200.

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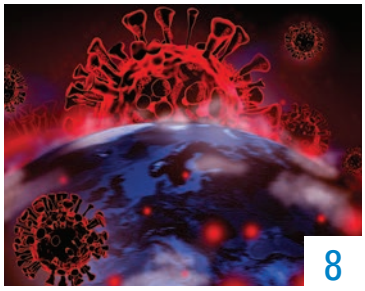

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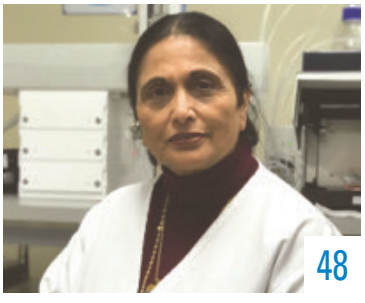

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In a 670 patient study funded by the International Society of Nephrology, the South Africa Medical Research Council and the University of Witwatersrand, Johannesburg, South Africa,
the Nova Point of Care StatSensor Creatinine/eGFR meter was more accurate than the central laboratory IDMS-traceable Jaffe methodology in estimating GFR when both methods were compared to MEASURED GFR (iohexol).[1]

- StatSensor measurements showed less proportional and constant error than respective IDMS Jaffe measurements when compared to iohexol measured GFR (mGFR).[1]
- StatSensor showed better accuracy than the IDMS Jaffe methodology at identifying patients with mGFR's <90 mL/min/1.73 m^2.[1]
- Of particular interest in the study, StatSensor showed better accuracy than the laboratory Jaffe methodology in the 60-89 mL min/1.73 m^2 range, where individuals with early disease may benefit from renal protective measures.[1]

Nova Biomedical StatSensor Creatinine Meter

1. George J et al. *Evaluating chronic kidney disease in rural South Africa: comparing estimated glomerular filtration rate using point of care to iohexol measured GFR. CCLM 2021.*

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Getting back on track with lab accreditation

By Kristine Russell
Executive Editor

As laboratorians, the priorities in our facilities depend on systems that focus on quality management. This would allow us to assist in the delivery of accurate diagnostics to our physicians that is integral to their ability to assist patients in their care.

Our ability to follow consistent standards and document our processes will ultimately result in patient safety, including our own lab personnel safety. As part of the process, there are a number of organizations who grade our ability to follow guidelines and standards by accrediting our actions within our labs.

According to Wikipedia – "Accreditation is the independent, third-party evaluation of a conformity assessment body (such as certification body, inspection body or laboratory) against recognized standards, conveying formal demonstration of its impartiality and competence to carry out specific conformity assessment tasks (such as certification, inspection and testing)."

The accreditation process does improve the ability to deliver accurate and rapid diagnostics and improves our efficiency resulting in error reduction. The process validates what we do and proves that we have a system of standard procedures that aims to improve quality and patient safety.

I recently attended an interesting session on lab accreditation that highlighted a number of areas in which clinical labs were struggling to keep up with accrediting standards and guidelines. The session was part of at the Executive War College in New Orleans in April. The presenters were from The Joint Commission, College of American Pathologists, COLA, and A2LA. The discussion reviewed common deficiencies found during accreditation surveys and areas that are overlooked when making your lab assessment ready.

As most would suspect, many of the problem areas they listed could be related to staffing levels and the time needed to ensure that these areas are covered consistently.

Top deficiencies mentioned by all four agencies included:

- Personnel competency assessments
- Procedure manuals
- Proficiency testing
- Equipment inspections and maintenance records
- Surveillance of patient results and records
- Evaluations of same test results performed with different instruments or at different locations
- Timely reporting of critical results of tests and diagnostic procedures
- Personnel or lab director not fulling responsibilities of their position

Accreditation should be embraced by our laboratory professionals as a welcome process that proves we have the ability and dedication to save lives – and we do every day!

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

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Fast Facts

Infection-induced SARS-CoV-2 seroprevalence

In December 2021, the B.1.1.529 (Omicron) variant of SARS-CoV-2, the virus that causes COVID-19, became predominant in the United States. Traditional methods of disease surveillance do not capture all COVID-19 cases because some are asymptomatic, not diagnosed, or not reported; therefore, the proportion of the population with SARS-CoV-2 antibodies (i.e., seroprevalence) can improve understanding of population-level incidence of COVID-19.

75%

of children and adolescents had serologic evidence of previous infection with SARS-CoV-2 as of February 2022, with approximately one third becoming newly seropositive since December 2021.

24.2%

was the overall U.S. seroprevalence increase from 33.5% in December 2021 to 57.7% in February 2022, for all age groups

31%

of children aged 0–11 years had increased seroprevalence in the same December 2021 to February 2022 time period

73,869

was the median sample size per 4-week period that the CDC sampled between September 2021–January 2022

28.6%

Was the greatest seroprevalence increase among persons aged 12–17 years, from 45.6% to 74.2%

27.2%

Was second highest seroprevalence increase among adults aged 18–49 years when it went from 36.5% to 63.7%

Source: CDC https://www.cdc.gov/mmwr/volumes/71/wr/mm7117e3.htm?

Antibodies fighting original SARS-CoV-2 virus weaker against omicron

A recent study from Johns Hopkins Medicine and the National Institute of Allergy and Infectious Diseases suggests vaccine-derived antibodies that prevent binding by the original strain of the virus, SARS-CoV-2, do not work as well with the omicron strain, leaving even vaccinated and boosted people open to breakthrough COVID-19, according to a news release.

Research findings were posted online, in the *Journal of Clinical Investigation Insights*.

"Previous research has shown vaccine-induced antibodies respond to the original strain of SARS-CoV-2 by inhibiting the virus's ability to bind to angiotensin-converting enzyme 2 [commonly known as ACE2], the receptor on a cell's surface through which SARS-CoV-2 gains entry," says study senior author Joel Blankson, MD, PhD, Professor of Medicine at the Johns Hopkins University School of Medicine. "Our study suggests those same antibodies yield less ACE2 inhibition with the omicron strain, opening the door to a breakthrough COVID-19 infection."

To conduct their study, Blankson and his colleagues analyzed both the humoral (SARS-CoV-2 specific antibodies circulating in the bloodstream and produced by B lymphocytes, or B cells) and cellular (direct attack on the virus by T lymphocytes, or T cells) immune responses in 18 healthy and fully vaccinated people, ages 23 to 62 (mean age of 30), who experienced breakthrough infections within 14 to 92 days (median of 50 days) after receiving a booster COVID-19 vaccine. Fourteen participants received a booster of the Pfizer-BioNTech messenger RNA (mRNA) vaccine, one was boosted with the Moderna mRNA vaccine, and the remaining three had an mRNA booster following their initial dose of the Johnson & Johnson viral vector vaccine.

The humoral and cellular immune responses of those participants with breakthrough infections were compared with those from a control group of 31 participants, ages 21 to 60, who received similar COVID-19 vaccinations and boosters, and had no prior infection with SARS-CoV-2.

Although the researchers were not able to document that the breakthrough infections were from the omicron strain, they say it's a strong probability because the omicron variant accounted for more than 90% of the COVID-19 cases treated at The Johns Hopkins Hospital (where the study was conducted) during the time when the study participants became symptomatic.

"When we tested antibody-mediated inhibition of SARS-CoV-2 spike protein binding to ACE2, we found that serum from study participants with breakthrough COVID-19 — most likely the result of omicron infection — had antibodies that strongly stopped binding by the original strain virus as expected but didn't carry out that function as well when responding to the omicron strain," says Blankson.

The levels of antibodies that inhibited spike protein binding to ACE2 — high for original strain virus but reduced for omicron — were similar for both the participants with breakthrough infections and those in the control group.

The specific reduction in ACE2-inhibiting antibodies responding to omicron, Blankson says, differs from what was seen in previously studied breakthrough infections with the alpha variant. In those cases, infected individuals were found to have lower overall antibody levels to the original virus strain.

This was shown in a second recent study, also co-authored by Blankson, looking at the blood plasma of 15 mRNA vaccine recipients.

"The comparable strong T cell responses for the original and omicron strains in both studies could explain why people, like our study participants, who have breakthrough COVID-19 cases typically experience only mild symptoms during the course of their illness," he explained.

Mothers with postpartum depression benefit from screening

Cedars-Sinai researchers identified comprehensive nurse training as key to successful hospital screening for mood disorders after childbirth. Nurse education is the key to successfully screening women for postpartum depression, which affects some 15% of mothers, according to a new quality improvement (QI) study from Cedars-Sinai.

"Training that helped nurses get comfortable with the topic of depression and to develop a non-judgmental attitude and openness to a patient's questions and concerns is critical," said Eynav Accortt, PhD, principal investigator of the QI review and Director of the Reproductive Psychology Program at Cedars-Sinai.

Depression and anxiety during pregnancy or in the first 12 months after delivery is one of the most common perinatal medical complications. Postpartum depression that sets in after childbirth is often characterized by per-

sistent sadness, fatigue, feelings of hopelessness and worthlessness and trouble sleeping or eating. Some women find it hard to care for their new baby.

Hospitals have been urged to institute postpartum depression screening and referral programs to identify and help women struggling with their mental health. Effective programs and procedures for screening can be challenging to develop. A new quality improvement (QI) initiative by Cedars-Sinai investigators in the Department of Obstetrics and Gynecology identified nurse training and education as key to successfully screening women in their care.

"Our research also revealed that framing the screening as part of the medical center's commitment to family wellness, as opposed to only using the term 'depression,' was helpful. It allowed us to normalize the challenging transition to parenthood these patients often experience," said Accortt, a Clinical Psychologist and Assistant Professor in the Department of Obstetrics and Gynecology.

The initiative, Implementing an Inpatient Postpartum Depression Screening, Education, and Referral Program: A Quality Improvement Initiative, is published in the *American Journal of Obstetrics & Gynecology–Maternal-Fetal Medicine.*

Nurses are often on the frontlines of screening programs for postpartum depression, but nursing schools rarely require training in mental health screening or education. Reviewing data involving over 19,500 women who gave birth at Cedars-Sinai allowed investigators to evaluate the benefits of additional training for the nurses charged with accessing new mothers for depression.

"We recognized that we needed to do a better job identifying patients at risk before they went home from the hospital," said Sarah Kilpatrick, MD, PhD, senior author of the QI study, and the Helping Hand of Los Angeles Chair in Obstetrics and Gynecology at Cedars-Sinai.

"We learned that it is a complicated process requiring dedicated collaboration between nurses, physicians, and information technology personnel to make the system work. Our framework should be reproducible in other hospitals, thus helping even more families recognize and better manage postpartum depression," said Sarah Kilpatrick, MD, PhD, chair of Cedars-Sinai's Department of Obstetrics and Gynecology.

An important tool for evaluating a patient for postpartum depression is a special questionnaire designed to identify the presence and seriousness of a mood disorder. Because many nurses called on to administer the questionnaire within two days of a patient giving birth had concerns about doing it correctly, an important quality improvement measure was in-service training; nurses observed a clinical psychologist demonstrate the process with a staff member playing the role of the patient.

If the results of a new mother's questionnaire suggest she needs help before she leaves the hospital, a visit with a social worker can be scheduled.

"The social worker begins by being a caring, nonjudgmental, listening ear and provides support and resources based on the patient's needs. She might consult psychiatry if the woman seems unstable and in need of a full psychiatric evaluation. Otherwise, she might provide a referral to our Reproductive Psychology Program or to our patient navigator, who can help connect her to care in the community," said Accortt.

The postpartum depression screening program at Cedars-Sinai has expanded to include outpatient follow-up. A screening initiative for women who have experienced a stillbirth or who are in the obstetrics intensive care unit has also been implemented.

"If we care about our patients' mental health, screening must be made routine, just like we screen pregnant patients for diabetes. It must be done in such a way that patients feel comfortable answering the questions truthfully, and there must be consistent follow-up of patients at risk for postpartum depression once they leave us," said Kilpatrick.

Asthma, hypoxia, and lung damage

New research from scientists at La Jolla Institute for Immunology (LJI), shows that hypoxia can activate the same group of immune cells that cause inflammation during asthma attacks, according to a news release.

Hypoxia, a lack of oxygen, can have long-term effects. In fact, doctors describe hypoxia as an "initial insult." As a person gasps for breath, these cells flood the airways with molecules that damage the lungs.

Experiencing hypoxia is a known trigger for developing and worsening lung conditions such as severe asthma, chronic obstructive pulmonary disease (COPD), and fibrosis. To treat and prevent these diseases, researchers need to understand why a lack of oxygen would affect the immune system.

"We show how lack of oxygen can be part of a feedback loop that can contribute to even worse inflammation," says LJI Professor and Chief Scientific Officer Mitchell Kronenberg, PhD, a member of the LJI Center for Autoimmunity and Inflammation. "This work gives us insight into the causes of fibrosis of the lung and severe asthma."

Kronenberg and his colleagues worked with a genetically altered mouse model to mimic the signals of hypoxia in the airway's epithelial cells, which line the paths to the lungs. They discovered that combining the hypoxia signals with inflammatory signals stimulated the "innate," or rapidly responding immunity, and an immune cell type called an ILC2.

An ILC2's job is to make signaling molecules (called cytokines) that quickly alert other immune cells to react to a pathogen. Unfortunately, ILC2s sometimes over-react and respond to harmless environmental allergens. In these cases, ILC2s churn out cytokines that drive mucus production and inflammation in the lungs. All this swelling and mucus leads to hypoxia.

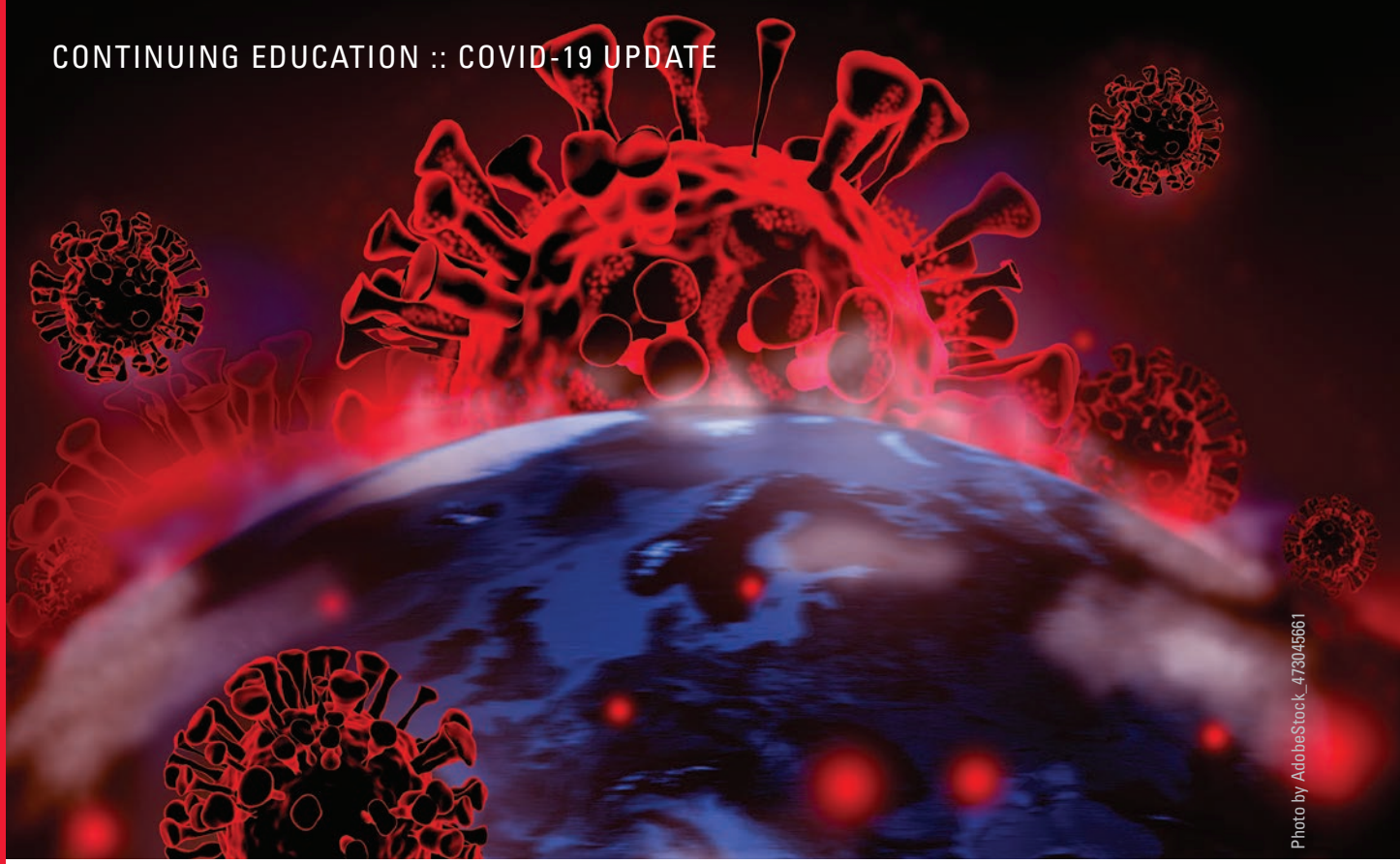
As they report in Journal of Experimental Medicine, ILC2s respond to hypoxia as well, adding to the lung damage already caused during an asthma attack.

"That hypoxia may then contribute further to inflammation," says Kronenberg.

The next step was to figure out exactly how epithelial cells activate ILC2 during hypoxia. LJI Postdoctoral Fellow Jihye Han, PhD, led the work to uncover an unexpected culprit: adrenomedullin (ADM). ADM is known for its role in helping blood vessels dilate, but until now it had no known role in immune function.

Kronenberg was surprised to see ADM involved—but not shocked. "We're finding that many molecules with no previously known role in the immune system can also be important for immune function," says Kronenberg.

The researchers showed that human lung epithelial cells exposed to hypoxia also produced ADM. This means ADM or its receptor could be targets for treating inflammatory and allergic lung diseases. The challenge is to find a balance between dampening the harmful immune response without leaving the body vulnerable to infections.



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SARS-CoV-2 sequencing for public health impact

By Noah Kojima, Eugenia Khorosheva, Lauren Lopez, Mikhail Hanewich-Hollatz, J. Cesar Ignacio-Espinoza, Matthew Brobeck, Janet Chen, Matthew Geluz, Victoria Hess, Sophia Quasem, Nabjot Sandhu, Elias Salfati, Maria Shacreaw, George Way, Zhiyi Xie, Vladimir Slepnev, and Jeffrey D. Klausner

Like many viruses, coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), mutates.[1] When mutations occur in key proteins, the virus can become more transmissible, become resistant to certain treatments, and gain the ability to evade antibody-mediated immunity. When that happens, the strain may be classified as a variant of concern.[2,3]

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LEARNING OBJECTIVES

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

1. List and describe COVID-19 variants that have swept through the US population.
2. Discuss the study performed in LA County and Riverside County as it relates to: participants, samples transportation, validation and useability.
3. Describe results and finding of the study performed in LA County and Riverside County.
4. Discuss how future variants will be tracked and ways to keep the spread under control.

Following the initial reports of SARS-CoV-2 infections in China and Italy, the United States was not prepared for a pandemic of a novel respiratory virus. The initial SARS-CoV-2 detection assay developed by the US Centers for Disease Control and Protection had performance problems,[4] the supply-chain for clinical diagnostic supplies was inadequate.[5] and the public health system was neither prepared for the volume of SARS-CoV-2 testing nor surveillance for SARS-CoV-2.[6] To have effectively responded to SARS-CoV-2, the rapid expansion of diagnostic testing and variant surveillance was needed early in the pandemic period.[7]

Following the initial wave of the wildtype strain of SARS-CoV-2, the first identified variant of concern was the Alpha variant (UK variant), which spread approximately 50% faster than the wildtype strain.[2] Following the Alpha variant of concern, the Beta (South Africa), Gamma (Brazilian), Delta and Omicron variants of concern were identified.[8,9] Currently, the Omicron variant with its sublineages is the most prevalent SARS-CoV-2 variant of concern in the United States,[10,11] with new variants actively being identified.[12]

As evidenced by the Omicron variant,[13] the transmissibility and ability to evade antibody-mediated immune protection can increase. Due to the major public health concern of SARS-CoV-2 and identified variants, we used a private SARS-CoV-2 clinical laboratory's infrastructure and newly developed clinical research and sequencing capacity to monitor SARS-CoV-2 variant frequency and distribution in two large counties in California.

Participant characteristics

We enrolled adults (18 years or older) in Los Angeles County and Riverside County who recently tested positive for SARS-CoV-2 by PCR (Curative, San Dimas, CA). Participants were required to have a positive SARS-CoV-2 RT-PCR result with a cycle threshold value less than or equal to 30 cycles within 5 days of enrollment and sample collection. Trained healthcare workers instructed participants to self-collect anterior nares specimens under direct observation. Individuals meeting eligibility criteria and providing written consent were enrolled in the study.

Subjects considered vulnerable including pregnant women, nursing home residents or other institutionalized people, prisoners, and persons without decisional capacity were excluded from the study. Written informed consent was obtained from each eligible participant prior to enrollment in the study and any specimen collection. The study was approved by Advarra Institutional Review Board under Pro00053729 on May 10, 2021. All research was performed in accordance with relevant regulations in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants.

Sample transportation

Specimens were placed into 10 mL collection tubes containing DNA/RNA Shield Stabilization Solution (Zymo Research, Irvine, CA). Samples were transported to the sequencing laboratory at 2°C to 8°C within 5 hours of specimen collection and stored at 4°C for up to 7 days before library preparation.

Ribonucleic acid (RNA) isolation

RNA extraction was performed using chaotropic agents/silica-based methods. Either manual silica column-based extraction,[33] or a modified automated magnetic silica beads-based extraction method were used. RNA was eluted in 60 mL of 10 mM Tris (pH 7.4). [34]

Library preparation and sequencing

The libraries were prepared using COVIDSeq protocol.[35] On a single 96-well plate, samples were processed alongside a positive control (SARS-CoV-2 BEI NR-52287 genotype A) and a negative control of human nasal specimen without SARS-CoV-2 RNA. Next, 96 indexed sample libraries from each plate were pooled together and quantified using a fluorometer. Four 96-well plates were combined at equimolar concentrations to a total of 384 samples and sequenced. Dilution and loading were performed as per the manufacturer's instructions. Dual-indexed paired-end sequencing was performed for 100 cycles or 200 cycles to get a deeper sequencing depth. Sequencing aimed to have 1 to 2 million reads per sample.[37]

Quality control of reads

Paired-end reads were filtered and trimmed to reduce low quality base calls in the analysis and to eliminate the presence of primers and adapters. A minimum quality score of 30 was selected (pTrimer-1.3.4 -a Primers.bed -q 30 -t pair).[14]

Mapping

Paired-end reads were then mapped against the 'Wuhan seafood market pneumonia virus isolate" Wuhan-Hu-1 genome (Accession number: NC_045512.2),15 using bwa.16 Each read was aligned (bwa aln -t 8 NC_045512.2.fasta), then alignments were paired with the sampe option. Alignment files were then subsetted using samtools view to consider only proper pairs with a quality score larger than 12 (samtools view -bS -q 12 -f 0X2).[17]

Validation

To validate the SARS-CoV-2 sequencing assay, BEI SARS-CoV-2 samples were used as control samples.[18] Sequencing libraries were prepared by two operators. Each operator would prepare 16 replicates of BEI 52287, which would be used as the positive control in clinical sample testing, and one library for each of the other 13 BEI standards. All extracted nucleic acids from the BEI samples were verified to contain SARS-CoV-2 RNA. Ct values were between 26 and 29 for each sample before proceeding to cDNA synthesis. cDNA synthesis and library were prepared. Finished libraries were enzymatically normalized and pooled. Pooled libraries were quantified with KAPA qPCR and pooled together in equimolar concentrations to make a standardized final pooled library. [38]The final pooled library was sequenced and analyzed with the protocol listed later.

Variant calling and consensus genome generation, mutation identification, and variant identification

Variable sites were generated, regardless of coverage depth assuming a haploid genome using bcftools (bcftools call -mv -Ov).[17]Variable sites were then filtered for quality (20) coverage (20x) and minimum allele frequency (0.25). Finally, the consensus genome was generated using the VCFcons.py script (VCFCons.py --input_depth TEMP.depth --input_vcf sample.vcf --vcf_type bcftools -c 10 -f 0.25 -q 20), part of a CoSa suite.[39] Consensus genomes were then run on the command line version of both: pangolin and nextclade.[19]

Ad-hoc analysis

Custom scripts were used to calculate sequencing, effort, and the percentage of reads used to assemble de novo genomes and base pair coverage. These can be found at (https://github.com/curative/bioinformatics).

Analysis of consensus sequences mutations and identifying similar isolates

A lineage comparison was done using Outbreak.info resource created by Scripps Research. A search for genomic sequences similar to the identified SARS-CoV-2 isolates was performed using Nucleotide BLAST 2.6.0+. Isolated were compared to all sequences available on the Global Influenza Surveillance & Response System (https://www.epicov.org/epi3/cfrontend#2c08bd). Data underwent alignment to identify gaps in generated consensus sequences and to match them with positions in amino acid sequences carrying hallmark mutations using software.[40]

Reporting

Results were submitted to Global Influenza Surveillance & Response System EpiCoV database for widespread data sharing and surveillance, a public surveillance service.[20,21] The accession numbers were added to the Global Influenza Surveillance & Response System.

Useability

From May 27, 2021, to January 11, 2022, 820 recently tested SARS-CoV-2 positive participants were enrolled and underwent specimen collection. Of those enrolled, there were 408 (49.8%) females, 570 (69.5%) vaccinated, and 351 (42.8%) of Hispanic or Spanish origin. Median age of participant was 43 years (IQR: 33, 53). Of the cohort, 803 (97.9%) participants had symptoms at time of collection. The time from specimen collection to sequence result was reduced to three days. During the study period, we observed a decreased prevalence of Alpha, Gamma, Iota, Lambda, which was replaced by Delta, then Omicron variant of SARS-CoV-2 **(Figure 1)**.

The view from here

In all, outpatient SARS-CoV-2 variant surveillance could be conducted by a private laboratory in a timely and accu-

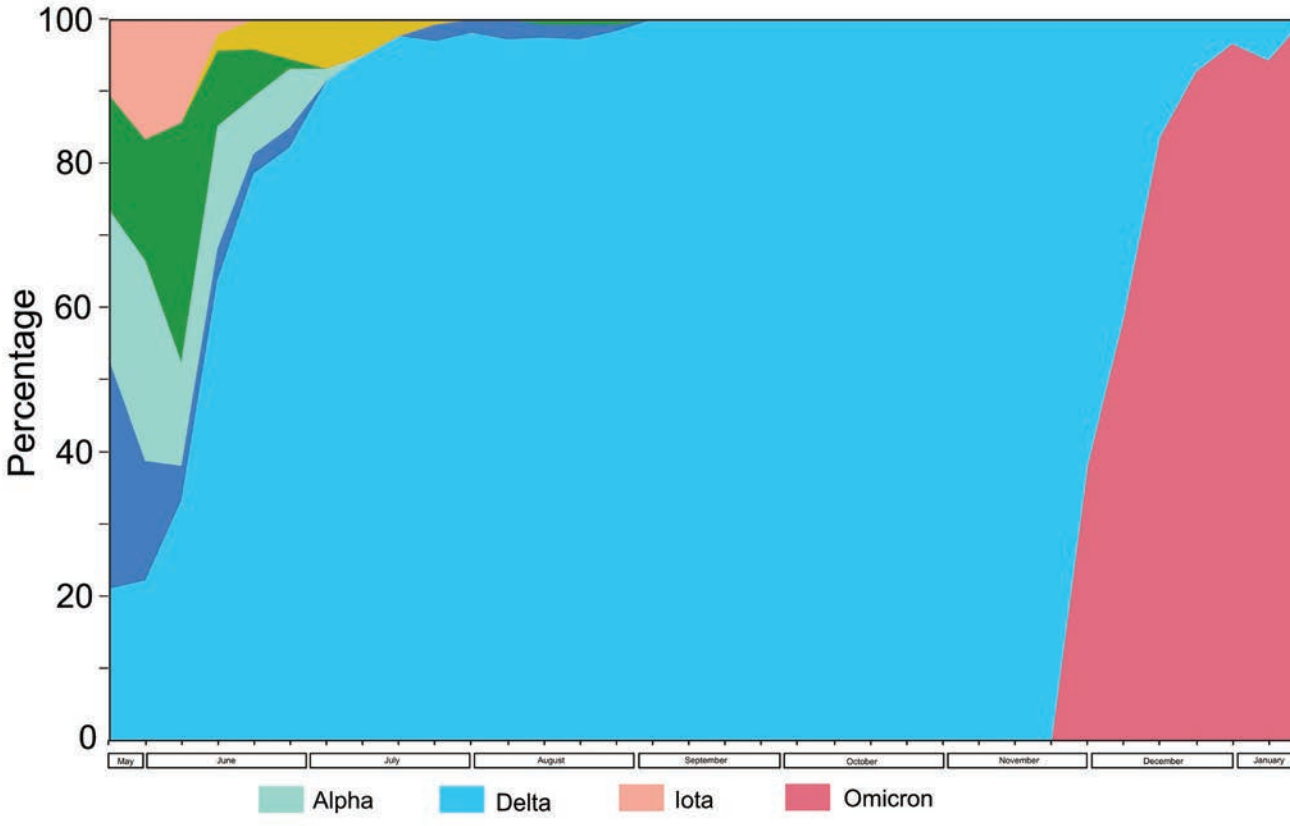

Figure 1. SARS-CoV-2 expanded lineage data over time from a cohort of outpatient participants in Los Angeles County and Riverside County, California, May 27, 2021 to January 1, 2022 (n= 820)

rate manner. Surveillance programs are needed to monitor SARS-CoV-2 variants to inform public health efforts. With the development of new genomic sequencing tools, it is possible for genomic data to be used to inform those public health responses. The World Health Organization proposed that a strong and resilient global sequencing network that provides useable and timely results is needed to maximize the public health impact of sequencing.[22]

The identification of new SARS-CoV-2 variants in a timely manner is critical to public health. While it is hard to prognosticate the future, it is possible to establish a method to prioritize research when new mutations are discovered on genetic coding segments of key proteins, like the SARS-CoV-2 spike protein.[23,24] Faster identification of new SARS-CoV-2 variants of concern and understanding the rates in their change of prevalence could be critical predictors of new waves of SARS-CoV-2 and met with changes in public health recommendations. This study demonstrates that private clinical laboratories may play a role in the surveillance of SARS-CoV-2 variants of concern.

The sheer number of people who have been infected and the total SARS-CoV-2 infected person-time has led to the rapid evolution of SARS-CoV-2. Local epidemics of populous areas creates a situation in which many new mutations can form due to the large amount of viral spread over a short period of time. Additionally, there are many reports of SARS-CoV-2 detected among many animal species that closely interact with people, which may become reservoirs of infection and future spillover events.[25]

Animal reservoirs

As long as SARS-CoV-2 infections persist, SARS-CoV-2 will continue to mutate, and new variants of concern will arise. So far, farmed mink and pet hamsters have been shown to be capable of infecting humans with SARS-CoV-2.[26] SARS-CoV-2 has also been identified among many domestic and wild animal species, e.g., bats, hamsters, ferrets, minks, cats, white-tailed deer, apes, and pigs.[25] There is evidence that SARS-CoV-2 can be spread among various animal species and between animal species.[27,28]

Some research suggests that spillback of SARS-CoV-2 into other animal species has been observed with accelerating frequency with concerns of rapid adaption that may hasten viral evolution and novel strain emergence.[29] Bashor, et al. observed rapid selection of SARS-CoV-2 variants *in vitro* and *in vivo* studies using cell-expanded SARS-CoV-2 inoculum and viruses recovered from cats, dogs, hamsters, and a ferret following experiment exposure. However, it is not clear how these animal reservoirs will contribute to endemic SARS-CoV-2 infections, mutation of new clinically significant variants of concern, or the risk of zoonotic spread. Given the severity of the pandemic caused by SARS-CoV-2, it seems prudent to not only monitor animal species known to harbor SARS-CoV-2 for presence of virus, but also for potentially dangerous mutations that could develop into new variants of concern.

Tracking future variants into the endemic phase

After the wave caused by Omicron variant of SARS-CoV-2 subsided, there has been a lower global prevalence of SARS-CoV-2 and many countries have rolled back public health

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measures used to prevent the spread of SARS-CoV-2.[30] However, as Tedros Adhanom Ghebreyesus, the Director-General for the World Health Organization, noted, the world will be living with COVID-19 for the foreseeable future.[30] While we now have the basic tools needed to address COVID-19—testing, treatment, and vaccinations, it is clear that areas of our surveillance, public health, and medical systems need to be bolstered. Vaccines importantly continue to prevent severe infections, however vaccine effectiveness against infection wanes with time, new variants of concern can partially evade the immune system, and large populations around the world have not had adequate access vaccinations for SARS-CoV-2.[31] While effective treatments have been developed for SARS-CoV-2, treatments are costly, have supply-chain issues for availability and distribution, and a lack of awareness of treatments causes them to be underutilized.[32] While many testing modalities for SARS-CoV-2 which have been developed including rapid testing and genomic testing, access to COVID-19 testing continues to be a problem, especially among the uninsured. Frequent and routine testing should be made available for the public to help guide public health measures to address local epidemics, and continued genomic sequencing is needed to assess SARS-CoV-2 mutations to monitor new variants of concern.

Conclusions

The tools needed to address SARS-CoV-2 have been developed; however, continued vigilance is needed as the frequency and distribution of SARS-CoV-2 transitions from a pandemic to endemic state. This study demonstrates that timely outpatient SARS-CoV-2 variant surveillance conducted by a private laboratory could be used to inform public health efforts to identify changes in SARS-CoV-2 strains in local communities. Government agencies should engage private clinical laboratories in the surveillance of diseases that threaten the public's health to supplement national disease surveillance networks.

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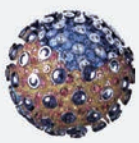	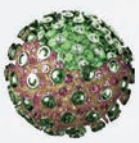	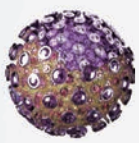			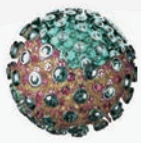	
- RdRP gene - HV69/70 del - E484K - N501Y	- W152C - K417N - K417T - L452R	- L452R - P681R - K417N	- F490S - P681R - L452Q - L452R	- L452Q - F490S - R346K - D950N	- RdRP gene - HV69/70 del - E484A - N501Y	- P681R

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1. What happens to a virus when proteins mutate?
- A. The virus can become more transmissible
- B. The virus becomes resistant to certain treatments
- C. The virus can gain the ability to evade antibody-mediated immunity.
- D. All of the above

2. Currently, which variant is the most prevalent SARS-CoV-2 variant of concern in the United States?
- A. Delta
- B. Alpha
- C. Omicron
- D. Beta

3. Where was the private SARS-CoV-2 clinical laboratory infrastructure and newly developed clinical research lab located?
- A. In two large counties in California
- B. In a large suburb of New York
- C. On a Louisiana college campus
- D. In the heart of Los Angeles' largest medical facility

4. What was one requirement for participation in the study?
- A. Participants must be below the age of 18
- B. Participants must have reliable transportation to and from the laboratory testing site
- C. Participants must have a positive SARS-CoV-2 RT-PCR result with a cycle threshold value less than or equal to 30 cycles within 5 days of enrollment and sample collection
- D. All of the above

5. Ideal subjects for the study include pregnant women and nursing home residents.
- A. True
- B. False

6. Specimens were placed into _____ collection tubes containing DNA/RNA Shield Stabilization Solution.
- A. 15 mL
- B. 10 mL
- C. 5 mL
- D. 0.5 mL

7. How was RNA extraction performed using chaotropic agents/silica-based method(s)?
- A. mmanual silica column-based extraction method
- B. modified automated magnetic silica beads-based extraction method
- C. A and B
- D. None of the above

8. During sequencing, what number of reads are aimed for, per sample?
- A. 100
- B. 200
- C. 1 to 2 million
- D. 5000

9. Regarding the quality control of reads, a minimum quality score is_____.
- A. 30
- B. 10
- C. 100
- D. 65

10. When mapping, paired-end reads were then mapped against the_____.
- A. Shanthi seafood market pneumonia virus isolate
- B. Shanghai beef processing plant viral isolate
- C. Guangzhou rice processing plant viral isolate
- D. Wuhan seafood market pneumonia virus isolate

11. What samples were used as control samples in order to validate the SARS-CoV-2 sequencing assay?
- A. Delta variant samples
- B. Gamma variant samples
- C. BEI SARS-CoV-2 samples
- D. cDNA samples

12. Variable sites were generated, regardless of coverage depth assuming a haploid genome using bcftools (bcftools call -mv -Ov).
- A. True
- B. False

13. Why did data need to undergo alignment?
- A. To identify gaps in generated consensus sequences
- B. To match them with positions in amino acid sequences carrying hallmark mutations
- C. A and B
- D. To rule out any environmental factors

14. Why were results submitted to Global Influenza Surveillance & Response System EpiCoV database, a public surveillance service?
- A. This step is mandated by law
- B. The database service is a safe, secure place to house the results
- C. For the safety of the laboratorians performing the tests
- D. For widespread data sharing and surveillance

15. What was the median age of the study's participants?
- A. 17
- B. 13
- C. 43
- D. 20

16. According to the World Health Organization, a strong and resilient global sequencing network that provides useable and timely results is needed to _____.
- A. maximize the public health impact
- B. allow labs to better schedule their daily testing
- C. help citizens find testing sites
- D. None of the above

17. Why are faster identification of new SARS-CoV-2 variants of concern and understanding the rates in their change of prevalence needed?
- A. So, the mask mandate can be removed
- B. So, large social gatherings can take place
- C. They could help parents make informed decisions about school children's social distancing practices
- D. They could be critical predictors of new waves of SARS-CoV-2

18. There are many reports of SARS-CoV-2 detected among many animal species, which may become reservoirs of infection and future spillover events. Which types of animal species are they referring to?
- A. Feral animals that roam wild
- B. Those that closely interact with people
- C. Air-born creatures
- D. Fish and game wildlife

19. While effective treatments have been developed for SARS-CoV-2, what causes them to be underutilized?
- A. Treatments are costly
- B. There is a lack of awareness of treatments
- C. People are afraid of injections
- D. A and B

20. What is one primary reason why access to COVID-19 testing continues to be a problem?
- A. People can't find testing sites
- B. People are afraid of injections
- C. People are uninsured
- D. People don't have reliable transportation to get to testing sites

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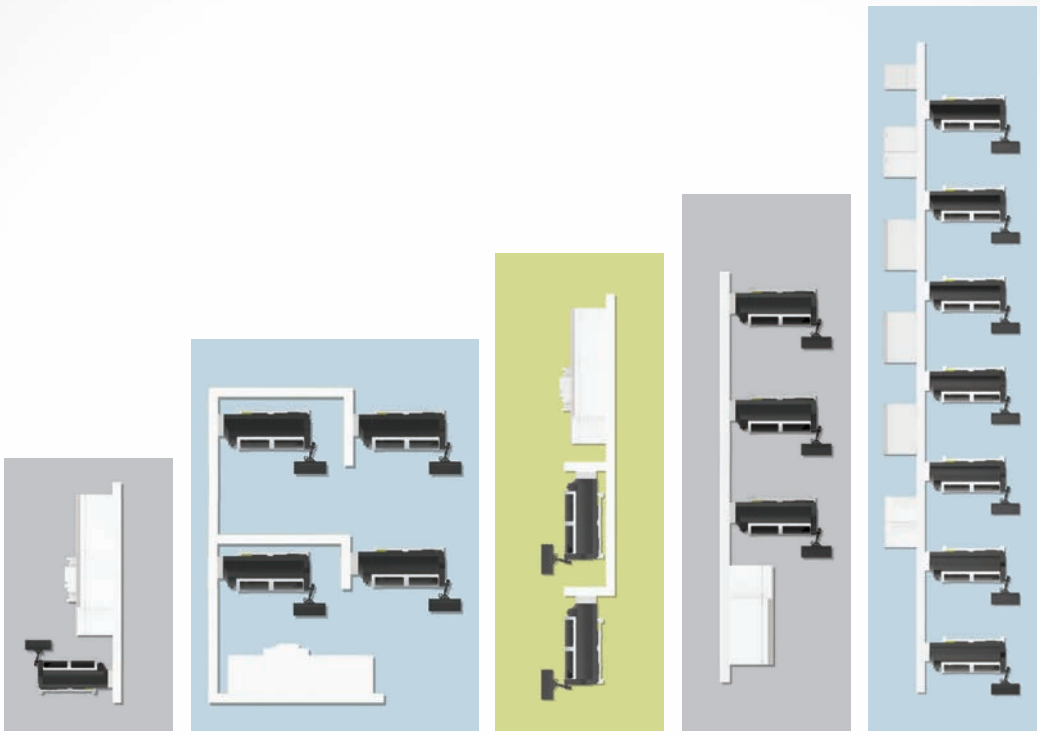

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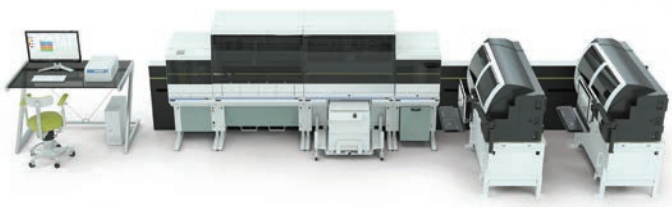

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The clinical value of next-generation sequencing integration within medical laboratories

By Stephen Vella Ph.D.

Infectious diseases (ID) remain at the forefront as the leading cause of morbidity and mortality globally. The intrinsic ability of ID to spread quickly, stealthily to surmount the immune system, and rapidly evolve through beneficial mutations conferred through natural selection is made no more evident through the global disruption caused by COVID19.[1,2] In 1977, Fred Sanger developed the first platform of DNA sequencing that was rapidly and significantly utilized for decades in research and clinical genetics.[3] Later in 1983, Kary Mullis invented the polymerase chain reaction (PCR). These two technologies served as the fundamental foundation of modern day microbial/molecular diagnostics, commonly referred to as nucleic acid amplification tests (NAATs).[2] Even with the advent of NAATs, traditional methodologies such as culture, strain identification, antigen, and antibody detection remain a key component of laboratory diagnostics.[2,4,5]

Sanger sequencing commonly utilizes clonal amplification of adaptor-ligated DNA fragments across the surface of a glass flow cell, yet it is limited in terms of low throughput and complexity.[6] Major improvements and advancements in molecular biology that were transitively incorporated into sequencing technologies led to the development of second and third generation sequencing methodologies, commonly termed next-generation sequencing (NGS). Such innovations led to the milestone achievement of completion of the human genome project.[1,3,6] Nowadays, sequencing turnaround time and cost have dramatically reduced, as well as have become more automated and compact since the early 2000s, thus enabling easier adoption and more practical widespread utilization within the clinician setting and beyond.[2,3]

An immense amount of curated clinical, genetic, and genomic data has emerged through NGS, helping foster the development of more precision based medicine, laboratory diagnostics, and clinical treatment.[2,3] In addition to microorganism identification, NGS has been utilized for detection of antibiotic resistance, single nucleotide polymorphism (SNPs), and the host immune response.[3] The clinical value of NGS has been exemplified, not only at the individual patient level, but as well as, NGS has been utilized to help govern and direct public health and (hospital) infection control strategies. For example, NGS contributed (and still contributes) to the discovery and tracking of SARS-COV2 variants including alpha, delta, omicron, and possible future variants throughout the course of the ongoing global pandemic and currently, Public Health England routinely employs whole-genome NGS to track spread of antimicrobial resistance of M. tuberculosis.[7,8]

Given these developments, the U.S. Food and Drug Administration (FDA) has outlined the guidelines for designing, developing, and validation of approved NGS tests.[3] Generally speaking, both second and third generation sequencing technologies share nearly identical three step workflows: (1) preparation and extraction of nucleic acid template; (2) preparation of library including clonal amplification; and (3) sequencing and alignment of short reads.[3]

Science and methodology of NGS within the laboratory:

Generally speaking, NGS can be divided into the Sequencing and Data analysis phase **(Fig 1A)**. With regards to the clinical lab, NGS possesses several steps and variables that must be taken under considerations if a clinician or laboratory manager desires to implement NGS within its clinician pipeline, the details of which are outlined in **Fig 1B**.

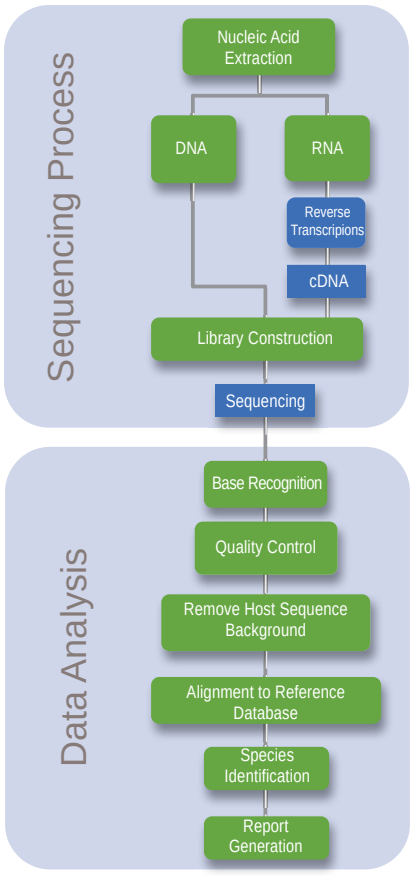
Sample Collection and Preprocessing: As with any diagnostic assay, optimal specimen collection with sufficient volume is fundamental to obtain meaningful sequencing results. The DNA of the intended target needs to be at a sufficient threshold for detection. Thus, the timing of specimen collection serves as an important factor and needs to be taken under significant consideration. For example, if samples are obtained from a patient that is undergoing or about to receive antibiotics, this treatment may adversely impact the levels of DNA needed for quality results.[5,9]

Nucleic Acid Extraction: Similar to nearly all NAAT based assays, the first step is nucleic acid extraction from the specimen. Due to the enhanced sensitivity and capability of detecting DNA or RNA from any organism, precaution needs to be taken to limit the risk of contamination of the extraction reagents. For example, the commensal flora of laboratory personnel can contaminate laboratory reagents and risk leading to inappropriate patient diagnoses.[5]

Library Preparation and Clonal Amplification: Post extraction of sample nucleic acid (whether it be DNA or RNA), the specimen is further processed in order to ensure compatibility and optimization for high-throughput sequence analysis. Library preparation is a delicate process comprising several steps that seek to preserve or enrich the pathogen sequences present within the sample, while maintaining the complex, native diversity, that is intrinsic to the sample. Depending on the type and target of the NGS assay (targeted, whole genome, or metagenomic, discussed later), pathogen genetic material can be selectively enriched using differential lysis, DNase or RNAse, mitochondrial and/or ribosomal RNA depletion, or whole genome hybridization. However, most clinical laboratories will likely employ an unbiased strategy utilizing total nucleic acid to more broadly identify for the presence of pathogen DNA. If a more targeted or refined approach is desirable, commonly, spiked targeted primers specific to conserved regions of either bacteria (16S rRNA), fungal (internal transcribed spacer region) or to different clades of viral targets will be added.[3,5,10]

The final step required for creation of the library is the addition of sample barcodes and sequencing adaptors, using standard, common techniques. Sample barcodes are short DNA sequences ligated to the ends of each sample library that allows for the pooling of multiple samples for sequencing analysis and sample identity using bioinformatics. Sequencing adaptors are specialized and specific oligonucleotide adaptors tailored to a given sequencing platform and are commonly added through either adapter ligation or transposase-mediated addition.[5]

(A)



Sequencing: Over the past decade, a massive amount of commercially available sequencing platforms has emerged that offer high-throughput analysis. To generate sufficient data for adequate sequencing analysis, most platforms will pool libraries for sequencing. Quantification of the pooled libraries can be employed using several approaches, such as total DNA quantification, quantitative PCR normalization, and bead normalization. Within the clinical setting, several factors need to be taken into consideration when performing or considering NGS sequencing. All sequencing platforms have an intrinsic error rate that needs to be considered for data analysis. Further considerations include the level of throughput for the number of total sequences obtained as well as their profile length; the number of base pairs obtained; the sequencing depth per sample; and the physical computational hardware for processing and storing large NGS data files.[5]

The Generations of Sequencing Platforms: Post the advent of first generation of sequencing technology of Sanger Sequencing, second and third generation have emerged has the technology has advanced. The umbrella term of NGS includes second and third generation sequencing. Second generation requires template amplification prior to sequencing, while third generation offer de novo assembly in real time without the need of template amplification.[6]

Platforms such as Ion Torrent, Pacific Biosciences, and Illumina are the current frontrunners of second generation sequencing technology.[3] Ion Torrent is unique in its detection method. Unlike other technologies that use fluorescence or chemiluminescence, Ion Torrent detects proton release during nucleotide incorporation of strand synthesis.[3]

Second generation sequencing has significantly revolutionized and advanced the field, yet the technology is not without flaws. Second generation sequencing typically has short sequence reads leading to sequencing gaps, alignment issues due to repetitive regions/pseudogenes, and PCR artifacts.[3] As a means to overcome these limitations, third generation sequencing, offering sequencing at the signal molecule level, was developed. PacBio SMRT and Oxford Nanopore Technologies are the current representatives of third-generation sequencing.[3,6]

PacBio SMRT has a similar library preparation except for specialized adapters to circularize double-stranded DNA fragments. The circularized DNA and DNA polymerase are immobilized and analyzed on a chip. The signal from the incorporation of fluorescently labeled nucleotides is measured via a CCD camera.[3]

Oxford Nanopore uses a novel technology called nanopores. Nanopores are tiny bio-pores with nanoscale diameter, capable of measuring current changes. Each of the 4 types of nucleotides will pass through the nanopore, altering the channel voltage, and lead to a distinct current change that is measured by the platform. Nanopore technology is advantageous of short turn-

(B)

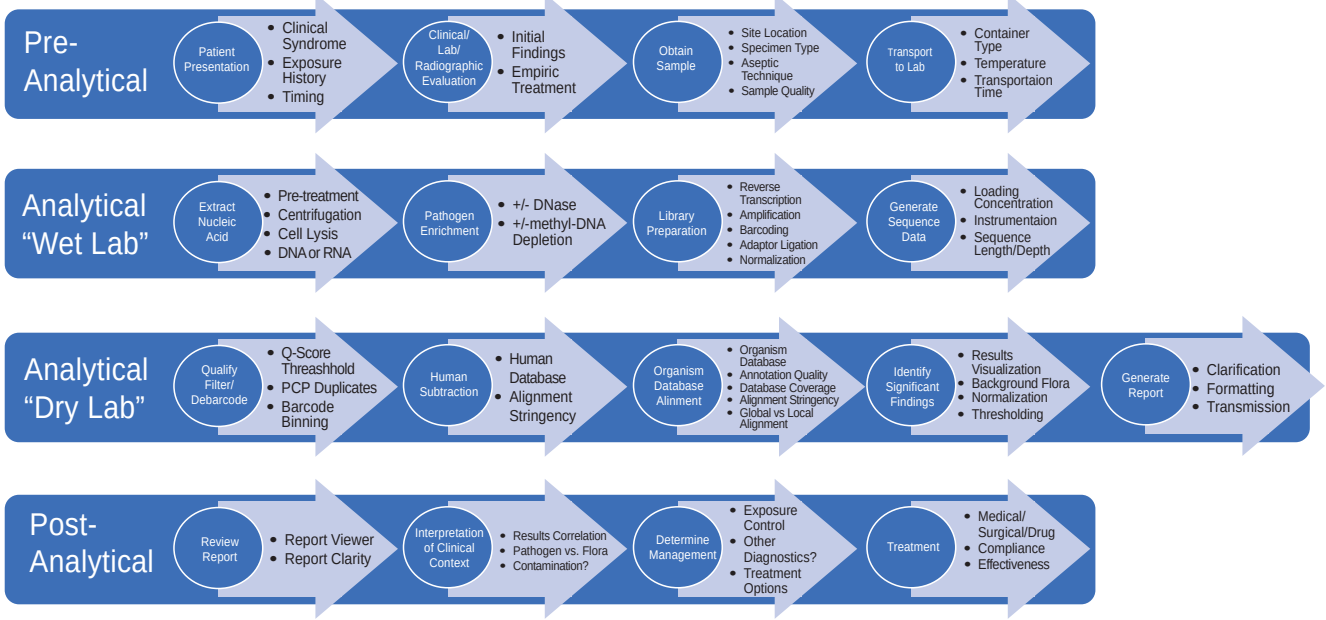


Figure 1: (A) General Flowchart of Next-Generation Sequencing. The general procedure displayed is representative of metagenomic next-generation sequencing. Adapted from Duan et al.[1] (B) Clinical Workflow Considerations of Next-Generation Sequencing. The 4 major steps of Next-Generation Sequencing are Pre-analytical, Analytical (Wet Lab), Analytical (Dry Lab), and Postanalytical. General Considerations and variables significant to clinicians are presented within the arrows. Adapted from Miller et al.[5]

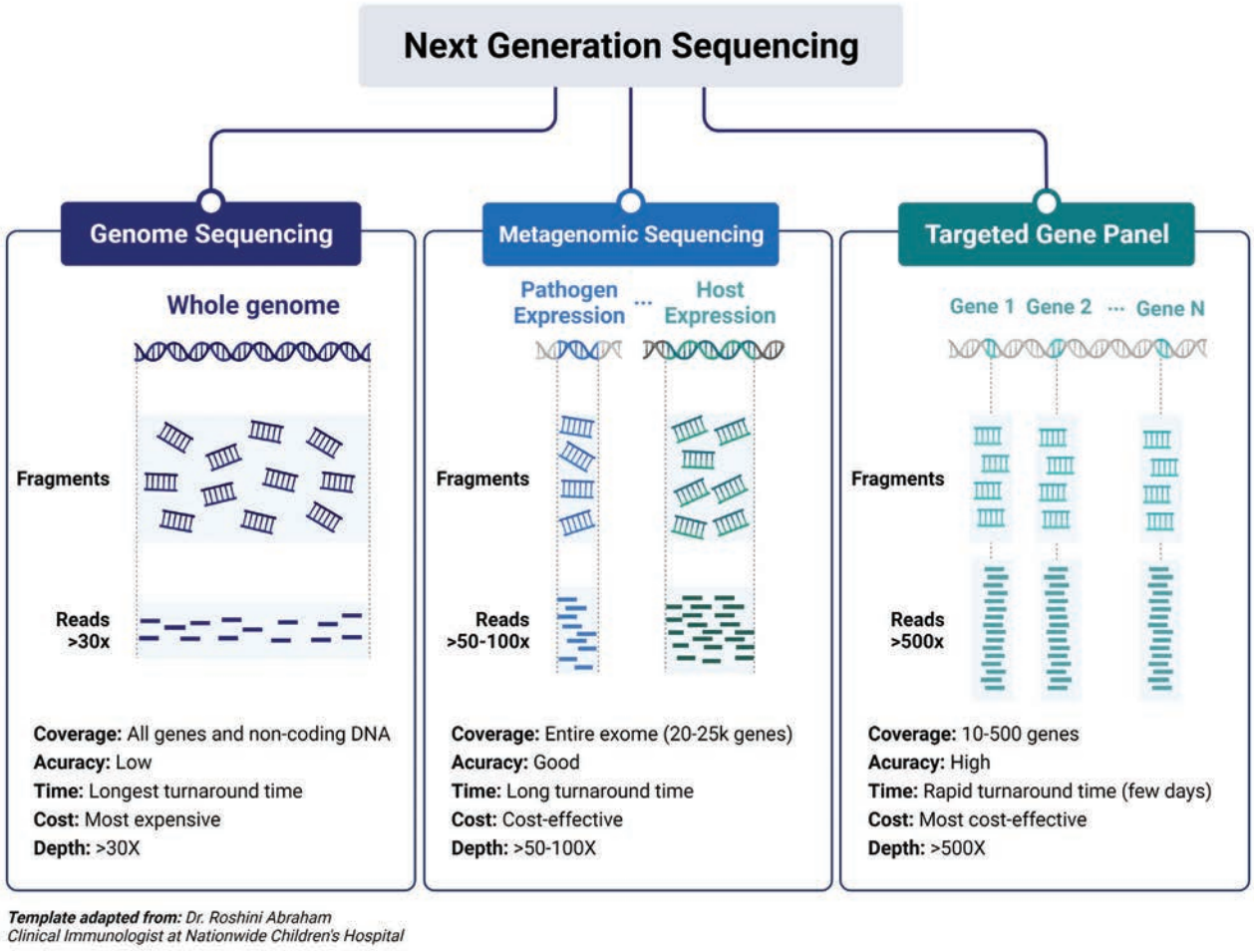


Figure 2: Types of Next Generation Sequencing. The 3 types of Next Generation Sequencing are outlined above and within the text of the manuscript. Figure created from BioRender with Publication License

around time and no GC bias, yet has the disadvantage of nanopore technology is its high sequencing error rate.[3]

Bioinformatic Data Analysis: Bioinformatic sequencing data analysis involves a multistep well-established pipeline as a means to identify any pathogen sequences present in the sample. Generally speaking, the sequential major steps are quality filtering, human subtraction, alignment to a (pathogen) database, taxonomic characterization, and genome mapping. The confidence of the sample is proportional to the number of sequence reads identified for the organism, normalized to the total number of reads present within the sample, and the overall genome coverage. Optional quantitative controls enable for the determination of the number of molecules per milliliter of organism DNA in the original sample to be determined.[5] The direct clinical application of NGS to detect infectious agents is contingent on the availability of a curated databases to provide a high level of confidence of matched reads against the organisms identified. For example, organism types may not be present in the database thus hampering their detection. Though nucleotide alignment is the most commonly employed analysis strategy, amino acid /protein can be utilized to identify possible divergent organisms.5 NCBI possess a vast amount of curated and uncurated databases that are ever expanding. For example, more than 376,000 bacterial genomes are currently available.[5,6]

In order to offset the magnitude of data achieved from NGS a number of software platforms have been developed, a significant investment cost that could likely hinder more universal acceptance within the clinical lab.[11] A number of software platforms, both commercially available (bioMérieux Episeq, Illumina, Bio-Rad's SeqSense, Qiagen's OmicSoft Suite) and open source software suites, are readily available. Episeq, designed developed by bioMérieux; as well as, several open source platforms provide cloud-based computing thus offering an attractive alternative to limited in-house analysis.[11]

Clinical utility and interpretation of the report analysis of NGS:

Similar to all diagnostic assays, the clinical, real-world utility of NGS testing is dependent on a number of critical factors to consider: (1) the patient presentation, symptom severity, and timing of sample collection; (2) the sample quality, location, and infection source type; and (3) the native operational characteristics of the assay, including but not limited to analytical sensitivity, specificity, and detection range.[5]

Post analyzation, a results report is generated with clinically relevant information including the organism(s) identified with associated relevant sequencing metrics and comments for potentially clinically significant results. For example, detection of contamination of endogenous or environmental flora or unusual or highly pathogenic organisms will likely be flagged with comments.[5]

The major clinical application within microbiology laboratories are: whole genome sequencing, metagenomic NGS (mNGS), and targeted NGS (tNGS) **(Fig 2)**.[3,10] Whole-genome sequencing involves sequencing and assembly of an entire template within a clinical sample, enabling simultaneous typing of any microorganism or virus genome; and in some cases, identifying resistance gene/mutations/prediction of antimicrobial susceptibility of a given strain.[2] Generally speaking, a pure sample

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of colony is needed for this approach.[8] A more mass and widespread approach, metagenomic sequencing, involves sequencing all available templates within a clinical sample including pathogen and human DNA and RNA. This approach is advantageous in that it does not requiring culturing and takes an unbiased approach, enabling for the detection of numerous pathogens (and the associated host response against them). Finally, targeted NGS is similar to metagenomic yet is more refined, focusing on a subset of genes. Targeted NGS first enriches for sequences of interest before the preparation to enhance analytical sensitivity. Contingent upon the focus of the specific disease or disorder, this can range from several to a few hundreds of gene targets.[3,10] For example, panels can be specialized to target bacteria, viruses, and eukaryotic pathogens.[3]

Whole genome sequencing's ability to sequence and assemble an entire genome with plasmids is advantageous within the clinical laboratory as a means to identify antimicrobial resistance profiles thereby influencing first-line drug implementations. Recently, whole-genome sequencing proved beneficial to detect and characterize the emergence of several patients suffering from pneumonia from an unknown cause from Wuhan, China. While the initial sequence was of unknown origin, later bioinformatic analysis identified similarity to beta-coronaviruses and termed SARS-CoV-2 thus exemplifying the benefit of whole genome sequencing in identifying novel organisms and/or mutations.[3,10]

Metagenomic NGS has proven beneficial when targeted or less comprehensive tests fail. Given its wide inclusivity and lack of requirement of previous knowledge of potential pathogens, several clinical tests have been developed from a variety of patient samples including: synovial fluid, CSF, feces, corneal tissue, blood, plasma, nasopharyngeal swabs, and joint fluid as a proxy to diagnose various types of infections.[3,10] Body fluid samples can possess significant complexity in terms of the biodiversity present and metagenomic NGS enables for detection of low-prevalence templates within the entire sample that would have likely been missed by other diagnostic means.[3]

A limitation of Metagenomic NGS is the disproportionate ratio of host to pathogen nucleic acid reads thus decreasing the analytical sensitivity of the assay. Targeted NGS improves analytical sensitivity by first enriching for highly conserved regions of pathogens, such as the 16S rRNA in bacteria. Targeted NGS has proven beneficial in terms of contributing to public health, such as enriching for SARS-CoV-2 RNA in clinical samples as a means to track the rise of variants.[3,10] Targeting NGS of both the host and its associated flor3a can serve as an indicator of the general well-being of the patient. For example, sequencing of the gene expression of a patient's immune response gene profile combined with sequencing of commensals and pathogen genomes lead to the correct identification of the causative agent with high sensitivity and specificity with a true negative predictive value of 100%. Likewise, sequencing of the virome within immunocompromised patients can serve to evaluate the competency of the host immune system, if viral loads dramatically increase under immunosuppressants.

These examples highlight just a few examples of the massive degree of publications available of NGS. It is wide-accepted that NGS possess immense value in contributing to the clinical utility within the healthcare setting. However, these assays are not without flaws. Contrarily, advances are ever ongoing to help contribute to easier adaption within the clinical lab and better patient outcomes.[3]

The Current Limitations to Widespread Implementation: It is accurate to claim that NGS sequencing as a diagnostic tool is still in its infancy.[10] Currently, the most commonly utilized NGS platforms are limited by short reads, reliant upon clonal PCR, have high error rate, requires advanced technical expertise, and guidelines are not universally standardized.[3,10] The process of implementing NGS sequencing requires significant resource investment, including test validation, bioinformatics support, data storage, and overcoming insurance cost hurdles.[3] Most testing is current limited to reference laboratories or academic research centers that can afford such upfront resource investment.[2,10] It is reasonable to assume that as the technology continues to improve to and advance, the threshold for more widespread adaption will decline.[10] As with any molecular based diagnostic assay, testing results alone do not guarantee infection and the asymptomatic colonization.[4]

Conclusion:

Within clinical practice NGS possess mass potential, but as it stands today the most optimal, practical utilization appears to be in patient populations where infection is strongly suspected, yet conventional testing is negative.[10] The field would significantly benefit from a prospective, controlled clinical trial evaluating the clinical utility for unbiased pathogen detection from clinical samples. As it stands today, the majority of publications comprise case reports and retrospective studies comparing the results to the traditional standard of care.[10] It is likely only a matter of time before completion of such types of studies; thus, such research articles would allow for a more convincing argument for clinicians to adapt the application more readily. Likewise, as continual refinements and improvements to the technology continually emerge, NGS can and will be more easily integrated and streamlined within the clinical setting.

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Point-of-care (POC) testing, in the appropriate patient care scenarios, provides significant benefits to patient care. The biggest advantage to POC testing is that by providing faster access to test results, diagnosis and subsequent treatment is expedited. However, to harness that rapid turnaround time (TAT), results must be captured at the point of care and made immediately available to the caregivers responsible for taking action based on those results.

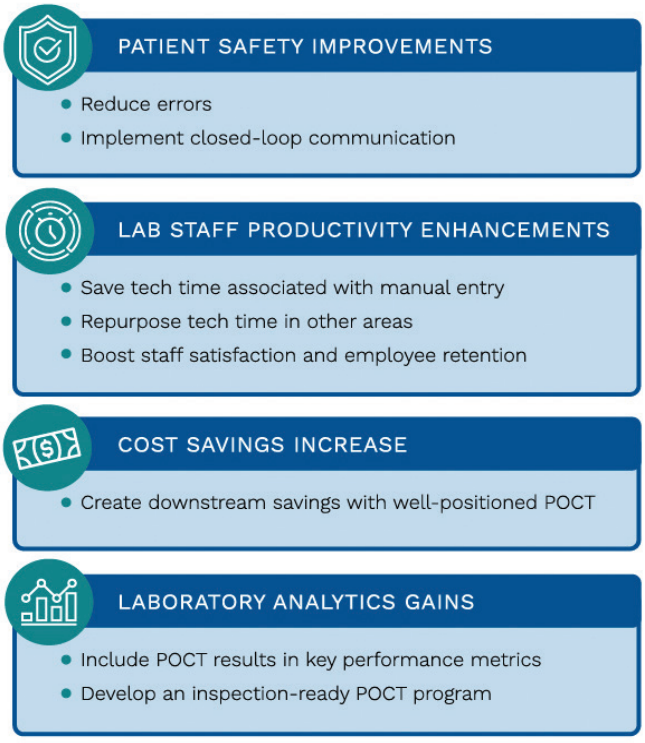
POC testing growth spurred by the pandemic

Prior to the COVID-19 pandemic, POC testing was already experiencing significant growth and broader acceptance. With a renewed focus on improving population health at more affordable costs, the case for POC testing is strong, especially in situations where a quick TAT can have a profound impact on downstream costs and patient outcomes.

With the pandemic came a greater recognition of the value of POC testing and the importance of rapid test results along with an increased demand for reliable testing methodologies. Vendors are responding to this demand with improved methodologies and interfaceable devices, which are also driving adoption.

Benefits of data capture at the POC

To achieve the real-time benefits associated with POC testing, not only does the test have to be performed at the point of care, but also the results need to be electronically captured and integrated into the patient's chart, making results immediately available to the care team. When this is the case, POC testing can improve the efficiency of providers and potentially improve patient outcomes.[1]



Benefits of data capture at the POC

Because POC testing sites can be widely scattered across a healthcare campus, it is important to have a robust POC testing management system to capture important test information and manage regulatory compliance.[2] Ideally, the POC testing program can be efficiently and effectively monitored from a remote location.

Few healthcare organizations have been able to successfully integrate their POC test results into their Laboratory Information System (LIS) and Electronic Health Record (EHR). Decentralization of POC testing makes connectivity more challenging and contributes to the fact that only 10% of POC test results are electronically integrated.[3] The full value of POC testing is only seen when those results are immediately accessible in the patient's EHR.

Opportunity for significant time & money savings

As a primary benefit to the laboratory, capturing POC results at the testing location can save laboratory professionals a significant amount of time when compared to the time it takes to manually type results into the LIS or EHR. Time saved translates into cost savings and efficiency improvements for the entire organization. Below are two examples of integrated POC testing saving technologists' time:

- **Integrated bedside glucose improves lab productivity**

Prior to integrating their bedside glucose testing, a healthcare organization in Nebraska was manually entering thousands of bedside glucose results. Laboratory staff were spending a significant amount of time writing down results at the bedside, traveling to the lab to manually enter results, and performing the required verification of those manually entered results.

Implementing a connectivity solution eliminated inefficiencies and errors associated with manual entry. Their laboratory saved more than 700 hours annually that staff can now use to focus on other tasks. With this example, the potential savings within a large healthcare facility add up to a substantial amount. For instance, a conservative estimate of annual bedside glucose testing volume in a large teaching hospital approaches $70,000 per year.[4] If each glucose takes one minute to manually enter, this is equivalent to 1,167 hours of staff time; multiplied by an average Medical Assistant (MA) hourly wage of $18 per hour,[5] this equates to about $21,000 per year spent in labor costs associated with the manual entry of bedside glucose testing. Calculated using the average Medical Laboratory Scientist (MLS) hourly wage of $36 per hour, it equates to more than $42,000 per year attributed to typing in glucose results.

- **POC testing connectivity saves more than 3,300 hours of tech time**

Prior to implementing a connectivity solution, POC testing operators at a large hospital in Ohio were manually typing results into the EHR or scanning instrument printouts for urinalysis (UA) testing. On average, manually entering results took 2.5 minutes because a UA contains ten or more components to enter; therefore, for every 24 UAs, entering results took an hour of tech time. To put this in perspective, their UA volume is approximately 80,000 per

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year, adding up to 3,333 hours spent manually entering results for that one lab test. Using the average MA wage for entering results, this means that their laboratory spent nearly $60,000 in one year in staff time allocated to this task alone.

In addition, to avoid the labor-intensive method of manually ordering and entering UA results, some of their testing locations were scanning the UA analyzer printouts or hand-written manual log sheets into the EHR because it was easier and faster. In this scenario, data mining for those test results is impossible because there is no discrete data. With a connectivity solution, the lab was able to eliminate this error-prone workflow and gain the efficiencies brought on by a comprehensive POC testing management and connectivity solution.

Patient safety boon

When results are not captured at the time of testing, the opportunity for errors and mishandling of test results increases. There is always the concern that caregivers and providers are not receiving results in a timely manner. Optimizing your organization's health information technology capabilities so that closed-loop communication is in place, via automated ordering and reporting of POC test results, helps ensure patient safety and improves patient outcomes.

Connectivity standards are improving POC testing data capture

Two decades ago, there was no electronic data management for POC testing; results were manually recorded in paper charts or on log sheets in the testing area. To improve connectivity for POC testing, in 2000, the Connectivity Industry Consortium developed POC testing connectivity standards that have since evolved into the Clinical and Laboratory Standards Institute (CLSI) POCT1-A. In 2005, the POCT1-A standard was upgraded to POCT-01-A2. The standard's purpose is to standardize POC test connectivity so that devices are easily interfaced to information systems. CLSI now has a consensus committee that oversees the development of ongoing POC testing standards.

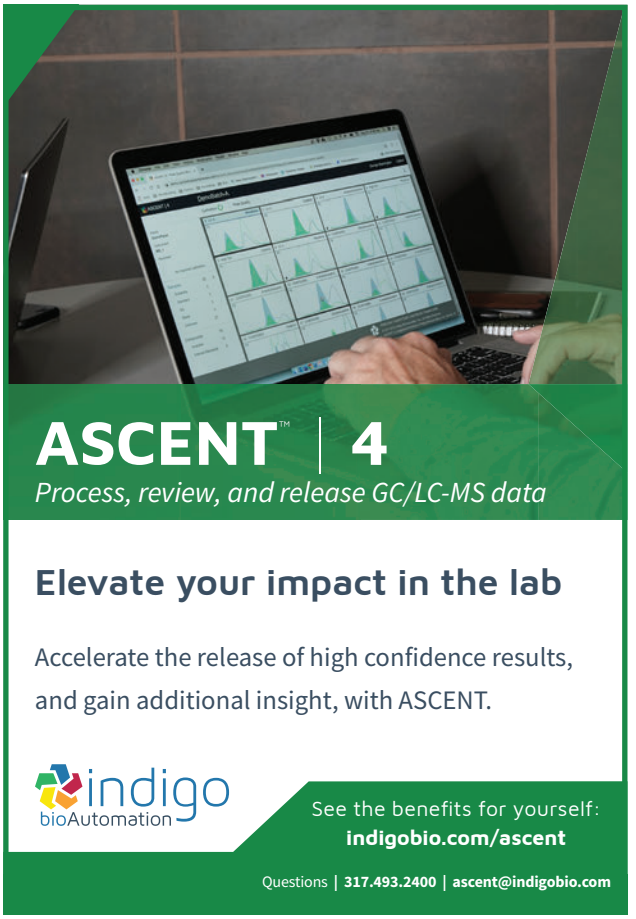
Today, many devices can reduce or eliminate operator and analytical errors, and POC testing management systems are available that enable automatic electronic flow of data from the devices to the LIS and EHR, as well as provide remote access to quality control (QC) and operator certification data.

POCT must be integrated to reach full potential

Having a strong POC testing management system and connectivity solution can dramatically reduce the amount of time spent typing in results, eliminate errors inherent to manually entered results, and facilitate real-time access to results so that providers can make timely care decisions.

When POC test results are captured at the time of testing, valuable savings in tech time are achieved, freeing staff to perform other tasks. Automatically capturing results through POC testing also provides tools that improve employee job satisfaction because laboratory professionals realize that their time and expertise are better used outside of manual result entry. Furthermore, having a closed-loop communication where the order is placed electronically and results transmit back into that system as soon as they are available reduces errors associated with manual entry and that, in turn, improves patient safety.

In the advancing arena of healthcare data analytics to support patient-centered care and population health management, it is no longer a luxury to have POC testing electronically integrated—it is a necessity. POC testing must be immediately available in the patient's chart so that the benefits associated with rapid TAT are fully realized, and the POC test data is included in the overall data snapshot of the healthcare organization to facilitate analytics-driven business decisions.



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Short and long-term effects of the COVID pandemic on cardiovascular patients

By Sean-Xavier Neath, MD, PhD

The COVID-19 pandemic has created a number of diagnostic challenges for clinicians and laboratorians world-wide. Even during the relatively quiet "off-peak" periods of acute COVID, there remain the challenges of helping the large group of patients left with the shrapnel of "long Covid." Kaufman and Meyer, in a recent edition of this journal,[1] present an excellent overview of the evolving long-term health consequences of COVID-19. This article will focus on the cardiovascular elements of acute COVID and long COVID with an emphasis on how deployment of known cardiovascular biomarkers can help aid in the identification, risk-stratification and treatment of patients.

While COVID-19 is primarily thought of as a respiratory illness, it became apparent early in the pandemic that the cardiovascular system is not spared from the effects of the disease. This makes sense mechanistically as the virus gains entry to human cells via the angiotensin-converting enzyme[2] (ACE2), which is ubiquitously present in the body, including the cardiovascular epithelium. Additionally, it became quickly clear that patients with preexisting cardiovascular conditions were at higher risk for going on to develop severe COVID-19 disease.[2] Similarly, patients hospitalized with severe COVID-19 even without pre-existing cardiovascular disease have had a significantly higher rate of cardiovascular complications such as myocardial infarction, heart failure, vascular thrombotic events, and myocarditis. Interestingly, myocarditis and heart failure can also be seen as rare but serious complications of mRNA COVID-19 vaccines absent any active viral infection, particularly in younger men.[3] In all these patient groups, there is diagnostic and prognostic utility of cardiovascular biomarker management using necrosis markers (cardiac troponin), natriuretic peptides (BNP or nt-proBNP), and thrombosis markers (d-dimer).

Throughout the pandemic, a number of biomarkers have been identified to risk stratify patients presenting to the ER with COVID. In particular, either a troponin or a d-dimer value twice the upper limit of normal is associated with severe disease.[5] Mueller and colleagues have published an overview of cardiovascular biomarkers in patients with COVID that helps differentiate some of the nuances in interpretation needed in patients with COVID.[6]

Troponin should be measured in hospitalized patients with COVID, and repeated if abnormal or if new clinical criteria arise. In non-critically-ill patients with COVID-19, modest elevations (up to 3 times the ULN) are often due to prior cardiac disease or myocardial ischemia related to respiratory failure. Higher concentrations (>3x ULN) are more likely to be due to the presence of specific acute cardiac disease such as myocardial infarction, myocarditis, or takotsubo syndrome.

Natriuretic peptides (NPs), such as BNP, nt-proBNP or MRpro-ANP should be measured if heart failure is suspected on clinical grounds. In patients who are not critically ill, NPs cut-offs for heart failure "rule-in" maintain high positive predictive value, even in patients with pneumonia. In contrast, currently recommended NP cut-offs should not be applied in critically ill in patients with ARDS or septic shock, as most critically-ill patients have substantial elevations in BNP/NT-proBNP, due to overwhelming hemodynamic decompensation.

D-dimers are generated by cleavage of fibrin monomers by plasmin, therefore, signal thrombus formation and resulting fibrinolysis. A d-dimer value lower than its assay specific cut-off has a high-negative predictive value to help rule out venous thromboembolism in low-risk patients. In more seriously ill patients, d-dimer can be used for the diagnosis and monitoring of disseminated intravascular coagulation associated with sepsis or shock. During the outbreak of COVID-19, a coagulopathy has been commonly observed in hospitalized patients that can be identified by d-dimer values. One mechanistic explanation is that severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2) has a high affinity to endothelial cells and may induce 'endotheliitis', which

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could explain why d-dimer is higher in COVID pneumonia than other historically seen forms of pneumonia.[7] Similar to the findings reported for cardiac troponin, in patients with COVID-19 the D-dimer values increase progressively in non-survivors whereas values remain around the upper limits of normal in survivors

In hospitalized patients with COVID, monitoring of coagulation parameters can aid to predict deterioration and potentially to guide therapeutic measures including the intensity of anticoagulation. Pharmacologic prophylaxis of venous thromboembolism (VTE) is recommended for all hospitalized patients with COVID (Kim). If VTE is suspected and detected, the patient's anticoagulation should advance from prophylactic to therapeutic dosing. In summary, d-dimer testing sheds light on important pathophysiological aspects of COVID-19 disease as well as contributes to more effective early risk assessment, on guidance on intensity of anticoagulation.

Cardiovascular issues in long-COVID

Post-acute sequelae of SARS-CoV-2 infection (PASC) colloquially understood as "long-COVD" is currently defined by the U.S. CDC as "Broad range of symptoms (physical and mental) that develop during or after COVID-19, continue for ≥2 months (i.e., three months from the onset), and are not explained by an alternative diagnosis."[8] Cardiovascular complaints are common in long-COVID patients. Chest discomfort/pain is frequent and appears to resolve slowly. Chest discomfort persists in 12 to 22 percent of patients approximately two to three months after acute COVID-19 infection. There are a large number of diagnostic and therapeutic modalities being investigated in cardiovascular long-COVID.[9] Suspected myocarditis and/or an unexplained troponin uncovered in a patient's evaluation should lead to a cardiac MRI. In persistently dyspneic patients, natriuretic peptides should be part of the initial workup to investigate for superimposed heart failure on top of any pulmonary disease. Hypercoagulability states typically manifest during acute-COVID and not long-COVID. However, monitoring for persistent, refractory, or recurrent disease should be done when clinically indicated and this evaluation is usually initiated with a d-dimer.

We are also seeing a significant number of patients who are not suffering directly from COVID but have developed cardiovascular issues due to delaying care during the COVID-19 pandemic. Fear of being exposed to COVID-19 in healthcare settings has kept many patients from seeking care in Emergency Departments for potentially life-threatening issues. Also, many routine primary care and specialty care clinic visits have unfortunately been cancelled, postponed, or converted to video visits where important physical exam findings may not get properly discovered. One example of a direct risk would be a patient moving into a more severe stage of heart failure due to delayed diagnosis. Indirect risks are patients that have increased risk factors of COVID-19 complications such as advanced age, coronary heart disease, high blood pressure, stroke survivors, congenital heart defects, and compromised immune systems not getting the care they need in a timely manner. Cardiovascular experts from across the globe have weighed in on the delays to care and the backlog of potentially life-saving interventions and procedures, with a concerning impact on health for many members of society.[4]

While the detailed epidemiologic future of the COVID-19 pandemic remains unfinalized at this writing, this fearsome disease has changed many features of acute cardiovascular care. This has included important new understanding of pathological mechanisms, diagnostics, and therapeutics. Fortunately, a number of excellent cardiopulmonary biomarkers had been developed pre-pandemic; and their performance characteristics have been readily deployed by clinicians and researchers to optimize the identification and risk stratification of the more vulnerable subsets of COVID patients. Many have critiqued our preparedness and our tools used in the course of this pandemic. I would argue that laboratory medicine was better poised to handle the challenges of this pandemic than at any time in the last century. For instance, it is sobering to consider that, if this pandemic had occurred 30 years ago, many of the biomarkers and nucleic acid tests effectively deployed in our current arsenal, including the tests discussed in this article, would not have existed. An unprecedented amount of inflammation and thrombosis accompany this particular viral disease, which may account for much of its ferocious nature. Cardiac troponin, natriuretic peptides and d-dimer testing are three highly useful tools for the clinician to discern the extent of these pathologic processes and intervene as early as possible during the patient's presentation. A "second punch" from COVID has come with the unusual features and complications of disease convalescence that we see in the group of patients suffering from long-COVID. Finally, access-to-care issues during the recent broad societal shutdowns have created a perfect storm of patients with brewing, advancing cardiovascular conditions for whom more rapid assessment and diagnostic evaluation will be essential in addressing these delayed, unaddressed health issues. Fortunately, there is a solid collection of cardiovascular tools already readily available to initiate the investigation and develop personalized treatment plans.

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WSLH Proficiency Testing

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Selecting the right analyzer technology to meet your laboratory's testing needs

By Kara Nadeau

A clinical laboratory's choice in analyzer technology impacts all aspects of its operations, from staffing and workflows to operating costs and quality of testing. With the broad range of analyzers available, lab leaders must carefully weigh their options and select the right technology that meets their lab's needs today and supports future testing volumes and growth.

To help lab professionals determine the right analyzers for their labs, we asked leading analyzer manufacturers to comment on the latest trends in this area, new platforms and features that address current pain points (e.g., staffing shortages, supply chain disruptions), and factors to take into consideration when evaluating the analyzer technology landscape.

Staffing shortages

Lab staffing shortages continue to be a problem across the United States, as evidenced by the results of MLO's 2022 Annual Salary Survey of laboratory professionals, where 43% of respondents said the current shortage has largely impacted their labs' operational efficiency.[1]

Laboratories should consider their immediate needs and the growth goals of the organization when evaluating diagnostic testing solutions, according to Andrea Diebel, Marketing Instrumentation Product Manager, DiaSorin.

"A lab challenged with staffing shortages might urgently need to introduce automated, higher-throughput methods to improve their workflow," said Diebel. "Those with growth mindsets should look closely at the test menu, especially unique offerings and tests in development, and consider the flexibility and capacity of the analyzer family and vendor to grow with them."

When evaluating analyzer technology, Diebel suggests lab leaders ask the following questions:

- Will this analyzer make work simpler for my technicians?
- Can this system reduce send out costs and consolidate testing from other equipment, or even other labs?
- Will this instrument shorten turnaround times, improving the experience for both providers and patients?

"Having these conversations with vendors will help labs recognize the value in their solution," Diebel added.

Process automation

Clinical lab professionals cite more reliable results, reduced errors, and the ability to view and analyze cumulative trends of data as key benefits of lab automation and informatics, yet 74% report that less than half of their lab operations are automated.[2] To meet increased demand for automation, manufacturers are designing analyzers that minimize manual steps and seamlessly integrate with connected systems.

"Total workflow efficiency - both to meet current and perceived future demands - should be the key consideration when looking into purchasing any new equipment for the lab," said Alejandro Mora, Head of Global Marketing, Workflow Solutions, Siemens Healthineers. "One of the key considerations in establishing the smartest workflow is process efficiency and the reduction of manual steps to improve quality, save time, and simplify workflows."

Mora says labs today have more choices than ever when it comes to automated technologies, stating:

"Advances in data and process management have further transformed lab operations by leveraging data to drive smarter workloads and continuous workflow improvements—from reductions in aliquots to save costs or advanced result management protocols to guide patient-specific reflexive testing, to name a few. Smart integration between IT, automation and analyzers is key to realizing these data-driven advances."

Siemens Healthineers has more than 140 workflow consultants that can help labs simplify processes and design optimal workflows, using simulator tools and process mapping to determine and map workflow processes. According to Mora, they can help guide labs in selecting an appropriate automation level, what tasks are automated, and where.

"Based on unique workflow and budget requirements, there are several automation options—from integrated automation to task-targeted automation, to total lab automation—that can enhance efficiencies in the lab," Mora added. "Every lab will have its own set of variables that will guide how to improve space utilization, reduce staff motion, improve the work environment, and reduce material transportation."

Siemens Healthcare Diagnostics Atellica Solution

One solution Siemens Healthcare Diagnostics offers to labs in search of analyzer integrated automation is the Atellica Solution, which consolidates sample management technology, intelligent software, and IT to provide workflow efficiency with the flexibility to automate critical tasks with little or no additional footprint.

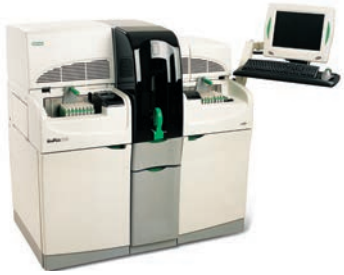
Workflow efficiency

Consolidation of platforms into a single, automated analyzer can help labs maximize their workflow efficiency and achieve LEAN processes, says Maria Crisostomo, BS, MBA, Sr. Sales Core Lab Product Manager, BioPlex 2200 Autoimmune/Infectious Disease Segment, Bio-Rad Laboratories. She recommends labs look for the following features and benefits when evaluating analyzer technology:

- Full automation with random-access sample processing
- Total Lab Automation (TLA) track line connectivity
- Reduced turnaround time, labor, and send-out tests
- Consolidation of tests and analyzers
- Highly secured web-based interface applications for remote monitoring, quality control data management systems and cybersecurity

"These aspects help today's clinical labs address the challenges of managing increasing testing volumes with less personnel and constrained operating budgets, while providing their physician clientele with high quality test results," said Crisostomo.

She notes how the Bio-Rad Laboratories BioPlex 2200 System provides clinical labs a testing solution for maximizing efficiency and productivity, streamlining workflows, and minimizing costs. With over 50 multiplex assays available today and more in development, labs



Bio-Rad Laboratories BioPlex 2200 System

can consolidate platforms for autoimmune, infectious disease, and vitamin D testing on one platform for full automation, trackline connectivity, streamlined workflows, improved turnaround time, and confidence in results.

"The BioPlex 2200 System is an easy-to-use, fully automated, random-access analyzer, utilizing powerful multiplex technology that can produce multiple results simultaneously," Crisostomo commented. "BioPlex 2200 makes managing test panels and complex algorithms as simple as running a single test."

Reliability and uptime

According to Delena Carite, U.S. Group Marketing Manager at Roche Diagnostics, high medical value and positive impacts to patient care are essential factors to take into consideration when choosing an analyzer. She notes how laboratory leaders reported instrument reliability and uptime as most critical for their needs, in addition to an extensive assay menu to complete or expand their offering.

"Understanding the performance of an analyzer in the hands of lab operators, including the length of time between repair

Roche Diagnostics cobas pro integrated solutions

visits or down time, is key," said Carite. "Given the importance of timely turnaround of test results and today's staffing challenges, speed, predictability, and the amount of required operator intervention make a big difference. Features such as continuous loading of reagents and consumables, automated maintenance and extended onboard stability for quality control and calibration can minimize operator intervention."

The Roche Diagnostics cobas pro integrated solutions is a scalable and modular solution for mid-to-high volume clinical chemistry and immunochemistry testing needs. Advanced features help labs optimize workflow, improve productivity, and enhance reliability and turnaround times to support patient care.

"Labs can boost efficiency with high-speed analytical units, intelligent sample routing, and industry-leading assay incubation times," Carite added. "cobas green packs provide more tests/pack and onboard stability of up to six months for chemistry and up to four months for immunoassays. The solution minimizes operator intervention with continuous loading of reagents and consumables, automated maintenance and automated calibration."

Operating costs

When planning capital budgets for 2022, 68% of lab professionals surveyed said they prioritized technology needed to improve quality/reduce costs.[1] Labs operating at lower volumes should evaluate their cost-per-test and turnaround-time, according to Carolina Liquid Chemistries COO Patti Shugart.

"For example, small clinical labs paying more than $5 per Comprehensive Metabolic Profile (CMP) should consider upgrading to a small benchtop chemistry analyzer such as the Medica EasyRA, which offers an extensive menu of urine drug screens and general chemistries with greater ease-of-use, throughput up to 240 tests per hour, and lower cost per test than many other benchtops," said Shugart. "Labs can quickly outgrow slow, expensive, dry reagent disk-based analyzers and should seriously consider upgrading to an analyzer such as the EasyRA."

Clinical considerations

With regards to analyzer throughput, Richard Noel, Director of North American Marketing, LumiraDx, says it really depends on the assay, analyzer, size of lab, and potential clinical impact of the results.

"For example, it's hard to justify running high sensitivity troponin as a batch test once per day if those results are used to determine a treatment pathway for a patient in the emergency room (ER)," he said. "It's interesting that many labs are choosing to bring in next-generation point of care analyzers that provide lab-comparable results in very short turnaround times. They are usually one test per analyzer but can be loaded and run right when a specimen arrives delivering results in minutes."

To speed up test turnaround time and eliminate "sample transport bottlenecks," Diebel suggests that some labs could benefit from a decentralized testing model.

"This model utilizes compact automated specialty testing analyzers to bring testing closer to the provider for better patient care," Diebel explains. "These analyzers may be small, but their innovative features and powerful software streamline the operator's experience. In addition to integrated QC software and LIS connectivity, newer analyzers have managed to eliminate daily maintenance while harmonizing walk-away with up front needs estimations, continuous reagent and sample loading, in-process controls, and improved traceability."

The DiaSorin LIAISON XS is a compact benchtop chemiluminescence immunoassay analyzer belonging to the scalable DiaSorin LIAISON Analyzer family. This random access, fully automated system enables efficient low to medium volume specialty testing capacity in any laboratory setting. Its unique menu includes Gastrointestinal testing, QuantiFERON-

DiaSorin LIAISON XS Analyzer

TB Gold Plus and PCT. All tests utilize DiaSorin's universal reagent Integral format, standardizing operations and results across all LIAISON systems.

As Richard Rollins, Sr. Marketing Manager, Nova Biomedical, explains, clinicians treating patients in high acuity areas, such as the intensive care (ICU), need to be able to make very rapid diagnosis, provide targeted therapy for many complex and rapidly changing diseases, and monitor effectiveness of therapy.

"Test menu, turnaround time, and connectivity are the most important considerations when hospitals select instruments for point-of-care testing in ICUs and hospital wards," said Rollins.

"Having an essential profile of stat tests while at the patient bedside is critical for clinicians to manage these high acuity illnesses."

Rollins points to the Nova Prime Plus blood gas/critical care analyzer, which has been specifically developed for point-of-care testing of high acuity ICU and hospital ward patients. Prime Plus provides the most comprehensive menu of critical care tests from a single 135 µL whole blood sample in about one minute at the point of care. Its menu of 22 diagnostic tests helps clinicians manage a broad spectrum of vital physiological functions, including respiratory function and blood gases; acid/base balance; electrolyte balance including ionized magnesium (one of the most important yet often unmeasured electrolytes); kidney function; fluid balance; anemia; tissue perfusion; and glycemic control.

Nova Prime Plus blood gas/critical care analyzer

Rollins notes how the Nova Prime Plus blood gas/critical care analyzer connects the test results to the patient record and makes them available for clinician review at the patient bedside. He states:

"They are easily connected to the electronic medical record and other data sites with Nova's extensive NovaNet middleware, which is already in use by more than two thirds of U.S. hospitals to connect Nova StatStrip bedside glucose measurements."

Quality control

According to Noel, clinical labs are discovering the utility of next generation point-of-need tests when it comes to quality control (QC), stating:

"Although software features like QC lockouts, operator certification expiration, and expired test strip lockouts were designed to support quality management outside the clinical lab, in conversation with lab directors some have indicated these are great features no matter the setting. The level of stringency may differ but the features themselves are impactful."

LumiraDx Platform is a next-generation point of care testing (POCT) analyzer designed to support a broad menu of tests with lab-comparable performance. The LumiraDx SARS-CoV-2 Antigen test is a rapid antigen test, but more specifically it is a Rapid Microfluidic Immunofluorescence assay.

"What sets our test apart from traditional lateral flow tests is our next generation microfluidic technology," said Noel.

LumiraDx SARS-CoV-2 Antigen test

"In contrast to the passive action of lateral flow methods, our microfluidic technology allows us to control every aspect of the test process including mixing, temperature, timing, incubation, magnetic capture, and signal detection. This next generation technology is how we attain near PCR sensitivity superior to lateral flow methods. Although this is designed to bring lab-comparable testing closer to the point-of-need, several large academic institutions are running this in their clinical lab due to the features discussed above."

Supply chain factors

Supply chain disruptions ushered in by the COVID-19 pandemic continue to impact clinical lab operations. Among lab professionals surveyed in 2022, 58% said they have utilized multiple testing platforms as a best practice to address supply-chain issues during the pandemic.[1]

"In addition to metrics such as throughput and footprint, clinical labs should also consider supply chain risks inherent in the global marketplace when evaluating a new analyzer," said Shugart. "For example, the CLC Family of Instruments from Carolina Liquid Chemistries offers options for testing chloride, potassium and sodium using either an Ion Selective Electrode (ISE) method or switching to a moderate complexity photometric method in the event of supply disruption. The CLC Family, comprising the very high-volume CLC6410, high-volume CLC1600, and mid-volume CLC800, are fully automated and have extensive test menus."

Individual lab needs

Martin Conway, Marketing Manager, Randox Laboratories, reminds laboratory professionals that the choice of analyzer ultimately comes down to each lab's specific needs, stating:

"Laboratories across the globe all differ in testing capabilities, size and experience. There are many different factors that laboratory users should consider such as the throughput of the instrument – does it meet their testing requirements, size of the instrument, ease of use, analyzer downtime/uptime, testing menu, sample types, sample volume, STAT capabilities, QC capabilities, ISE testing and time and cost to the laboratory."

"Laboratory automation and analyzer versatility has driven the demand for larger throughput instruments in the

Randox RX Modena fully automated chemistry analyzer

market such as the Randox RX Modena," Conway added. "However, for some laboratories, smaller benchtop platforms and semi-automated instruments meet particular needs, most importantly, the time and cost savings over dry and wet chemistry laboratory testing, like that of protein specific testing where laboratories can install an RX instrument over a nephelometer."

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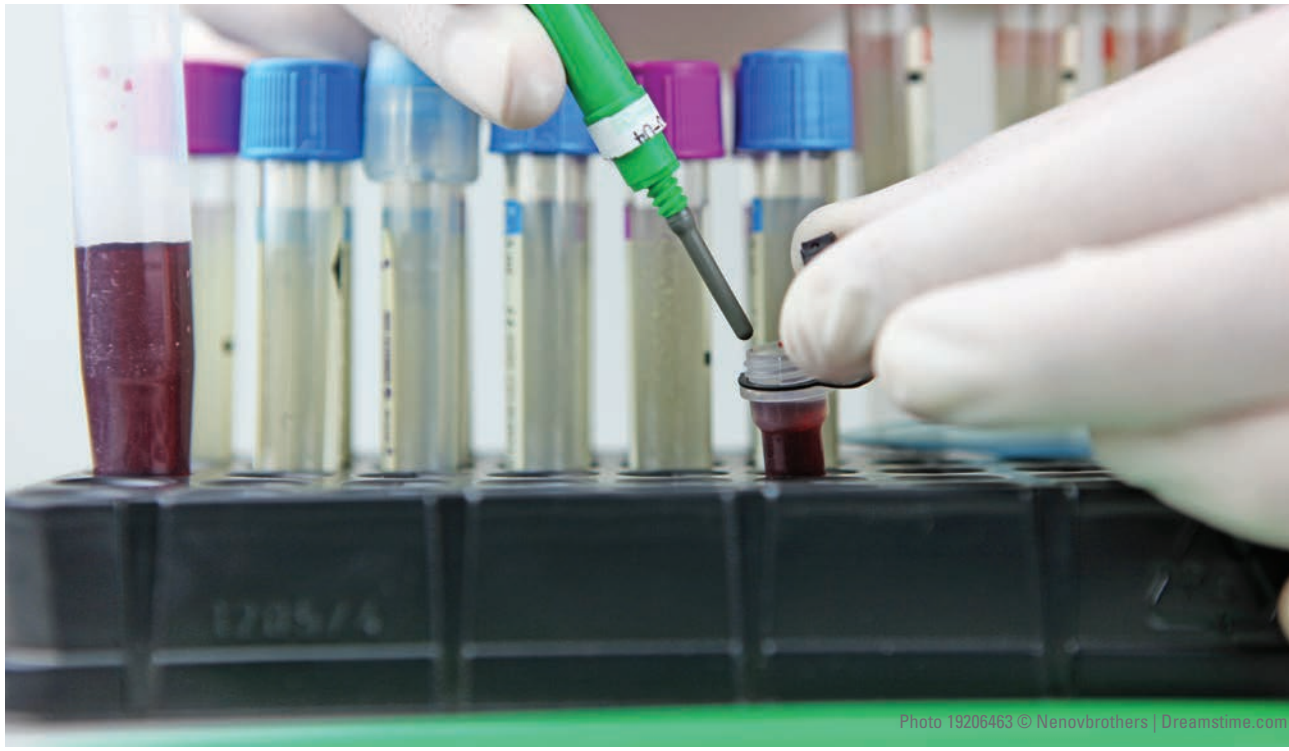


COVID-19's impact on testing practices for sexually transmitted infections

By Kara Nadeau

In April 2022, the Centers for Disease Control and Prevention (CDC) released its 2020 STD Surveillance Report, based on data that "provide(s) the clearest picture yet of COVID-19's impact on the U.S. STD epidemic."[1]

According to the CDC, reported cases of sexually transmitted diseases (STDs) declined during the first few months of the pandemic, which the agency attributes to a drop in testing. Because healthcare facilities were overwhelmed with COVID-19 patients, and others temporarily shut their doors, there were fewer places for individuals to turn for STD screening.

Comparing lab reporting of STDs from April 2019 to April 2020:

- 30% decrease overall in total number of positive STD test results via electronic laboratory reporting (ELR), 40% drop in positive tests via paper reporting
- 38% decrease in positive reactive syphilis serologies via ELR, 49% via paper
- 32% decrease in positive chlamydia results via ELR, 40% via paper
- 15% decrease in positive gonorrhea results via ELR, 34% via paper[2]

The CDC data shows a resurgence in STDs by the end of 2020, as testing once again became widely available, with reported cases of gonorrhea, syphilis, and congenital syphilis surpassing 2019 levels.

"The COVID-19 pandemic put enormous pressure on an already strained public health infrastructure,"said Jonathan Mermin, MD, MPH, Director of CDC's National Center for HIV, Viral Hepatitis, STD, and TB Prevention. "There were moments in 2020 when it felt like the world was standing still, but STDs weren't. The unrelenting momentum of the STD epidemic continued even as STD prevention services were disrupted."

Under its Clinical Prevention Guidance, the CDC describes five major strategies for the prevention and control of STDs - also referred to as sexually transmitted infections (STIs) - with three focused on testing and diagnosis.

1. Accurate risk assessment and education and counseling of persons at risk regarding ways to avoid STIs through changes in sexual behaviors and use of recommended prevention services
2. Pre-exposure vaccination for vaccine preventable STIs
3. *Identification of persons with an asymptomatic infection and persons with symptoms associated with an STI*
4. *Effective diagnosis, treatment, counseling, and follow-up of persons who are infected with an STI*
5. *Evaluation, treatment, and counseling of sex partners of persons who are infected with an STI*[1]

With STD screenings on the rise, clinical labs are faced with higher volumes of tests to process with fewer staff members and shortages of laboratory consumables, including blood specimen collection tubes.

Manufacturers of laboratory equipment and supplies share their insights on the challenges faced by labs in screening for STDs and steps labs can take to diagnose patients with greater accuracy and efficiency.

Process automation

"The pandemic aggravated the pre-existing laboratory staffing shortages brought on by overdemand and burnout," said James Walker, VP of MDx Core & Women's Health and Cancer, BD."Plus, the pandemic saw many more experi-

enced laboratorians retiring. And on top of that, the pandemic forced many people to postpone health screenings."

"Now, as patients get back to doctors' offices to catch-up on delayed screenings, we're likely to see testing volumes rise to pre-COVID numbers or higher," Walker continued. "That means those same already short-staffed labs will be—forgive the word choice—sorely tested themselves. It's a perfect storm of reduced staff—and less senior staff—coupled with higher demand as well as supply chain challenges to secure inventory of the actual tests themselves.

Walker says labs need to take full advantage of automated- and AI-driven or supported processes. He notes how remote system monitoring, redundancy of sub-systems and long walkaway times can help reduce the likelihood of human error while helping meet the demand challenges presented by staffing shortages and increased patient demand on testing resources.

"Integrated automation of the pre-analytical workflow, as well as onboarding capacity of reagents and specimens, enable delivery of several hundred more test results than a human worker can produce with limited intervention – and in a much shorter timeframe,"Walker added.

BD CTGCTV2 assay for the BD MAX System

Sample transport

When patients are waiting hours, days, or even weeks for the results of STD tests, the last thing they want to hear is that the testing was inconclusive and will have to be performed again. Preservation of the specimen during transport from the point of testing to the lab for processing is critical to accurate test processing.

"Efficient collection and accurate results are critical aspects of all patient testing," said Virginia Templet, Director of Marketing, Puritan Medical Products. "When testing for STIs that can be identified through specimen collection with a swab, consider Puritan's UniTranz-RT universal transport media product. This medium is available in 1ml and 3ml vials or combined with a flock swab, designed with the patient in mind. For your gynecological patients, choose Puritan's large rayon tip swab, Histobrush and the Rovers family of cervix brushes, all from Puritan."

Some STD viruses are more susceptible to damage during transport. One of the most common STDs, the herpes simplex virus (HSV), is highly sensitive to desiccation and pH inactivation, and the virus infectivity is heat labile. Therefore, the "specimen should also be transferred quickly to a diagnostic virology laboratory on ice (+4°C)."[4]

HPV Testing

As the Centers for Disease Control and Prevention (CDC) reports, Human Papillomavirus (HPV) "is so common that nearly all sexually active men and women get the virus at some point in their lives."[5] In the U.S., there are an estimated 42.5M HPV infections - new or existing – at any given time.[6]

"It's important to consider HPV when talking about STI screening because almost all cervical cancer is caused by high-risk HPV," said Walker. "There are 14 high-risk HPV genotypes, and each high-risk genotype is associated with a different level of risk of progression to cervical pre-cancer and cancer. BD Onclarity HPV Assay is the only FDA-approved assay with extended genotyping, reporting six high-risk HPV genotypes individually, including HPV 31. The assay with extended genotyping, is a more precise, accurate way to measure a woman's risk for developing cervical pre-cancer and cancer."

Run on the BD COR System, Walker says labs using the BD Onclarity HPV Assay can provide clinicians with more advanced insight on women's health and more informed treatment options for clinicians. The BD COR System integrates and automates the complete molecular laboratory workflow from pre-analytical processing to diagnostic test result, transferring the sample from the liquid-based cytology (LBC) collection to a molecular aliquot tube for HPV testing. It replaces labor-intensive and error-prone manual processes with automated ones, and the system is modular and scalable, designed to address multiple laboratory needs for expanding molecular testing and increasing test volumes.

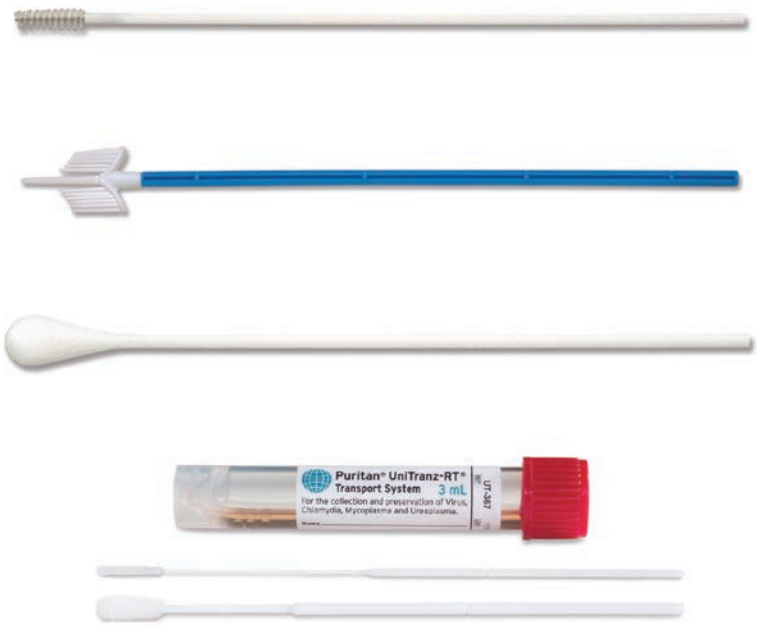
Syphilis testing

While STDs, such as syphilis and gonorrhea, have been widely recognized for centuries, clinical labs still struggle with the accuracy and efficiency of diagnostic tools. With the rise in highly infectious primary and secondary (P&S) syphilis rates since a historic low in 2001,[7] researchers are focusing on ways to achieve earlier diagnosis.

A Comparative Analysis of Molecular and Serologic Testing for Primary Syphilis, published in the *Frontiers in Cellular and Infection Microbiology* in April 2021, describes how "syphilis serology is imperfect and requires interpretation of multiple tests while molecular diagnostics allows for potential yes-no identification of highly infective, primary anogenital lesions."[8]

The researchers performed a retrospective analysis of adult patients with anogenital lesions who were screened for syphilis and herpes simplex (HSV) 1/2 in Alberta, Canada using polymerase chain reaction (PCR) to evaluate Tp-PCR versus serology to diagnose primary syphilis.

The researchers concluded that "molecular testing using Tp-PCR for primary syphilis appears to be a highly specific test with low sensitivity that is, therefore, most useful in confirming the diagnosis rather than as a screening test." They added, "Concurrent testing with syphilis serology remains necessary to ensure all cases are identified to manage the worsening



Puritan UniTranz-RT universal transport media product

epidemic and further work is required for the development of superior diagnostic assays that are both sensitive and specific."

Testing for multiple STD diagnosis

The CDC recommends certain populations be screened for multiple STDs. For example, all pregnant women should be tested for HIV, syphilis, and hepatitis B surface antigen (HBsAg), at their first prenatal visit, and hepatitis C virus (HCV) during each pregnancy, except in settings where the HCV infection rate is <0.1%.

The agency urges sexually active women who are under the age of 25 or who have new or multiple sex partners to get annual tests for chlamydia and gonorrhea. Sexually active gay and bisexual men should get tested for syphilis, chlamydia, and gonorrhea at least once a year, or every three to six months if they have multiple sexual partners, according to CDC guidelines.[9]

"It is critical for labs and healthcare systems to offer STI tests that have a quick time to result and user-friendly techniques for processing," said Walker." BD offers the BD CTGCTV2 assay for BD MAX System, a test that simultaneously and separately diagnoses the three most common non-viral STIs: Chlamydia trachomatis (CT), Neisseria gonorrhoeae (GC), and Trichomonas vaginalis (TV)."

Walker says TV is often not included in STI testing, but it should be. According to the CDC, there were more than 2 million TV infections in the U.S. in 2018, but only 30% of those individuals infected develop symptoms.[10]

"The BD assay diagnoses TV using the highly sensitive CDC-recommend NAAT technology," Walker explained. "For GC diagnosis, the assay has a dual-target design, meaning detection of both GC genes is needed to produce a positive result. This makes a big difference because it provides confidence in your result, confidence that a positive IS a positive, and that you are providing the physician and ultimately the patient with an accurate result."

Walker says the GC test is run on the BD MAX System, a benchtop instrument that can process 24 samples in about three hours. Plus, the BD CTGCTV2 assay uses a variety of specimen types: clinician and self-collected vaginal swabs (in a clinical setting), urine, liquid-based cytology (CT & GC only), and endocervical swabs.

Looking ahead

Preliminary CDC data on STD rates in 2021 reveal a continued increase in infections, specifically for primary and secondary syphilis among adults. Cases among women are up 34% and among men 9%. In addition, syphilis among newborns is up 6%, with 2,268 cases already reported in the preliminary 2021 data, which the CDC will continue to report through the fall of 2022.[11]

Laboratories are just beginning to see the front end of increased STD screenings coming out of the pandemic and will likely experience higher volumes in the months and years ahead as more patients resume regular screening.

As the CDC states in its April 12, 2022 press release:"There is much to be done to rebuild, innovate, and expand STD prevention and control in the United States—and this will require many groups working together, including local healthcare systems, clinics, and community-based organizations; public and private sectors; health care providers; and public health workers."[12]

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Diabetes cases continue to rise from SARS-CoV-2 complications

By Kristine Russell

According to a number of studies regarding the effect of SARS-CoV-2 and diabetes, data shows that people with diabetes are not more prone to SARS-CoV-2, the virus that causes COVID infections, but if they develop an infection, the disease is much more severe and seems to progress quicker.

In addition, SARS-CoV-2 infections are associated with the worsening of diabetes symptoms, and persons with diabetes are at increased risk for severe COVID-19. SARS-CoV-2 infection might also induce newly diagnosed diabetes, according to a report from the Centers for Disease Control and Prevention (CDC).

According to a report from Mayo Clinic, people with diabetes have more inflammation in their body. Therefore, with COVID, that inflammatory state gets worse much more quickly. People with diabetes also may be more prone to having problems with their circulatory systems. It also appears to happen with both type 1 and type 2 diabetes, and both seem to be prone to more severe disease. However, Type 1 patients may have better outcomes because they are younger.[1]

Risk of diabetes after COVID

In the report from the CDC, *Risk for Newly Diagnosed Diabetes >30 Days After SARS-CoV-2 Infection Among Persons Aged <18 Years — United States, March 1, 2020–June 28, 2021* ,[2] published in January 2022, persons aged less than 18 years with COVID-19, were 116%, according to data from IQVIA (a database of adjudicated healthcare claims from closed U.S. health plans used to provide a complete view of patient care across all care setting), more likely to receive a new diabetes diagnosis 30 days after infection than were those without COVID-19 and those with pre-pandemic acute respiratory infections. The report also indicated that non-COVID respiratory infections were not associated with an increased risk for diabetes.

The observed association between diabetes and COVID-19 might be attributed to the effects of SARS-CoV-2 infection on organ systems involved in diabetes risk. COVID-19 might lead to diabetes through direct attack of pancreatic cells expressing angiotensin converting enzyme 2 receptors; through stress hyperglycemia resulting from the cytokine storm and alterations in glucose metabolism caused by infection; or through precipitation of prediabetes to diabetes.[10]

A percentage of these new diabetes cases likely occurred in persons with prediabetes, which occurs in one in five adolescents in the United States. Steroid treatment during hospitalization might lead to transient hyperglycemia; however, only 1.5% – 2.2% of diabetes codes

Papers in 2021 Continue to Show Certain Glucose Meters Cause Serious Adverse Events Due to Interferants

"We report a case that probably resulted in the death of a patient from an erroneous interpretation of POC BG readings due to interference from high-dose vitamin C." [1]

AACE Clin Case Reports, 2021

"High Dose vitamin C treatment in combinations with Accu Chek II and Hemocue BGMs in patients with acute kidney failure may cause misinterpretation with potentially fatal consequences." [2]

Clin Chem Lab Med, 2021

"Yet, vitamin C has been associated with multiple reports of factitious hyperglycemia and harmful iatrogenic hypoglycemia causing death in at least one report." [4]

J Med Care Reports, 2021

"While the Nova StatStrip glucose meter effectively detected the presence of ascorbic acid interferant and suppressed glucose results, the Roche Inform II and Abbott Precision Xceed Pro demonstrated falsely increased results that could have impacted patient care (delayed PET scan) or possibly led to inappropriate patient treatment." [3]

J Diabetes Sci and Tech, 2021

Nova's StatStrip Glucose Meter Has No Known Clinical Interferences and is the Only Meter FDA Cleared for use on Critically Ill Patients.

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1. Orija IB et al. Pseudohyperglycemia Secondary to High-Dose Intravenous Vitamin C Managed as Diabetic Ketoacidosis: An Endocrinological Catastrophe. *AACE Clin Case Reports* 2021.

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Database/Characteristic	No. (%)				
	Pediatric overall	COVID-19	Non–COVID-19	ARI	Non-ARI
IQVIA					
Total no. of patients	1,698,753	80,893	404,465	404,465	808,930
Age, mean (SD), yrs	12.3 (4.3)	12.3 (4.3)	12.3 (4.3)	12.3 (4.3)	12.3 (4.3)
Age group, yrs					
0–4	124,530 (7.3)	5,930 (7.3)	29,650 (7.3)	29,650 (7.3)	59,300 (7.3)
5–11	483,273 (28.4)	23,013 (28.4)	115,065 (28.4)	115,065 (28.4)	230,130 (28.4)
12–15	592,830 (34.9)	28,230 (34.9)	141,150 (34.9)	141,150 (34.9)	282,300 (34.9)
16–17	498,120 (29.3)	23,720 (29.3)	118,600 (29.3)	118,600 (29.3)	237,200 (29.3)
Female sex	850,857 (50.1)	40,517 (50.1)	202,585 (50.1)	202,585 (50.1)	405,170 (50.1)
Hospitalized at index encounter	6,473 (0.4)	566 (0.7)	614 (0.2)	1,602 (0.4)	3,691 (0.5)
New diabetes diagnosis†					
Overall	**937 (0.06)**	**68 (0.08)**	**132 (0.03)**	**227 (0.06)**	**510 (0.06)**
DM type (% of all newly diagnosed diabetes)					
Type 1 or Type 2	891 (95.1)	64 (94.1)	124 (93.9)	210 (92.5)	493 (96.7)
Due to underlying condition/Other	31 (3.3)	3 (4.4)	6 (4.5)	8 (3.5)	14 (2.7)
Drug or chemical induced	15 (1.6)	1 (1.5)	2 (1.5)	9 (4.0)	3 (0.6)
DKA (% of all newly diagnosed diabetes)	241 (25.7)	33 (48.5)	18 (13.6)	50 (22.0)	140 (27.5)

abbreviations: ARI = acute respiratory infection; DKA = diabetic ketoacidosis; DM = diabetes mellitus; ICD-10-CM = International Classification of Diseases, Tenth Revision, Clinical Modification.

TABLE 1. Characteristics of matched pediatric groups with and without evidence of COVID-19 or acute respiratory infection and number of new diabetes diagnoses, by age, sex, and preceding COVID-19 or acute respiratory infection diagnosis IQVIA PharMetrics Plus United States, March 1, 2020–June 28, 2021. Chart courtesy of CDC, https://www.cdc.gov/mmwr/volumes/71/wr/mm7102e2.htm

were for drug- or chemical-induced diabetes, with the majority of codes being for type 1 or type 2 diabetes.

Alternatively, COVID-19 might have indirectly increased diabetes risk through pandemic-associated increases in body mass index, a risk factor for both serious COVID-19 illness and diabetes. The authors commented that future studies addressing the role of comorbidities and increases in body mass index in post–COVID-19 diabetes are warranted.

Although this study provides information on the risk for diabetes following SARS-CoV-2 infection, additional data are needed to understand underlying pathogenic mechanisms, either those caused by SARS-CoV-2 infection itself or resulting from treatments, and whether a COVID-19–associated diabetes diagnosis is transient or leads to a chronic condition.

Increases in pediatric type 1 diabetes

Evidence of increased pediatric type 1 diabetes has been reported during the COVID-19 pandemic.[3,4] Among persons aged <18 years with COVID-19 and new diabetes diagnoses in this study, nearly one half had diabetic ketoacidosis (DKA) at or around the time of diagnosis. This number was higher than that in comparison groups, and higher than previous reports of DKA among incident type 1 diabetes cases before the pandemic (28%) .[11]

Increased frequency of DKA at time of diagnosis of type 1 diabetes during the pandemic has previously been reported and was thought to be due to delayed care-seeking for diabetes.[5] However, the observed association of increased risk for diabetes diagnosis following SARS-CoV-2 infection would not be explained solely by delayed care. COVID-19 has disproportionately affected racial/ethnic minority groups, and those aged <18 years in these groups are also at increased risk for type 2 diabetes.[12]

An association between COVID-19 and new pediatric diabetes diagnoses might disproportionately affect racial/ethnic minority groups. Race/ethnicity data were unavailable in the present data sets; however, future studies should address racial and ethnic disparities in COVID-19 and diabetes, and whether persons aged <18 years who are at risk for COVID-19 are also those at risk for delaying medical care.

Healthcare providers should screen for diabetes symptoms in persons aged < 18 years with a history of SARS-CoV-2 infection. These symptoms can include frequent urination, increased thirst, increased hunger, weight loss, tiredness or fatigue, stomach pain, and nausea or vomiting.

The stats

The increased diabetes risk among persons aged <18 years following COVID-19, highlights the importance of COVID-19 prevention strategies in this age group, including vaccination for all eligible persons and chronic disease prevention and treatment.

The COVID-19 pandemic has disproportionately affected people with diabetes, who are at increased risk of severe COVID-19. Increases in the number of type 1 diabetes diagnoses and increased frequency and severity of DKA at the time of diabetes diagnosis have been

reported in European pediatric populations during the COVID-19 pandemic.

The study included 80,893 patients with COVID-19 in the IQVIA database, the mean age was 12.3 years, 50.1% were female, and 0.7% were hospitalized at their index COVID-19 encounter. In the IQVIA database, diabetes incidence was 316 per 100,000 person-years in the COVID-19 group, 118 per 100,000 person-years in the pandemic period non–COVID-19 group, 126 per 100,000 person-years in the pre-pandemic acute respiratory infection group (ARI), and 125 per 100,000 person-years in the pre-pandemic non-ARI group.

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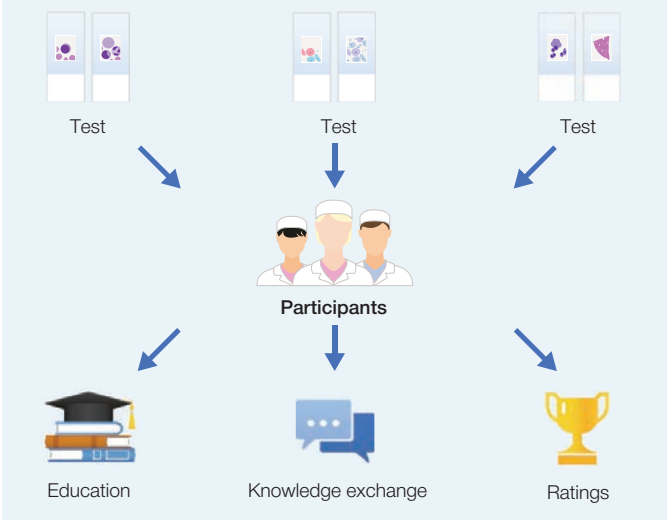

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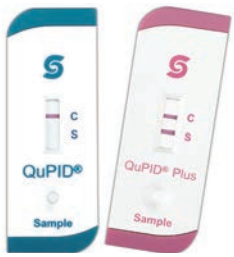
Copan, FLOQSwabs optimize the efficiency of the target analyte collection with improved patient comfort. A FLOQSwab has no internal core that could trap the specimen. The tip of the applicator is coated with soft Nylon fibers that allow for uptake and elution of more than 90% of sample, a considerable improvement over traditional wound fiber swabs.

Copan



Fast urine or serum pregnancy testing

QuPID hCG test range of one-step cassette platforms for urine or urine/serum pregnancy testing is available in packs of 25 or 50. A quick-clearing background ensures easy to interpret results, from two drops of sample in as little as 10 seconds, minimizing need for re-testing even with low level specimens. Accuracy and specificity is >99%.

EKF USA

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Marketlab

In-vitro analyzer for simplified processing

The CE-IVD marked SuperFlex Automated Chemiluminescence Analyzer delivers hands-free, ultra-sensitive detection of biological molecules using labeled antibodies and antigens in serum, plasma and blood. It can be incorporated with point-of-care cardiovascular and inflammation detection kits that analyze 1 - 12 samples with the same or different assays within 15 minutes.

Perkin Elmer

Trichomonas rapid test

The OSOM Trichomonas Rapid Test for the qualitative detection of trichomonas antigens from vaginal swabs is accurate (sensitivity 96%; specificity of 95%), fast (result in 10 minutes), simple (CLIA waived; no equipment needed), and cost-effective (collection swabs and QC included).

SEKISUI Diagnostics

Automatic cell imaging analyzer

The West Medica Cell Imaging Analyzers provide automatic scanning and analyzing the whole slide image for creating digital sample. The latest achievements in AI support the development of Application Modules for precise analysis of digital slides.

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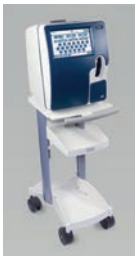

Stat Profile Prime Plus® whole blood critical care analyzer combines maintenance-free cartridge technology for sensors and reagents with patented, non-lysing whole blood co-oximetry technology. Test menu includes blood gases, electrolytes, metabolites, Hb, Hct, MCHC, CO-Ox, and estimated plasma volume, with results in about one minute.

Nova Biomedical

Aptima® CMV Quant assay – Coming Soon

The Hologic Aptima® CMV Quant assay will bring the Panther® assay menu to 19 FDA-approved tests on a single platform, offering consolidation, assay performance, workflow efficiency while working with a trusted partner.

Hologic

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Peezy Midstream urine specimen collection device is designed to obtain a clean catch urine sample helping provide more accurate results, diagnosis and treatment.

Owen Mumford

Safety SubCulture Unit 2 - Needleless Subculture Procedure

Safety SubCulture Unit 2 enables a safe and needleless subculture of positive blood culture bottles to slides and media plates. Other subculture devices transfer samples with exposed needles. **Protect staff with a safety-oriented subculture solution.**

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LumiraDX

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Werfen - Hemostasis

Four Respiratory Tests in One

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LABORATORY INNOVATOR

Molecular and point-of-care experience helps overcome lab challenges

By Kristine Russell

Ghazala Nathu, MD, MS, PhD, FACB, Medical/Molecular Laboratory Director of Clinical Pathology, Director of Point of Care and Blood Bank/Tissue Compliance Officer, at Bassett Healthcare Network – Cobleskill Regional Hospital.

Cobleskill Regional Hospital (CRH) is located in Cobleskill, New York. CRH is a 25-bed critical access facility and is the only hospital for 50 miles in any direction. The hospital has a full service Emergency Department but no maternity or critical care. CRH excels at stabilizing and transporting of patients to another hospital when needed.

What made you decide to pursue a career in medicine?

Both my parents were physicians. My father, who is 85 years old, still practices medicine. Both my parents had a passion for patient care. I became an MD because of my parents and because I wanted to challenge myself and to help patients through clinical pathology.

Why did you become a Molecular director for your lab?

Genetic and molecular testing is the future of clinical pathology. Artificial intelligence is catching up fast and is being used to help analyze genetic and molecular testing results. I studied these fields in order to improve patient care. For example, CRISPR is being used in clinical trials to engineer a cure for Sickle Cell Anemia. Pharmacogenetic testing is used to determine how genes affect the body's response to certain medications.

What do you enjoy most about being the Director of Point of Care?

I am board certified in point-of-care (POC). POC is well regulated by regulatory agencies. One of my greatest passions is being able to help patients and assure that they get a high standard quality of care. POC can also improve patient treatment outcomes because the physician receives results almost immediately and they can institute the treatment necessary to help the patient without any delays.

How does your PhD in Neuroscience help you address and overcome challenges as a Lab Director?

Obtaining a PhD in neuroscience has helped me in many ways with my passion for seeing that patient's receive a high quality standard-of-care. In the process of obtaining my PhD, I learned to think outside the box. I learned the fundamentals of basic research. I obtained a better view of the whole picture when it comes to taking care of patients. That knowledge enabled me to understand pre-analytic, analytic, and post analytic phases of testing. I was able to promote and develop a laboratory developed test (LDT) in-house that was FDA approved and had clinical utility. The test is an Extraction free SARS-CoV-2 RNA detection by RT-Real Time PCR (polymerase chain reaction). In addition to being the Medical Director of CRH and the Molecular Director for BMC, I was also the Medical Director for a large reference laboratory. The reference laboratory performed 10,000+ COVID-19 tests per day. The development of the LDT, which was approved by CLIA and the local Department of Health, helped overcome shortages of materials.

Will you describe the role your lab has played as a regional healthcare center in New York in response to the pandemic?

We normally have two negative pressure rooms. But New York State allowed us to make six more rooms into temporary negative pressure rooms. There were so many COVID-19 patients in New York City and downstate, that the upstate hospitals were required to accept COVID-19 patient transfers from downstate. We had our fair share of COVID-19 patients. Patients who needed critical care were shipped to other facilities that had ICU beds available. With our two Abbott ID Now's, we did a great deal of COVID-19 testing and flu testing. For a while, there was an executive order for any patient sent for testing, to be tested for both flu and COVID-19. In the beginning, we were the only facility in the area to offer a rapid COVID-19 test. A lot of patients came to our Emergency Department for testing after they were exposed to people who had COVID-19. I was overseeing, as a solo Molecular Director, for all of the Bassett Network to support the healthcare team and system in the immediate response for the diagnosis and prompt treatment of patients and employees. I was in constant communication with my staff, Bassett Network Medical Directors, and the supply chain vendors to ensure constant feed of supplies to avoid any possible interruption in patient care.

What is the current vacancy rate at your lab? What strategies have you found to be successful in recruiting and/or retaining staff?

We are currently fully staffed in our laboratory. We did not have a staffing problem during the pandemic because, previously, we had to attract and keep workers. We are close to the Capital District area, which includes Albany, New York, so we had to be competitive to obtain staff. We changed to 12- hour shifts. Our hospital employees were treated equally and with respect. I used a team approach and was always positive with the staff. If I had to talk to an employee about something negative, I would always start with something positive and then bring up the negative aspect.

Are there particular 'lessons learned' you wish to share with fellow Laboratory Directors?

I learned that a single person or laboratory cannot do everything. During the pandemic, everyone learned that a collaborative approach got things done; this included outside agencies as well as internal personnel. The New York State Department of Health and Governor Cuomo had emergency powers and were able to cut much of the red tape. CLIA also made exceptions with regard to the pandemic. The FDA and CDC also made exceptions with the pandemic. I learned that the collaborative team approach works best in handling emergent situations. This includes the Department of Health, Federal agencies, executives, governors, and other persons.

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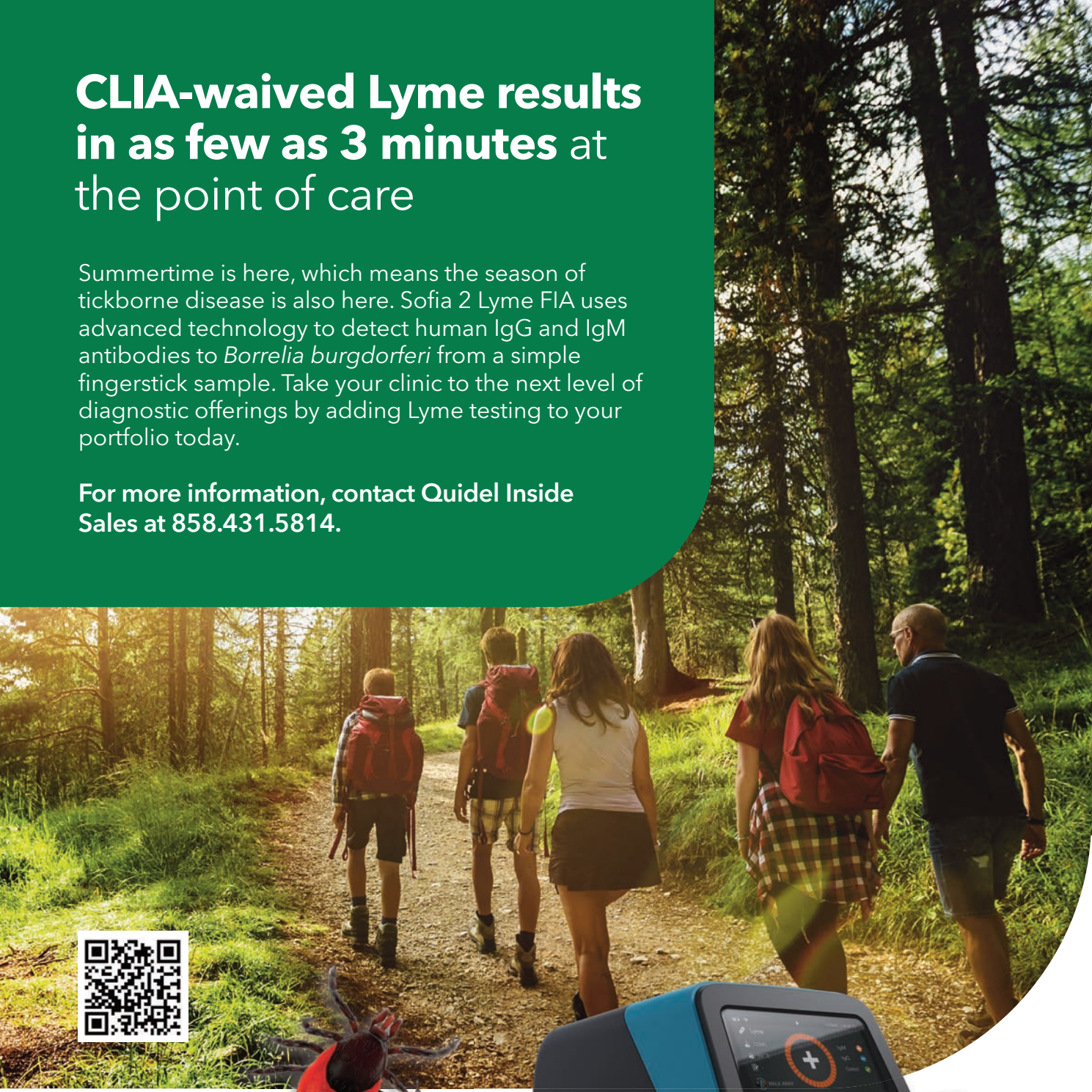

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