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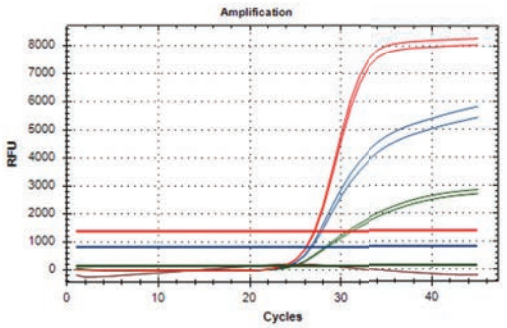

WT K417, WT N501, E484K variant result. FAM (K417) and HEX (E484K) shows amplification while Quasar670 (Cy5 N501Y variant) shows no amplification.

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

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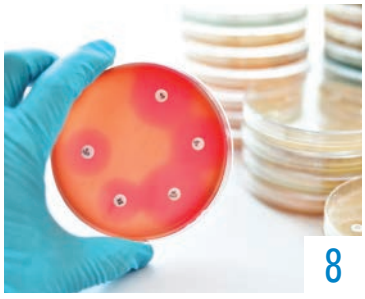

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Serial screening and SARS-CoV-2

By Linda Wilson
Senior Editor

The federal government has added more tools recently to the COVID-19 testing arsenal for serial screening initiatives.

As the United States races to outpace the spread of new SARS-CoV-2 variants through a massive vaccination effort, it makes sense to both manage and monitor the activity of the virus using a wide variety of testing types and strategies.

Serial screening at the individual level will help us control community transmission of SARS-Cov-2 and resume activities safely. When combined with population-level surveillance activities, genetic sequencing, and serology testing, serial screening plays a role in monitoring where SARS-CoV-2 is spreading and how well prior infections and vaccines protect people from COVID-19 – both now and in the future.

Clinical labs will help their communities with these testing efforts. They will continue to test respiratory specimens from people suspected of being infected with SARS-CoV-2, as well as blood samples from people who have developed immunity either through infection or vaccination.

But laboratorians also can help provide expert advice for serial testing efforts that occur outside the walls of the lab. As people become vaccinated and communities resume pre-pandemic activities, more testing – or at least specimen collection – will occur in homes, businesses, schools, and other community settings.

The government has approved point-of-care (POC) and in-home tests to help with these efforts.

The U.S. Food and Drug Administration (FDA) in early April issued an emergency use authorization (EUA) for the Symbiotica COVID-19 Self-Collected Antibody Test System, which the agency said is the first antibody test authorized for use with dried blood spot samples collected at home. The samples are then sent to Symbiotica's laboratory for analysis.

The FDA also approved in April amended EUA requests for multiple tests, expanding over-the-counter (OTC) and point-of-care serial testing options for COVID-19. The approved tests include Quidel QuickVue At-Home OTC COVID-19 test (OTC at-home serial screening), Abbott BinaxNOW COVID-19 Antigen Self Test (OTC at-home serial screening), Abbott BinaxNOW COVID-19 Ag Card 2 Home Test (OTC at-home serial screening with telehealth), Abbott BinaxNOW COVID-19 Ag 2 Card (POC serial screening without a prescription), and BD Veritor System for Rapid Detection of SARS-CoV-2 (POC serial screening with a prescription).

The Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) also have gotten involved in serial testing efforts.

They launched "Say Yes! COVID Test," which will be rolled out in Pitt County, NC, and Chattanooga, TN. Residents will have access to free rapid antigen tests that they will administer themselves three times a week for one month. NIH plans to provide the tests and evaluate if frequent self-administered COVID-19 testing helps reduce community transmission of SARS-CoV-2.

Those community members also may choose to volunteer for a survey-based research study that will determine whether frequent self-administered testing makes a difference in behavior, knowledge about preventing spread of the virus, and thoughts about COVID-19 vaccination.

These announcements are probably just the beginning. I expect that we will hear about other initiatives in upcoming months. As laboratorians know, testing of all types plays a big role in allowing the so-called "new normal" life to happen safely.

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

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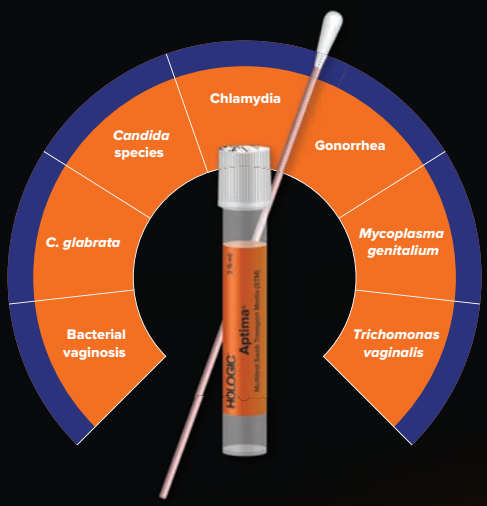

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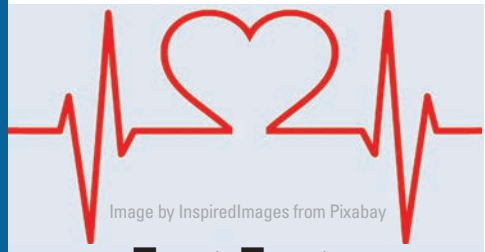

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Fast Facts Noncommunicable Diseases (NCD)

Treatment and prevention of noncommunicable diseases globally has been severely impacted by COVID-19, according to the World Health Organization (WHO).

41 million
people die from noncommunicable diseases (NCD) each year

71%
of deaths globally are from NCD

85%
of premature death for people aged 30-69 are due to NCD

42%
of cancer treatments were disrupted by COVID-19

49%
of treatments for diabetes were impacted by COVID-19

31%
of cardiovascular emergencies had disrupted services from COVID-19

94%
of ministry support staff in areas of NCDs were reassigned to COVID-19

20%
of countries discontinued some health services during the pandemic

58%
of countries are using telemedicine

Source: https://www.who.int/news/item/01-06-2020-covid-19-significantly-impacts-health-services-for-noncommunicable-diseases

SARS-CoV-2 variants evade most – but not all – antibodies

New research indicates that three new, fast-spreading variants of the virus that cause COVID-19 can evade antibodies that work against the original form of the virus that sparked the pandemic. Whether such antibodies were produced in response to vaccination, natural infection, or were purified antibodies used as drugs, researchers found more antibody is needed to neutralize the variants.

However, several highly neutralizing monoclonal antibody cocktails, including those developed at Vanderbilt University Medical Center, showed intact or only mildly diminished activity against the variants tested, possibly because they target sites on the spike protein other than the highly mutable E484K residue.

The findings, from laboratory-based experiments and published in *Nature Medicine*, suggest that COVID-19 drugs and vaccines developed thus far may become less effective as the new variants become dominant, as experts say they inevitably will. The researchers looked at variants from South Africa (B.1.135), the United Kingdom (B.1.1.7) and Brazil (B.1.1.248, also known as P.1.)

The multi-center research was led by Washington University School of Medicine in St. Louis. In addition to Vanderbilt University Medical Center, University of Texas Medical Branch also participated in the work.

The virus that causes COVID-19, known as SARS-CoV-2, uses a protein called spike to latch onto and get inside cells. Consequently, spike became the prime target for COVID-19 drug and vaccine developers. And potent anti-spike antibodies were selected for development into antibody-based drugs for COVID-19.

The researchers tested the variants against antibodies in the blood of people who had recovered from SARS-CoV-2 infection or were vaccinated with the Pfizer vaccine. They also tested antibodies in the blood of mice, hamsters and monkeys that had been vaccinated with an experimental COVID-19 vaccine, developed at Washington University School of Medicine, that can be given through the nose. The B.1.1.7 (United Kingdom) variant could be neutralized with similar levels of antibodies as were needed to neutralize the original virus. But the other two variants required from 3.5 to 10 times as much antibody for neutralization.

They also tested monoclonal antibodies: mass-produced replicas of individual antibodies that are exceptionally good at neutralizing the original virus. When the researchers tested the new viral variants against a panel of monoclonal antibodies, the results ranged from broadly effective to completely ineffective.

Since each virus variant carried multiple mutations in the spike gene, the researchers created a panel of viruses with single mutations, so they could parse out the effect of each mutation. Most of the variation in antibody effectiveness could be attributed to a single amino acid change in the spike protein. This change, called E484K, was found in the B.1.135 (South Africa) and B.1.1.248 (Brazil) variants, but not B.1.1.7 (U.K.).

CMS addresses CLIA certification violations

As a result of a recent record check, the Centers for Medicare and Medicaid Services (CMS) issued 171 cease-and-desist letters to facilities that did not have proper certifications in place as outlined in the Clinical Laboratory Improvement Amendments of 1988 (CLIA). CLIA certification is important, because it verifies that laboratories meet federal performance, quality and safety standards to properly diagnose, prevent and treat diseases.

CMS said that every facility that conducts COVID-19 testing is considered a "laboratory" and must be certified under CLIA. To make certification easy, CMS implemented an expedited review process at the beginning of the public health emergency and recently released a quick-start guide to help laboratories with the application process. CMS said that it is imperative to public safety that facilities apply for CLIA certification and only operate within the scope of that certification to prevent false results that could adversely alter diagnosis or treatments and contribute to the further spread of COVID-19.

False positive results possible with Roche test

The FDA announced that false positive results can occur with the Roche Molecular Systems cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System.

Roche's assay tubes may sporadically leak, causing an obstructed optical path in the Liat analyzer, producing abnormal PCR growth curves, leading to invalid or erroneous posi-

tive results, particularly for the Flu B test. If a tube leak occurs, later testing runs may have an increased likelihood of false positive Flu B results.

Roche also determined that abnormal PCR cycling in the reaction tubes may produce abnormal PCR growth curves, caused by simultaneous factors, such as hardware positioning, volume movement, and curve interpretation. This issue may cause false positive results for multiple analytes (Influenza A, Influenza B and/or SARS-CoV-2) in a single testing run.

The FDA recommends users of the cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System:

- Watch out for unexpected clusters of positive Flu B results, as this may indicate the cobas Liat System has experienced a tube leak.
- Repeat tests when two or three analytes are positive. Different results on the repeat test may indicate abnormal PCR cycling.
- Stop using the cobas Liat System and contact Roche if you suspect either of these two issues has occurred.

NIH scientists develop breath test for methylmalonic acidemia

Researchers at the National Institutes of Health (NIH) have developed a breath test that measures how well patients with methylmalonic acidemia (MMA) respond to receiving liver and/or kidney transplantation. Researchers used the test to assess the severity of the disease in people and help determine if they would benefit from surgical or experimental genomic therapies that target the liver.

MMA is a rare genomic disease that impairs the body's ability to metabolize certain proteins and fats. This causes toxic build up, causing kidney disease, pancreatitis, movement disorders, intellectual impairments, organ complications, or, in severe cases, death. Currently, MMA is incurable, and some patients receive liver and/or kidney transplants to help restore normal levels of metabolic proteins.

One form of MMA is caused by mutations in the methylmalonyl-CoA mutase gene (MMUT), which encodes for the MMUT protein. People with this form of MMA have a deficiency in the MMUT protein, which plays a pivotal part in metabolism by breaking down food, fats, cholesterol and amino acids.

MMUT helps break down food into a chemical byproduct called propionate, which is followed by oxidation, where a healthy body converts propionate into energy and carbon dioxide, which is exhaled, but that process is faulty for people with MMA.

Because MMUT protein function is compromised in people with MMA, the team chose to assess how well the MMUT protein helped break down propionate in both patients who did and not did not receive treatment.

To detect if the MMUT protein was functioning properly, researchers gave patients a dose of the heavier, less abundant version of carbon – carbon 13 – via a commercially available food additive.

The team recruited 57 study participants, including 19 MMA patients who had received transplants (liver, kidney or both) and 16 healthy volunteers. Researchers gave participants a dose of the food additive containing carbon 13 via a drink or through a feeding tube, and then collected their breath samples after a two-minute wait.

The researchers measured how much of the exhaled carbon dioxide contained the usual carbon 12 compared to added carbon 13. MMA patients who did not receive any treatment had lower levels of carbon 13 than healthy volunteers. By contrast, MMA patients with liver transplants had higher levels of carbon 13, similar to the healthy volunteers.

FDA updates on COVID-19 testing

The U.S. Food and Drug Administration (FDA) recently granted emergency use authorization (EUA) for numerous COVID-19 tests.

These include the Quidel QuickVue At-Home OTC COVID-19 test for OTC at-home serial screening; Abbott BinaxNOW COVID-19 Antigen Self Test for OTC at-home serial screening; Abbott BinaxNOW COVID-19 Ag Card 2 Home Test for OTC at-home serial screening with telehealth; Abbott BinaxNOW COVID-19 Ag 2 Card for POC serial screening without a prescription; BD Veritor System for Rapid Detection of SARS-CoV-2 for POC serial screening with a prescription; and the Symbiotica COVID-19 Self-Collected Antibody Test System, which is the first antibody test authorized for use with home collected dried blood spot samples.

The FDA also warned that false positive results can occur with antigen tests to detect SARS-CoV-2, particularly when users do not follow the instructions, including routine follow-up testing (reflex testing) with a molecular assay when appropriate, and by considering the expected occurrence of false positive results when interpreting test results.

When using antigen tests, the FDA said to follow instructions in the package insert about handling test cartridges/cards, such as ensuring they are not stored open, and reading test results at the appropriate time. Use caution when processing multiple specimens in batch mode because the process may make it challenging to ensure the correct incubation time for each specimen. Minimize the risks of cross-contamination when testing patient specimens, which can cause false positive results.

As the impact of SARS-CoV-2 variants on diagnostic test results is another issue facing laboratories, the FDA created a new web page: SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests | FDA.

The FDA revised an announcement regarding the doses per vial available for the Moderna COVID-19 vaccine.

The FDA first clarifies the maximum extractable doses per vial is 11, with a range of 10-11 doses. In the second revision, the agency authorized the use of an additional multi-dose vial that contains a maximum of 15 doses, with a range of 13-15 doses that can potentially be extracted.

Depending on the type of syringes and needles used to extract each dose, there may not be sufficient volume to extract more than 10 doses from the vial containing a maximum of 11 doses or more than 13 doses from the vial containing a maximum of 15 doses.

Because the Moderna COVID-19 vaccine does not contain preservatives, any further remaining product that does not constitute a full dose should not be pooled from multiple vials to create one full dose. If one vial becomes contaminated during use, pooling doses from multiple vials can spread contamination to other vials.

Common needs and interventions for COVID-19 and drug-resistant infections

By Diane Flayhart, MBA

We began this year living in a world with a nearly untreatable virus. At no time in recent history has there been a series of events or circumstances that challenged organizations and individuals to engage in new actions and behaviors as exists today due to COVID-19. The COVID-19 pandemic has been an acute shock to the world, as the novel coronavirus has affected the health of millions and the lives and livelihood of billions.

This circumstance provides a glimpse of what the future is likely to become more broadly if we do not mobilize a sufficient global response to drug resistant infections caused by antimicrobial resistance (AMR), which occurs when drugs lose their effectiveness. It occurs when bacteria, viruses, fungi, and parasites change over time and no longer respond to medicines, making infections harder to treat and increasing the risk of disease spread, severe illness and death. [1]

Antimicrobial resistance occurs when drugs lose their effectiveness. It occurs when bacteria, viruses, fungi, and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death.

As the bacteria that cause infections become increasingly drug resistant, even common medical procedures – including surgery, childbirth, and chemotherapy – can become increasingly life-threatening.

While the urgent and immediate threat of the novel coronavirus is of utmost priority for governments and healthcare systems, we must ensure that the lessons we are learning today from COVID-19 shape continued actions to combat AMR now and in the years ahead. The global strategy to curb drug resistance, initiated in 2016 by the UN InterAgency Coordination Group on AMR, [2] provides an effective framework for AMR action plans at the global and national level. The experience with the COVID-19 pandemic presents a unique opportunity to reexamine, adjust and reset our approaches through the lens of what actually happens when a nearly untreatable infection impacts the entire world.

Clinical and research laboratories have played a critical role in the COVID-19 pandemic. Laboratory testing results provide data to clinicians and allows patients to be put on the optimal treatment path. This data also informs surveillance, infection prevention practices, and antibiotic stewardship.

The impact of surveillance data

Tracking the spread of COVID-19 has been critical to the global public health response. This information allows hospitals to prepare for surges, governments to deploy testing strategies, and citizens to modify their behavior appropriately. But while information about COVID-19 is readily and publicly available, the world still struggles to monitor and track the spread of drug resistant infections.

It is critical that we improve tracking of drug resistant bacteria. Bacteria causing drug resistant infections move quickly across

Images used with permission from The Pew Charitable Trusts

Figure 1: How NDM-1 spread around the world: 2006 to 2016
Images used with permission from The Pew Charitable Trusts

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LEARNING OBJECTIVES

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

1. Describe how antimicrobial resistance occurs, what problems it causes, and examples of several drug-resistant organisms.
2. Discuss why tracking of drug-resistant organisms is important and tracking tools available today.
3. Discuss the role of infection prevention and control in preventing drug-resistant infections.
4. Discuss the role of diagnostic testing in improving antibiotic stewardship.

Global reported cases of *C. auris* by country

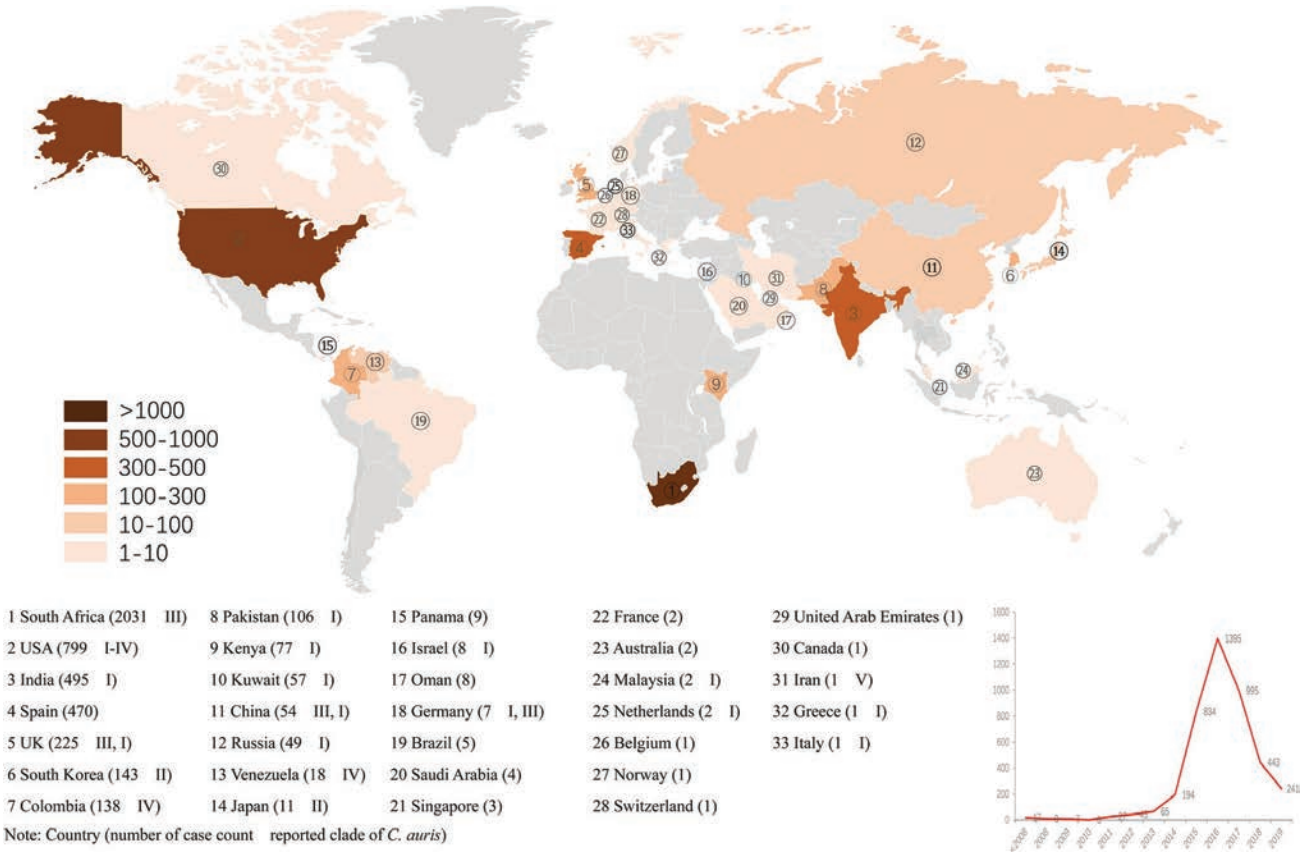

Figure 2: The reported case count of patients with *C. auris* and clade(s) in different countries were represented in descending order. An epidemic curve showing case count of *C. auris* by year was also portrayed based on publication data (adapted from Robinson projection map).

the globe via multiple carriers. The quick movement of these multi-drug resistant organisms has been demonstrated with two of the newer superbugs. NDM-1 is a resistance gene that can be found in Enterobacteriaceae and results in the production of the *New Delhi metallo-beta-lactamase*. NDM-1 bacteria are part of a larger group known as carbapenem-resistant Enterobacteriaceae and are resistant to penicillin, cephalosporin, and carbapenems. NDM-1 infection was initially identified in the mid-2000s and quickly spread to more than 80 countries, according to a comprehensive review of the literature conducted by the Pew Charitable Trusts in early 2017, which tracked the spread over a nine-year period.[3]

> Why is global surveillance needed?
> "AMR is not a problem that can be solved by any one country, or even any one region. We live in a connected world where people, animals, and food travel, and microbes travel with them."[5] Jim O'Neill from Superbugs: An Arms Race Against Bacteria

Candida auris is considered a "superbug fungus," which has caused worldwide concern and has been classified as an Urgent Threat by the Centers for Disease Control and Prevention (CDC).[4] *C. auris* is resistant to most first-line antifungal medications and spreads easily between patients. In 2020, Chen, et.al., completed a systemic review and meta-analysis of the global epidemiology and mortality of *Candida auris*. The analysis included studies from 2009 to 2019. Initially identified in Japan in 2009, there have been more than 4,733 cases of *C. auris* reported in more than 33 countries. Bloodstream infection was observed in 32% of the cases. The overall mortality of C. auris infection was 39%.[5] This retrospective analysis shows the global spread of this pathogen and the critical need to have real-time surveillance to track these life-threatening pathogens.

There are several tools available today to track drug resistant organisms. The CDC is prioritizing domestic antimicrobial resistance surveillance through the CDC Antibiotic Resistance Laboratory Network. The network includes labs in 50 states, including seven regional labs and the National Tuberculosis Molecular Surveillance Center. Comprehensive lab capacity and infrastructure utilizing cutting-edge technology, like DNA sequencing, provides data needed to combat AMR. The Global Antimicrobial Resistance Surveillance System (GLASS) supports global surveillance and research to strengthen the evidence base on antimicrobial resistance (AMR) and help to inform decision-making and drive national, regional, and global actions. Recently, the Surveillance and Epidemiology of Drug-resistant Infections Consortium (SEDRIC) launched a map to collect details of research projects focused on the surveillance of drug resistant infections. There are systems at local, regional, and global levels collecting data on drug resistance. We need to expand the capabilities of these surveillance systems and create real-time accessible platforms, so data can be acted upon quickly, slowing the spread of drug resistant organisms.

As Jim O'Neill, author of the book, *Superbugs: An Arms Race Against Bacteria*, explains, "AMR is not a problem that can be solved by any one country, or even any one region. We live in a connected world where people, animals, and food travel, and microbes travel with them."[6]

Using infection prevention and control to stop infections before they start

Preventing drug resistant infections reduces the use of antibiotics and improves patient outcomes. Infection control practices, from simple handwashing to global vaccination, and the use of effective infection prevention measures are key tools to combat COVID-19 and AMR.

Within healthcare systems, infection prevention measures are not specific to one pathogen and can have a broad impact. A recent study by Wee, et.al., evaluated the impact of a multimodal IPC strategy originally designed for the containment of COVID-19 on the rates of other hospital-acquired-infections (HAIs). With enhanced IPC measures introduced to contain COVID-19, they saw a decrease in hospital-wide MRSA acquisition rates together with central line-associated bloodstream infections rates. The rates of CRE, *C. difficile* infections, and device-associated HAIs remained stable. Respiratory infections were prioritized for interventions; however, good adherence to IPC impacted HAI rates as well.[7]

In a study by Bentivenga, et.al., researchers reported a significant reduction in the incidence of total MDR bacterial infections observed during the pandemic compared to in pre-pandemic years ($p < 0.05$). The study concluded that maintaining a high level of preventive measures could help tackle an important health problem, such as the spread of HAIs and multidrug resistant bacteria (MDRB).[8]

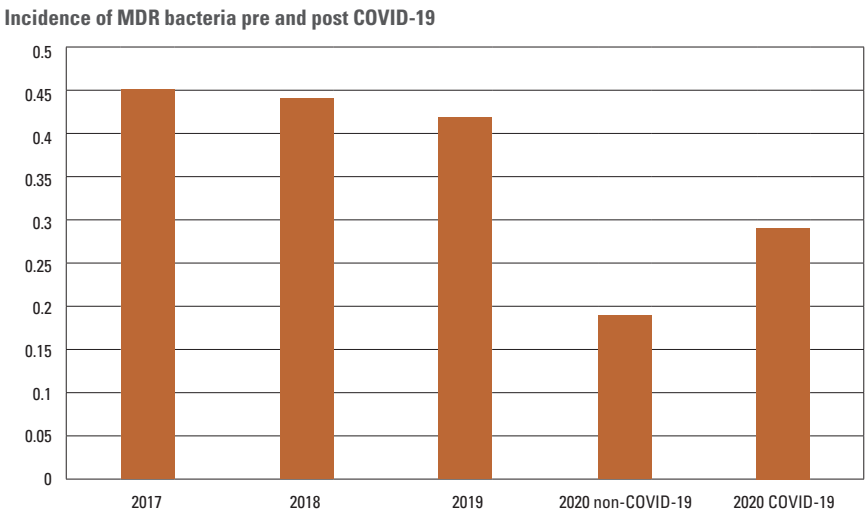

Figure 3. Data from medical departments between March 1 and June 30. The ordinate axis represents the infection incidence of MDR bacteria. The abscissas axis represents time.[8]

The COVID-19 pandemic and its associated healthcare efforts allowed researchers to better understand effective measures for HAI and MDRB prevention. These studies, limited to individual healthcare systems, demonstrate how effective infection prevention measures can reduce the rates of multi-drug resistant bacteria. In some settings, due to a higher risk case-mix, shortages of equipment, and staff shortages, an increase of nosocomial infections was seen. As laboratory technologies continue to evolve, the integration of real-time data into infection prevention programs will have a direct impact on the success of these programs.

There are tools available to learn more about best practices for infection control and how they link to AMR.

- The CDC has tools available to assess infection prevention practices and guide quality improvement.
- The websites for the World Health Organization (WHO), UNICEF, and WaterAid's provide information on WASH (Water, Sanitation and Hygiene) and IPC in all healthcare systems – both of which are required to combat AMR globally. In many low to middle-income countries, WASH is inadequate, with 1 in 3 healthcare facilities lacking hand hygiene materials at point of care, and more than 900 million people using healthcare facilities with no water service.

The COVID-19 pandemic has highlighted the critical role of vaccines in controlling infectious disease outbreaks. Vaccines are an effective infection control tool for bacterial infections as well. A recent report by Wellcome Trust[9] states that "vaccines do have some unique advantages and therefore, bringing additional, and more effective vaccines, to market could have a huge impact on AMR." Vaccines play a critical role, with a track-record of reducing AMR. Both *H. influenzae* b and *S. pneumoniae* vaccines have resulted in a reduction in disease burden and have been associated with decreased incidence of resistant strains. Additionally, both vaccines have an additional "indirect" effect on AMR by reducing antibiotic usage and, therefore, selection pressure on pathogens. Evidence shows that universal coverage with 13-valent S. pneumoniae vaccination could avoid 11.4 million days of antibiotic use per year in children under five. The report is available on the Wellcome Trust's website.

Diagnostic and antibiotic stewardship

The pandemic has demonstrated the critical role of diagnostic testing to steer our public health response. It has been shown that diagnostic testing for bacterial and fungal infections results in improved use of antibiotics and antibiotic stewardship. Whereas testing for COVID-19 has benefited from innovation and rapid uptake, testing for drug resistant infections remains underutilized. Antimicrobial resistance is a complex challenge - it is not a single pathogen like COVID-19; it can and does spread silently across healthcare, community, and the environment.

Diagnostic stewardship refers to the appropriate use of laboratory testing to guide patient management, including treatment, to optimize clinical outcomes and limit the spread of antimicrobial resistance. The diagnostic microbiology laboratory has a vital role to play in facilitating antimicrobial stewardship. Timely reporting of results increases the confidence of prescribers that they are treating infection appropriately with empirical antibiotics and allows treatment to be focused.

In recent studies by Mahrous, et.al and Claeys, et.al, an antimicrobial stewardship benefit was shown in their hospitals from the reporting of rapid-diagnostic testing in combination with pharmacist intervention.[10,11] The detection of resistance genes can also facilitate a considerable reduction in reporting time, as explained by Bianco, et. al.[12] The combination of diagnostic and antimicrobial stewardship has demonstrated improved antibiotic use; however, a recent publication from the CDC found that 56% of antibiotic use was unsupported in patients being treated at U.S. hospitals in 2015.[13] The study included patients with community-acquired pneumonia, urinary tract infections, or who were treated with fluroquinolones

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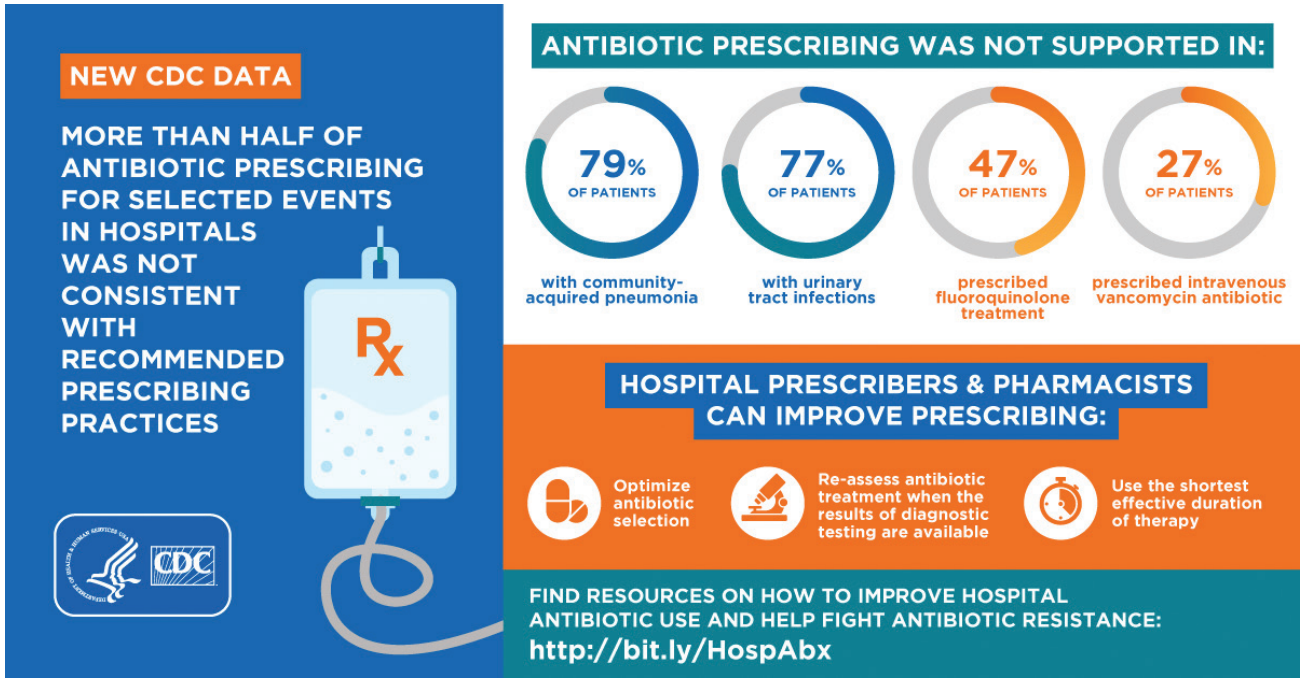

Figure from CDC

or vancomycin. Researchers defined the antibiotic use as unsupported when the patients didn't have specific signs or symptoms of infections, the wrong antibiotic was prescribed, or the length of treatment was too long. One of three calls to action was to re-assess antibiotic treatment when the results of diagnostic testing are available, reinforcing the importance of the rapid reporting of diagnostic testing.

Diagnostics are critical to slowing the spread of AMR. Better diagnostics can guide faster, more appropriate treatment to ensure patients receive the right drug for their infection, at the right time, for the right duration. Diagnostics can help us to preserve antibiotics and ensure they remain effective when they are needed most.

Dedicated funding and strong market need can and have driven rapid innovation. As we've seen, COVID-19 diagnostic tests were developed within weeks of the outbreak along with public health capabilities to address the pandemic like digital data collection, local manufacturing, and global distribution. There have been platforms built to collate data, resources marshaled, and creativity unleashed. We should capitalize on this innovation for AMR across the board, but we should certainly continue to move diagnostics for antibiotic-resistant pathogens forward.

The role of cross sector collaboration

Governments, researchers, and industry partners around the world have mobilized to develop diagnostics, therapeutics, and vaccines for COVID-19. The development of new recommendations and practices continue to be deployed to slow the spread of COVID-19. The burden of drug-resistant infections will likely surpass COVID-19. Drugs like antibiotics are a vital tool in modern medicine to prevent and treat infections. As drug-resistant infections are becoming more common, modern medicine as we know it is at risk, and much like COVID-19, these infections have the potential to overwhelm our healthcare structure.

In an article by Williams, et.al., the authors state that antimicrobial resistance is a threat to global health and food security. The emergence of COVID-19 in 2020 has focused attention on yet another global health challenge. The difference is that the pandemic is seen as a proximate public health crisis requiring immediate action. Consequently, relatively less attention has been directed towards antimicrobial resistance and climate change, which also pose urgent threats to lives and livelihoods, and in the end, may have worse global consequences.[14]

There are several tools available to learn more about how a cross sector approach will drive an improved focus, leading to a positive impact on the risk of drug resistant infections:

- A new podcast series, *Superbugs and You*, addresses the global AMR crisis through conversations with patients, clinicians, and researchers to discover how superbugs are affecting people and healthcare systems globally.[15]
- The recently released U.S. 2020-2025 National Action Plan accelerates response to antibiotic resistance by presenting coordinated, strategic actions to improve the health and well-being of all Americans across the One Health spectrum.[16] One Health is a collaborative, multisectoral, and transdisciplinary approach – working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.
- A new report from Wellcome Trust - The global response to AMR momentum, success, and critical gaps – was released in November 2020. This report gives an update on the status quo, recent developments and remaining critical gaps in the AMR response globally. One of the notable recent successes that was highlighted in the report was "the AMR community has grown into a broad, multi-sectoral coalition of actors that come from a range of sectors, including human health, animals and agriculture, and the environment."[17]

Surveillance, infection prevention, and diagnostic stewardship have been deployed successfully to combat the global COVID-19 pandemic. Continued focus on these practices with improved antibiotic stewardship efforts need to be deployed to combat the insidious threat of drug resistant infections.

REFERENCES:

1. Antimicrobial resistance. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance#:~:text=Antimicrobial%20resistance%20(AMR)%20is%20a,public%20health%20threats%20facing%20humanity. Accessed March 1, 2021.

2. No time to wait: securing the future from drug-resistant infections. World Health Organization. https://www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/. Accessed March 28, 2021.

3. Talkington K. Superbugs don't respect borders. October 2017. The Pew Charitable Trusts. https://www.pewtrusts.org/en/research-and-analysis/articles/2017/10/10/superbugs-dont-respect-borders.Accessed February 25, 2021.

4. Candida auris. Centers for Disease Control and Prevention. https://www.cdc.gov/fungal/candida-auris/index.html. Accessed February 26, 2021.

5. Chen J, Tian S, Han X, et al. Is the superbug fungus really so scary? A systematic review and meta-analysis of global epidemiology and mortality of Candida auris. *BMC Infect Dis*. 2020;20(1):827. doi:10.1186/s12879-020-05543-0.

6. Hall, W, McDonnell, A, O'Neill J. Superbugs: An Arms Race Against Bacteria. Cambridge, MA: Harvard University Press; 2018.

7. Wee LEI, Conceicao EP, Tan JY, et al. Unintended consequences of infection prevention and control measures during COVID-19 pandemic [published online ahead of print, 2020 Nov 4]. *Am J Infect Control*. 2020; S0196-6553(20)30963-9. doi:10.1016/j.ajic.2020.10.019.

8. Bentivegna E, Luciani M, Arcari L, Santino I, Simmaco M, Martelletti P. Reduction of multidrug-resistant (MDR) bacterial infections during the COVID-19 pandemic: a retrospective study. *Int J Environ Res Public Health*. 2021;18(3):1003. doi:10.3390/ijerph18031003.

9. Vaccines to tackle drug-resistant infections: an evaluation of R & D opportunities. Wellcome Trust, https://vaccinesforamr.org/. Accessed March 28, 2021.

10. Mahrous AJ, Thabit Pharm DAK, Elarabi S, Fleisher J. Clinical impact of pharmacist-directed antimicrobial stewardship guidance following blood culture rapid diagnostic testing. *J Hosp Infect*. 2020; 106 (In Press): 436-446. doi.org/10.1016/j.jhin.2020.09.010.

11. Claeys K, Heil E, Hitchcock S, Johnson J, Leekha S, Management of gram-negative bloodstream infections in the era of rapid diagnostic testing: impact with and without antibiotic stewardship. Open Forum Infectious Diseases. 2020; 7(10): ofaa427. https://doi.org/10.1093/ofid/ofaa427.

12. Bianco G, Boattini M, Iannaccone M, Sidoti F, Cavallo R, Costa C. Detection of antibiotic resistance genes from blood cultures: performance assessment and potential impact on antibiotic therapy management. *J Hosp Infect*. 2019; 102: 465-469. doi.org/10.1016/j.jhin.2019.03.007.

13. Magill SS, O'Leary E, Ray SM, et al. Assessment of the appropriateness of antimicrobial use in U.S. hospitals. *JAMA Netw Open*. 2021;4(3):e212007. doi:10.1001/jamanetworkopen.2021.2007.

14. Stewart Williams J, Wall S. The AMR emergency: multi-sector collaboration and collective global policy action is needed now. *Glob Health Action*. 2019;12(sup1):1855831. doi:10.1080/16549716.2019.1855831.

15. Superbugs and you: true stories from scientists and patients around the world. Antimicrobial Resistance Fighter Coalition. 2020. https://antimicrobialresistancefighters.org/podcasts. Accessed March 25, 2021.

16. U.S. national action plan for combating antimicrobial-resistant bacteria (national action plan). Centers for Disease Control and Prevention. 2020. https://www.cdc.gov/drugresistance/us-activities/national-action-plan.html. Accessed March 25, 2021.

17. The Global response to AMR momentum, success, and critical gaps. Wellcome Trust. November 2020. https://cdn.eventsforce.net/files/ef-lpifs4q56r2a/website/785/wellcome-global-response-amr-report.pdf. Accessed March 29, 2021.

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CONTINUING EDUCATION TEST

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TEST QUESTIONS

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1. **What is the term used to describe when bacteria, viruses, fungi, and parasites change over time and no longer respond to medicines, making infections harder to treat and increasing the risk of disease spread, severe illness and death?**
   - A. super viral
   - B. antimicrobial resistance
   - C. tired response
   - D. ineffective bacteria

2. **What was published by United Nations Interagency Coordination Group on AMR, providing an effective framework for global and national AMR action plans?**
   - A. pandemic response report
   - B. United Nations COVID plan
   - C. UN variants report
   - D. global strategy to curb drug resistance

3. **What informs surveillance, infection prevention practices and antibiotic stewardship?**
   - A. laboratory testing results
   - B. global pandemic report
   - C. variants strategy
   - D. the ATF

4. **What allows hospitals to prepare for surges, governments to deploy testing strategies, and citizens to modify their behavior appropriately?**
   - A. tracking
   - B. White House briefs
   - C. MLO-online.com
   - D. hand washing

5. **Bacteria causing drug resistant infections move quickly across the globe via _____.**
   - A. trucks
   - B. coughing
   - C. fleas
   - D. multiple carriers

6. **What can be found in Enterobacteriaceae?**
   - A. *Candida auris*
   - B. COVID-19
   - C. NDM-1
   - D. Polio

7. **What superbug is resistant to penicillin, cephalosporin, and carbapenems?**
   - A. *Candida auris*
   - B. COVID-19
   - C. NDM-1
   - D. E. coli

8. **What is considered a superbug fungus?**
   - A. Candida auris
   - B. COVID-19
   - C. NDM-1
   - D. E. coli

9. **A study showed the overall mortality of C. auris infection was ____.**
   - A. 27%
   - B. 32%
   - C. 36%
   - D. 39%

10. **What does the CDC use to prioritize domestic antimicrobial resistance surveillance?**
    - A. CDC COVID-19 Variants Tracking Resource
    - B. CDC Antibiotic Resistance Laboratory Network
    - C. FDA Superbug Directory
    - D. Drug Resistance Abuse Education

11. **What is the acronym for The Global Antimicrobial Resistance Surveillance System?**
    - A. TGASS
    - B. GRASS
    - C. GARS
    - D. GLASS

12. **Who launched a map recently to collect details of research projects focused on surveillance of drug resistant infections?**
    - A. SEDRIC
    - B. NIH
    - C. FDA
    - D. WHO

13. **Preventing drug resistant infections reduces the use of _____ and improves _____.**
    - A. steroids, morale
    - B. antibiotics, patient outcomes
    - C. anti-virals, IQ
    - D. doctors, statistics

14. **Key tools to combat COVID-19 and AMR include:**
    - A. media, marketing, and the internet
    - B. nasal swabs, pipettes, and agar
    - C. analyzers, AI, and genetic testing
    - D. handwashing, global vaccination, and prevention

15. **Infection prevention measures are specific to one pathogen.**
    - A. True
    - B. False

16. **With enhanced IPC measures introduced to contain COVID-19, they saw a decrease in hospital-wide acquisition rates of _____ together with central line associated bloodstream infections.**
    - A. COVID-19
    - B. Candida auris
    - C. MRSA
    - D. NDM-1

17. **Good adherence to IPC impacted _____ rates as well.**
    - A. HAI
    - B. recovery
    - C. hospital return
    - D. insurance

18. **In some settings due to a higher risk case-mix, shortages of equipment, and staff shortages, _____ of nosocomial infections was seen.**
    - A. a decrease
    - B. recovery
    - C. a plateau
    - D. an increase

19. **_____ of antibiotic use was unsupported in patients being treated at U.S. hospitals in 2015.**
    - A. 12%
    - B. 27%
    - C. 56%
    - D. 75%

20. **More than _____ people are using healthcare facilities with no water service.**
    - A. 900 million
    - B. 300,000
    - C. 5 trillion
    - D. 900,000

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ANTIMICROBIAL RESISTANCE FIGHTER COALITION

The availability of more accessible, automated solutions means NGS can now be run cost-efficiently with lower sample volumes.

Insourcing next-generation sequencing supports patient care at community hospitals

By Garret Hampton, PhD

A year ago, most people outside of the science and healthcare community were unfamiliar with the concept of next-generation sequencing (NGS). Fast-forward to today, and you cannot read the news without hearing concerns about new SARS-CoV-2 variants spreading across the globe, and the increased need for viral genome sequencing to better identify and track emerging virus mutations.

While sequencing has only recently become headline news, the approach has been used for years to enable fundamental biomedical discoveries and has seen the progressive transition to clinical testing settings. In oncology, for example, targeted NGS has been instrumental in helping the healthcare community deliver on the promise of precision medicine by enabling clinicians to access precise data about a tumor's genetic makeup and match patients with targeted treatments to improve outcomes. What began as a revolutionary research tool in large academic medical centers a decade ago has emerged as an important platform for clinicians to accelerate the most effective treatment of their patients.

In 2020, the U.S. Food and Drug Administration (FDA) approved 20 new personalized drugs and biologics.[1] For patients who are candidates for targeted therapies, these therapies are often more efficacious and also less toxic than existing front-line therapies, such as chemotherapy or radiation. As more targeted therapies become available, demand for multi-biomarker testing to match patients with these treatments is growing – creating a case for more hospitals to offer NGS assays to their patients.

Five years ago, NGS for clinical assessment was typically performed in academic medical centers with a deep understanding of the technical aspects of sequencing and knowledge of what to do with the vast amounts of information. However, technological advancements have now enabled targeted genomic sequencing with faster turnaround times, reduced tumor specimen requirements and increased ease of use, requiring less training and hands on time. As a result, an insourced sequencing model is becoming a very attractive proposition for many hospitals, including community-based hospitals where the majority of cancer patients are diagnosed and treated. In other words, bringing testing closer to the patient.

Faster results

Faster turnaround times are critical to identify patients who may be eligible for targeted, potentially more effective, therapies, particularly for late-stage patients who do not have time to spare. In lung cancer, as one example, patients usually do not demonstrate symptoms until their disease has progressed. Their cancer often goes undiagnosed until stage IV.[2] The five-year survival rate for advanced lung cancer is less than 25 percent,[3] but a recent drop in lung cancer deaths indicates that new treatments, such as immune checkpoint inhibitors and targeted therapies, are improving patient outcomes.[4] For patients to benefit from these treatments, comprehensive molecular test results are needed – quickly. In one survey, 76 percent of oncologists responded that improvement in turnaround times would lead to improved patient care. [5]

While insourced NGS is becoming more tenable, many hospitals continue to rely on single-gene testing. Not only does sequential single-biomarker testing fail to offer a comprehensive view of the molecular profile of a patient's tumor, due to the difficulty of obtaining large amounts of a tumor sample through

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[1] Kellum JA et al. Targeting acute kidney injury in COVID-19. Nephrol Dial Transplant (2020) 35: 1652–1662.

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biopsy, there is often insufficient cancer tissue to generate more than two or three test results.

As the utility of NGS for clinical assessment has become clearer, clinicians have sought ways to get these tests done. However, to get a comprehensive view of a tumor's molecular profile, clinicians have had to send a patient's tumor sample out to a centralized reference lab for NGS testing, a process that can take 10 days or more. In addition, there may be higher failure rates due to compromised material during shipment or lack of sufficient material.[6] For many cancer patients, waiting for this amount of time to even begin treatment is simply not an option. In the absence of the information needed to match a patient's tumor profile with a targeted therapy, a patient may have already been started on a conventional treatment, such as chemotherapy or radiation, in an attempt to take quick action.

Today, however, it is possible for a pathology lab at an accredited community hospital to perform NGS and generate test results in one to two days. Some community hospitals are already putting this new technology into action. As one example, William Osler Health System (Osler) in Ontario, Canada, recently began insourcing comprehensive genomic sequencing with a fully automated solution. Previously, the hospital's care teams would wait up to two months to receive actionable results from outsourced molecular profiling. Then, Osler brought biomarker testing in-house and was able to rapidly accelerate turnaround times, with test results available 94 percent of the time in a patient's first consult, compared to just 17 percent of the time when they were outsourcing testing. Now, by adopting an automated NGS solution, with just one test, Osler clinicians can access a more comprehensive view of a patient's tumor with the same rapid turnaround times.

Enhanced efficiency

Research has shown that therapy selection by NGS is also economical. A 2018 University Hospitals Cleveland Medical Center study on late-stage non-small cell lung cancer patients demonstrated how in-house NGS enabled clinicians to identify a broader set of actionable drug targets 50 percent faster than the time recommended by National Comprehensive Cancer Network (NCCN) guidelines – at no additional cost to the hospital.[7]

Previously, NGS was only economical for high throughput applications, but the availability of more accessible, automated solutions means NGS can now be run cost-efficiently with lower sample volumes. In addition, new, fully automated systems can be run by one lab technician, rather than a team of highly trained technicians or researchers, allowing labs to adopt this capability with existing staff and minimal training. The automation of NGS also minimizes hands-on time to reduce the risk of human error while accelerating time-to-results.

Improved patient outcomes

In-house testing means patients can benefit from the stronger collaboration that naturally occurs between pathologists and oncologists. Molecular tumor boards are becoming more common, in which oncologists, molecular pathologists, and staff meet to formulate the best treatment options for each patient. The board provides a forum in which oncologists can ask questions about a patient's particular gene mutation to gain information that will impact prognosis or the selection of therapy. Similarly, the pathologist becomes part of the patient's care team, rather than just the issuer of a written report, and facilitates translation of the NGS results to inform clinical treatment.

The future of NGS in community hospital settings

Over the last several years, an increasing number of community hospitals have embraced the role that NGS can have on informing patient care. Unfortunately, the coronavirus pandemic has forced many hospitals and patients to cancel or postpone oncology visits and tests. In the interim, some oncology labs have leveraged their expertise in molecular testing to join global SARS-CoV-2 surveillance efforts, especially as new strains have fueled a call for increased sequencing to understand these variants, including whether they are more transmissible, increase disease risk or demonstrate vaccine escape.

In addition to creating new capabilities for oncology labs with existing NGS programs, the pandemic has also accelerated adoption of NGS in labs that have not previously been exposed to this technology. While increased SARS-CoV-2 sequencing will remain important even as vaccination rates increase, wider prevalence of community-based access to NGS will open the doors for increased use of this technology for applications beyond COVID-19 research. Some labs that have adopted NGS technology for SARS-CoV-2 research are also speaking with local health systems about sequencing cancer patient samples, for example.

Ultimately, the pandemic has raised the profile of NGS and accelerated adoption by more labs that can immediately find utility sequencing SARS-CoV-2 samples and later apply this same technology to oncology and other disease areas, increasing the accessibility of precision medicine throughout more communities. The goal is to ensure *all* patients have access to comprehensive test results that can guide more effective, targeted therapy selection and improve health outcomes. The democratization of NGS is a huge step forward in making this possible.

REFERENCES

1. Personalized medicine at FDA: the scope & significance of progress in 2020. Personalized Medicine Coalition 2020: 7-8.
2. What is stage IV lung cancer? Cancer Treatment Centers of America. 2020. https://www.cancercenter.com/cancer-types/lung-cancer/stages/stage-iv-lung-cancer. Accessed March 31, 2021.
3. Your chances of surviving lung cancer. WebMD. 2019. https://www.webmd.com/lung-cancer/guide/lung-cancer-survival-rates. Accessed March 31, 2021.
4. Sharpless N. Lung cancer deaths are declining faster than new cases. Advances in treatment are making the difference. August 13, 2020. *STAT*. https://www.statnews.com/2020/08/13/lung-cancer-deaths-declining-faster-than-new-cases-due-to-advances-in-treatment/. Accessed March 31, 2021.
5. Menezes J; Joy V; Vora A. What can we learn from oncologists? A survey of molecular testing patterns. Poster presented at: AMP 2018 Annual Meeting; November 1-3, 2018; San Antonio, TX.
6. Heeke S et al. Comparison of tumor mutational burden using the Ion Ocomine TML and FoundationOne assays with routine clinical FFPE tissue samples to predict durable clinical benefit in lung cancer and melanoma patients – a multivariate analysis integrating PD-L1 and CD8+ evaluation. Paper presented at: AACR Annual Meeting 2019; March 29-April 3, 2019; Atlanta, GA.
7. Sadri N; Miller T; Yang M; Dowlati A; Friedman J; Bajor D; Chang R; Willis J. Clinical utility of reflect testing using focused next generation sequencing for management of patients with advanced lung adenocarcinoma. *JCO*. 2018; 36(15), e24199-e24199. doi: 10.1200/JCO.2018.36.15_suppl.e24199.

Garret Hampton, PhD, is President of Clinical Next-Generation Sequencing and Oncology at **Thermo Fisher Scientific**.

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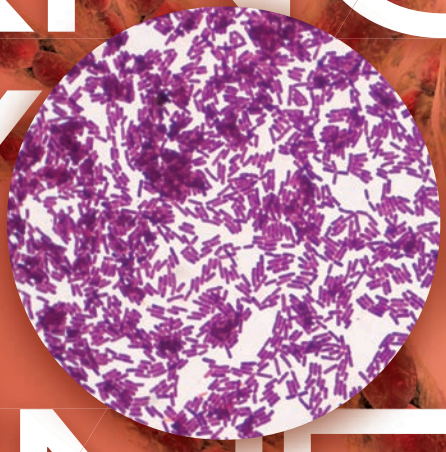

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Alameda Health System's survival strategy for COVID-19

By Marisa L. Williams

Seegene TECHNOLOGIES

At the MLO Forum on COVID-19,

Alameda Health System's Clinical Laboratories described their survival strategy put in place during the COVID-19 pandemic. From accessing test kits, supplies and reagents, to balancing test reagent/supply allocations to meet ever-changing testing demand, this experience allowed Alameda Health System's laboratories to identify factors critical for the selection and successful implementation of a new SARS-CoV-2 test method by partnering with Seegene.

The speaker at the Forum was Valerie Ng, Ph.D., MD, Chair of Laboratory Medicine & Pathology at Alameda Health System (AHS) and Laboratory Director of the health system's clinical laboratories, who is also Professor Emeritus in the Department of Laboratory Medicine, UCSF.

She has served on the board of directors for the Clinical and Laboratory Standards Institute and the external advisory board for the University of Georgia College of Pharmacy.

Currently, she is the Chair of the Laboratory Medicine Editorial Review group for Doody Enterprises, a member of the California Hospital Association's Hospital Laboratory Workforce Initiative (HLWI), a member and current Chair of the Centers for Disease Control and Prevention's Clinical Laboratory Improvement Amendments Committee (CLIAC), a member of the CARB-X Scientific Advisory Board, and an ad hoc external reviewer for the Moore Inventors Fellows Program of the Gordon & Betty Moore Foundation.

The emerging pandemic

While the first case hit the States on Jan. 21, 2020, Dr. Ng shared that the testing was not widely available until a month later. Mid-March, Quest came up with their test, but demands were soaring. At the end of March, there was a failure in the public health lab testing, and Ng personally had to drive samples 30 miles away. June 22, 2020, was the first time the lab was able to implement testing in-house for COVID-19. The rapid antigen test did not become available until Dec. 1, 2020, and by mid-December, they had implemented Seegene RT-PCR testing as well. Towards the end of January, a rapid antigen test was added to the repertoire, marking the ninth test that was implemented in a 10-month period.

March through December, there was additional paid time off allowed for the COVID-19 pandemic and mandated by the government, resulting in a massive shortage of staff. In September and October, the facility ran out of urine collection tubes, and for November and December, they ran low on agar media in the microbiology lab, leaving them unable to set up cultures to identify pathogens and determine susceptibility. Add to that the worldwide plastic shortage, and it was hard to get micropipette tips. Only able to produce a set number of tests each day with a demand at least triple what could be performed forced them to reach out to fellow labs for assistance.

Speeding up TAT

Having a Turn-Around-Time (TAT) of 2-3 days was too long in the midst of outbreaks, lengthened by the need to manually enter results. They had been watching the global status of tests being performed each day. They noted that South Korea was producing more tests than needed and was exporting their surplus. They were quite nervous to partner with a vendor from another country, especially with buyer beware stories of people ordering nasal swab supplies from international vendors only to receive makeup applicators instead.

Ng was very attracted to the idea of automation for high throughput labs. Seegene offered a line of instrumentation to make testing easier, essentially a walk-away PCR which met her needs. Seegene's Walnut Creek location was only ten minutes from the lab, so Ng's coworkers loved the idea of being able to drive over and knock on their door if they were having problems. They also sought a one-stop shopping supply chain. Hoping Korea's control of the COVID-19 pandemic meant less local test supply-demand and more available for international use, they decided to partner up with Seegene for 'one-stop shopping' – i.e., reagent kits, PCR primers, liquid handler, real-time PCR instrument, plate sealer, pipette tips, PCR tray, swabs, and another personal computer.

Offering related products, such as the one-tube primary screening for SARS-CoV-2, Flu, and RSV by real-time PCR, with results available within a few hours after extraction with an automated platform and auto-interpretation, was also of interest (but not yet implemented) to Ng. Seegene has also been developing assays capable of detecting and identifying SARS-CoV-2 variants.

For more information, visit www.seegenetech.com

Alternate non-invasive specimen collection solution for Sars-CoV-2

By Marisa L. Williams

SARS-CoV-2 marched its way around the globe, igniting a crisis the world was not prepared for. As demands for solutions increased, there were supply shortages and increased needs in sample collection, as laboratories saw an influx in demand for Sars-CoV-2. Many labs pivoted their daily operations entirely, scaling up, with some demands going from hundreds to millions. More labor was needed, with supplies, training and other changes and many turned to lab-developed saliva kits.

No problems, only solutions

With the mindset of no problems, only solutions, Thermo Fisher Scientific explored alternatives to crisis challenges, such as creating alternative specimen collection options. They looked to use something other than the nasal swab, which had many complaints of discomfort from end users and wasn't optimized for high frequency sample collection. They also wanted to create a kit that was optimized specifically for saliva unlike the lab-developed saliva kits so labs can automate their entire protocol helping them save time and money. Their solution is the new Thermo Scientific SpeciMAX Saliva Collection Kit.

The presentation at the MLO Forum focused on this new saliva collection kit and how Thermo Fisher Scientific responded to Sars-CoV-2 issues earlier in the year by ramping up their magnetic bead productions and continues to innovate sample preparation solutions. Sara Brown, Director of Global Product Management for Reagents in Sample Preparation at Thermo Fisher Scientific detailed their rapid response to the global crisis. Brown's education speaks volumes, as she earned a PhD and a Bachelor of Science in Biochemistry from the University of Wisconsin – Madison and a Master of Science in Molecular, Cellular and Developmental Biology from Yale University.

Brown leads global portfolio strategies, manages day-to-day operations for top-line growth and profitability, and provides leadership in the development of innovative solutions focused on manual and automation reagents at Thermo Fisher Scientific.

Surveillance testing

Thermo Fisher Scientific's Forum session showed how to mitigate the effects of SARS-CoV-2 through surveillance testing, with high frequency and high throughput testing using saliva samples, as opposed to nasal swabs or lab-developed saliva kits, in order to expand collection sample possibilities. Their easy-to-use kit, containing a tube, funnel, and cap is optimized for saliva collection and a 6 mL standardized size to fit into automation racks. With this innovation, there is no need for manual pipetting of saliva, so labs can save hours on manual labor when using a liquid handler/automation system.

Getting it right

Thermo Fisher Scientific worked with labs globally to get it right. By partnering with new suppliers and going to 24-hour manufacturing operations, they shortened processes that originally took six weeks to a couple days.

By October first of last year, Thermo Fisher Scientific delivered more than 145 million sample prep kits and 4,500 sample prep instruments worldwide. They continue to support Sars-Cov-2 solutions through their new SpeciMAX Saliva Collection Kits.

For more information, visit https://www.thermofisher.com

Improving existing QC practices

By Nico Vandepoele, BSc and Curtis Parvin, PhD

Quality control (QC) management is one of the most important tasks that takes place in the clinical laboratory. There are different regulations available for guidance, such as CLIA and ISO 15189, which outline mandatory QC practices for in the lab. Accreditation bodies – such as COLA, CAP and TJC review – audit laboratory QC processes and practices and are sources of information, too.

While QC practices should be reviewed periodically to improve or enhance them, labs usually don't do this for well-established processes. This may be because revising a process will frequently lead to follow-up tasks and updates to documentation. If the changes are made to a practical process, changes to standard operating procedures (SOP) and retraining of the staff may also be needed.

However, new and updated guidance for improved QC practices continues to be developed and promoted. Laboratories should be aware that some of their current practices may have been updated, or their current practices in use might need revisions. This article highlights a few QC practices that themselves may be in place at some level, but might not be current with updated guidance – which can provide useful insights and other benefits, such as time and cost savings.

QC targets

One of the most important tasks in quality control is establishing a QC target and range, or standard deviation (SD), for controls. Both the mean and the SD must be estimated by the lab when starting with a new quality control lot. The outdated historical practice of measuring 20 results over 20 days was revised in 2016 via Clinical and Laboratory Standards Institute (CLSI) C24 A4.[1]

Under the revised standard, a crossover study – based on a rigorous statistical analysis – can be performed faster with fewer QC materials to provide initial QC targets. By updating their practice in this regard, laboratories can also benefit from significant time and cost savings, while improving their initial QC target estimation.

Calculating the new target mean can now be done by measuring 10 QC results over 10 different days. When multiple instruments or instrument modules are running the same tests, the 10 new lot measurements are spread over the different instruments (for example: 5 QC results on two different instruments over 5 days), thus lowering the time to establish a new mean even more. There is no longer a need to establish a new SD or coefficient of variation (CV). The lab can simply use its current QC long-term CV – and use that CV to calculate the new SD. Alternatively, the lab can copy the current CV to the new lot. After a period of time, the lab would then review QC data and may update the range as indicated by performance.

QC Frequency and Testing Volume

Another QC practice that has been defined by regulatory bodies is the frequency of running quality control.

Testing two levels of QC once per day has been the fixed minimum for many U.S. laboratories – with the exception of blood gas, hematology and coagulation QC, which are run more frequently. With almost all of today's modern instruments running in a continuous testing mode, the QC schedule (or when to test QC) is now as important as how many QC processes are tested and what QC rules are applied.

To limit reporting of erroneous patient results, it is not the time between QC events that is most important, but the

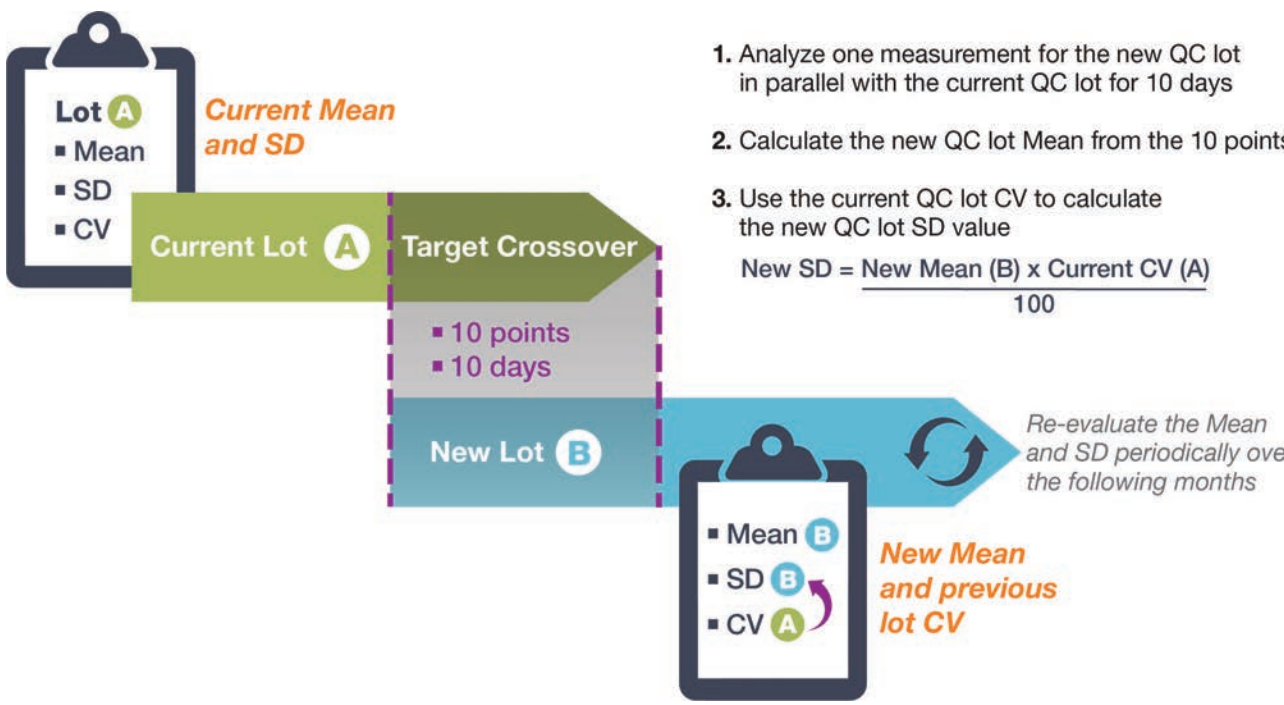

Figure 1: Crossover Study Process

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Figure 2: Sequence of events leading to patient harm from reporting an incorrect patient result[4]

number of patients samples run between these QC events. If they only run their QC once per day, a lab running 50 patient samples a day and a lab running 5,000 patient samples a day have distinctly different levels of risk of reporting incorrect patient results.

It is very important to know the number of patient samples run between QC events. Based on this number, labs should attempt to make the time between QC events shorter than the time needed to recover from an out-of-control condition.[2] Many labs are forced to spend extra time identifying, pulling, and retesting suspect patient results, because they allowed too much time to pass between QC procedures. The solution is to shorten the time between QC events.

QC Frequency and Critical Control Points

Besides the number of patient samples run between QC events, another important consideration in terms of enhancing QC practices is the concept of critical control points.[1] For example, it is important to end a testing run that occurs before a critical event with QC. These critical events are tasks that might adversely impact the measurement procedure, such as replacing reagents, performing maintenance, or calibrating instruments. The QC process confirms that the instrument was still performing within normal specifications throughout the testing run that occurred before the critical event. After execution of the critical event, a lab should start the new run with another QC procedure to ensure the critical event did not negatively impact instrument performance.

QC procedures also should be executed at the end of the day. Many smaller laboratories will start the day with a QC run, after they have performed maintenance, replaced reagents and performed calibrations. If this process is only repeated once a day, it can become challenging for the laboratory to effectively confirm if the patient samples tested throughout the previous day were produced while the instrument was still performing within acceptable specifications. The only way to confirm this is for labs to end the day with a QC run. If this run is accepted, patient results can be reported. This process enhancement is also called "bracketing QC."

All these suggested practices are part of the laboratory's QC strategy, and they should be based on quality requirements and performance goals based on the risk of harm to patients. Patient risk-based QC practice guidelines, such as CLSI EP-23,[4] provide a formal approach, which the laboratory can use to establish policies and procedures to help prevent or reduce patients' risk of harm. Labs should evaluate the different kinds of malfunctions or errors that an instrument might produce and the frequency they could occur. The probability of occurrence of patient harm depends on a measurement procedure's reliability, the effectiveness of the laboratory's QC strategy (to limit the number of erroneous patient results that get reported when out-of-control conditions occur) and the likelihood that erroneously reported results could lead to patient harm.

With these patient-risk guidelines, the laboratory should devote more QC to analytes with a higher probability that erroneous results will lead to patient harm and also to analytes, where the expected severity of harm is higher.[3] This helps to maintain the focus of the lab's QC on patient safety, as well as instrument performance.

Conclusion

The focus of quality control is no longer centered around the instrument alone. It is important to think about the final use of the test results. Not all tests are equal; therefore, the QC strategy does not need to be exactly the same for all tests. It is easy to use the same practice across all tests (same frequency, QC rules, number of QC levels, etc.). However, this approach leads to situations in which some tests might be doing "too much QC," while other tests might not have sufficient levels of error detection, potentially leading to patient harm if not detected in time.

Defining QC practices is an ongoing task for any laboratory. With new tests, instrumentation, methodologies and updated guidance documents emerging all the time, the availability of a good QC plan and QC practices is very important.

REFERENCES

1. C24 A4: Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions, 4th Edition. CLSI., Wayne, PA, 2016.

2. Parvin C. QC design: it's easier than you think. *Medical Laboratory Observer*. 2013. https://www.mlo-online.com/home/article/13006005/qc-design-its-easier-than-you-think. Accessed March 31, 2021.

3. Parvin C. Six QC recommendations to consider today. *Medical Laboratory Observer*. 2017 https://www.mlo-online.com/continuing-education/article/13009039/six-qc-recommendations-to-consider-today. Accessed March 31, 2021.

4. CLSI EP23-A: Laboratory Quality Control Based on Risk Management; Approved Guideline. CLSI: Wayne, PA, 2011.

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Curtis Parvin, PhD, is retired from **Bio-Rad**, where he was Manager of Advanced Statistical Research. Prior to joining Bio-Rad, Parvin was the Director of Informatics and Statistics at the faculty of Washington University School of Medicine.

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Forecasting the laboratory supply chain use

By Marisa L. Williams

This past year culminated in unforeseen supply chain challenges for clinical laboratories, forcing many lab directors to reevaluate their inventory levels, sources, and the value of forecasting.

Focusing on inventory strategies, operational efficiency, reagent efficiency and test utilization stewardship, labs can leverage their suppliers' analytic capabilities to mine data from instruments and/or middleware to generate an analysis that provides detailed breakouts on the use of reagents, calibrations, quality control (QC), repeats and troubleshooting.

Reviewing usage and ordering levels allows lab directors to establish their average daily and weekly forecast levels of supplies needed, providing insight on testing volumes, which can be leveraged to eliminate reagent waste for low-volume assays, improving inventory management of both reagents and consumables, and eliminating excess QC testing.

Track supply utilization and keep records

Lab directors should review reports on supplies ordered, as compared to the number of invoiced tests. Utilization goes beyond the lab to the entire organization. A facility's chief medical officer can help review the tests the organization runs, educating peers on Lab Stewardship and eliminating unnecessary supply ordering.

Mark Krhovsky

According to Mark Krhovsky, Vice President of Laboratory Sales, Medline Industries, there are three primary areas that lab directors should focus on: (1.) consumable standardization, (2.) instrumentation and capital contracts, and (3.) distribution programs.

He noted that hospital labs can be notorious for product variation. "The lack of purchasing oversight has allowed each individual clinician [his or her] own procurement power, leading to a more fragmented sourcing approach. There are undoubtedly areas where high brand preference is excusable and even necessary, but many of the general consumable categories offer prime opportunity for standardization." Review the costs of basics, such as microscope slides, and even slightly more complex products, like pregnancy tests, for potential savings.

A key benefit of knowing the supply needs is cost savings. To capitalize on savings, a number of sources advise reviewing reagent rentals contracts, and considering lower-cost alternatives. Rethink "big-box closed systems," requiring use of a supplier's proprietary reagents and consumables after buying the supplier's analyzer.

"Instrumentation, and their subsequent reagents, are typically one of the highest spend categories within any hospital lab," Krhovsky said. "This includes, but is not limited to, chemistry, immunoassay, hematology, molecular, centralized urinalysis and blood bank. The majority of these contracts are manufacturer-direct, run five-plus-year terms, and the amount to spend that can quickly get into the tens of millions of dollars. Incredibly clinical in nature, there is undoubtedly a technical element to these decisions that is rooted in the needs, dynamics and testing requirements for that particular lab. That being said, there is always room for supply chain to be involved with product negotiations and contract review."

Being aware of individual situations, what is and is not offered and available at specific locations, some laboratory departments prefer to operate on their own unique circumstances, processes and technology, regardless of rudimentary skills in contracting, negotiating and procurement. A lab director might not know the questions to ask or what to look for, but supply chain, finance and other organizations can help labs forecast their inventory needs.

The ability to forecast and predict volume fluctuations can help with more than potential savings, as suppliers advise clients on an improved and balanced structure between instruments, reducing time for quality control and calibration. If there is a fluctuation or change in volume, suppliers can also advise on creating a new operating model. Reviewing instrumentation and capital contracts is important, as is the distribution programs.

Photo by Louis Reed on Unsplash

Plastic pipette tips and tubes are amongst the supplies that labs report in high demand.

"If you compare lab distribution to the current standard of medical/surgical distribution – where supply chain has been an integral partner for decades – the disparity is hard to ignore," Krhovsky noted. "And yet the lab is as important as any clinical department at the hospital, so why the lack of change to the status quo? I believe lab clinicians and leaders are busier than ever, and also experiencing the pressure of more impactful outside stressors. Their focus has been on turnaround times, staffing, reimbursement changes and other tangible elements that are paramount to their long-term relevance and viability."

In looking long-term, dedicating departmental resources and helping to build relationships can make a big difference, too, according to Barbara Strain, MA, SM (ASCP), CVAHP, Principal, Barbara Strain Consulting

A ship stuck in the Suez Canal has created international shipping delays, including for lab supplies.

LLC, formerly Director of Value Management at University of Virginia Health System, and current member of MLO's Editorial Advisory Board. Strain has experience in helping labs apply value analysis to its decision-making.

"Assign specific buyer and contracting staff to the clinical laboratory, including, but not limited to, the core laboratory and specialty testing laboratories, [such as] microbiology, molecular, immunology, toxicology, pathology, phlebotomy and blood bank," Strain recommended. "This assures that the supply chain values the laboratory operations and wants to have a firsthand understanding of their needs."

Barbara Strain, MA, SM (ASCP)

Together, they should set up a lab-centric inventory management program.

"If one does not already exist, co-designing an inventory management system to guarantee laboratory reagents, test kits, PPE and other products needed for patient testing are ordered and delivered on time every time is key," she continued. "Supply chain and the laboratory might also draw on internal process improvement coaches or use services offered by laboratory supplier contracts to assist in 5S and other LEAN activities to organize workflow and create nearby supply availability locations."

Labs that have embraced value analysis, according to Strain, recognize that the process helps to keep initiatives on track by:

- presenting contracting options
- organizing supplier meetings and presentations
- assisting in collecting and providing product evaluation reports
- scheduling end-user reference account calls
- analyzing current versus estimated new costs, ROI and other analytics
- facilitating consensus decision making
- establishing key performance indicators (KPIs) to monitor efforts in meeting their goals

Forecasting challenges

When trying to forecast the supply chain, one tiny mishap can put a kink in the entire chain, resulting in unexpected delays across the globe.

"The Suez Canal blockage is a huge impact on laboratory supplies at the moment," explained John C. Masserant, MD, a retired OB/GYN who now analyzes stocks, noting events that impact supply chain issues and the stock market. "They say around 12% of the world trade flows through that canal, and that was blocked for nearly a week. Add to that the increased demand of lab supplies from the pandemic, with a worldwide demand of swabs, lab media, syringes, and anything else associated with checking for infection or administering vaccines."

Masserant pointed out that some areas have decreased the amount of recycled plastic during the pandemic, which increases the need of new plastic production. "Plastic is made from petroleum. Increasing cost, with a decreased supply of petroleum, shipping delays, and the whole situation is compounded by the shortage of domestic supply." Pipette tips and centrifuge tubes have been in short supply since the plastic shortage.

Labs have been feeling the impact, reporting supply shortages for blood agar, an enriched culture medium used to grow and identify bacteria; Mueller Hinton (MH) media, a type of growth to measure antibiotic susceptibility of bacteria; chocolate agar; fungal culture media; viral transport media; vaginal panels;

chromogenic agar plates; selective agar for streptococci; tryptic soy broth; buffered charcoal yeast extract agar; sabouraud dextrose agar; calcofluor white stain; and BD MAX Enteric Bacterial Panels, resulting in some labs resorting to Gram stain, fungal culture and PCR, instead of the panels.[1]

Effective demand management emerges from a chain of events focusing on supply chain visibility, supply network mapping and real-time data accessibility, analysis and transparency, according to Ranna Rose, Vice President, Operations and Customer Success, Resilinc.

Rose shared that there are currently multiple ripples intersecting through the supply chain ecosystem. COVID-19 is still disrupting global supply chains with sudden extreme and widespread demand shifts. "In the last 12 months, we've seen a record hurricane season, California fires, multiple large factory fires globally, a Texas freeze, semiconductor shortage, container shortages, plastics shortages and most recently, the Suez Canal delay. Due to these factors, we forecast a three- to six-month delay in global supply chains for most products, including materials needed to make lab equipment and other healthcare-related goods."

Rose added, "COVID-19 has been a black swan event of historic proportions and has opened the eyes of procurement officers and supply chain professionals who quickly realized they had limited information about their suppliers' global operations, and most dramatically, they learned they had little visibility to their suppliers' suppliers. Many woke up to the fact they needed greater visibility into their second, third or fourth-tier suppliers. It took many unprepared companies more than three months to react to the impacts of COVID-19 and get their mitigation efforts stabilized and moving forward."

Best practices from the bench

According to a recent MLO State of the Industry survey[3] conducted in February and the resulting report, recommendations from lab directors included a review of their test platforms and working with public health officials to forecast supply level needs.

The survey found that:

- 64% used multiple testing platforms
- 57% worked with state public health officials to gain access to needed testing supplies
- 45% implemented standing orders for crucial supplies
- 24% switched to reusable types of PPE
- 20% revamped their product evaluation process

Due to insufficient supply levels, lab directors mentioned paying extreme prices to secure products, having to use multiple suppliers, resorting to doing daily inventory updates system-wide, and using additional areas to store supplies to prevent running out when they could procure additional inventory.

Another strategy included using a bartering system, which has seen an upsurgence during the pandemic, as labs have traded supplies with each other during shortages, pooling resources. Pooling physical inventory includes sharing supply resources, and not having accurate information will only make a shortage worse, especially when some facilities overbought "just in case." Facilities attempting to out-stock their rivals can lead to time-sensitive supplies expiring, being wasted and having to be destroyed.

Good forecasting of needed supplies is critical for managing supply bottlenecks and shortages. Try to pinpoint potential bottlenecks and address them, before they become an issue, being proactive, instead of reactive, looking at the entire supply chain, supplier capacity, demands and rates of consumption. While urgent shortages need to be addressed, be aware of lurking shortages of other supplies in the future, as the sooner they are identified, the better to address it, before the need becomes acute.[4]

These worldwide shortages have inspired many scams and substandard equipment, creating a buyer beware environment. Valerie Ng, MD, PhD, of Almeda Health System shared her worry of purchasing at the MLO Forum on COVID-19, after hearing a story of a lab ordering nasal swabs, only to receive makeup applicators.[5] March: MLO FORUM (swoogo.com).

Creative solutions to supply shortages

With the U.S. International Trade Commission reporting an increase in imports of filter plastic pipettes and a double-digit percentage increase in the imports of surgical gloves from Malaysia and other places, it still was not enough to quench the need of laboratories and healthcare professionals. Recycling has come back to the forefront of lab professionals' minds, scrubbing cellular swab tubes to be used for a buffer, as well as reusing gloves for non-sterile work.

With personal protective equipment in high demand, places like Michigan Technological University have joined in on the 3D printing trend, recycling plastic into new creations to try to help fill the void.

After surveying the community to find what PPE were in short supply, Michigan Technological University's Open Sustainability Technology (MOST) Lab designed and developed three new tools to help: a high-temperature 3D printer, a firefighter mask and a printable, emergency-use ventilator. Nicki Gallup, a Biomedical and Mechanical Engineering student, worked alongside Joshua Pearce, PhD, a Richard Witte Endowed Professor of Materials Science and Engineering, helping with the 3-D printing of COVID-19 face shields, testing swabs, ventilators, and air filtration parts.

With the ingenuity of David Holden, Manager of Technology and Innovation and Michigan Tech, and John Schneiderhan, Michigan Tech's Library Technology Specialist, a mini manufacturing center was set up in Michigan Tech's library to produce needed PPE during the spring and summer months of 2020 to help distribute in the rural areas of the Upper Peninsula.

The pandemic inspired some creative thinking to solve real world problems, while bringing to the forefront the future needs of labs via forecasting. Amidst the chaos, it's easy to forget the supply chain of command, where one seemingly insignificant detail hinges on another, and something as silly as a boat stuck in a sandstorm can impact labs on the other side of the globe.

REFERENCES

1. Hagen, A., 2020. Laboratory supply shortages are impacting COVID-19 and non-COVID-19 diagnostic testing. American Society for Microbiology. Available at: https://asm.org/Articles/2020/September/Laboratory-Supply-Shortages-Are-Impacting-COVID-19. Accessed April 1, 2021.
2. News, C. 2021. Lab-supply shortages strike amid global pandemic. Nature.com. Available at: https://www.nature.com/articles/d41586-021-00613-y. Accessed April 1, 2021.
3. MLO State of the Industry survey Best practices while surviving COVID-19 chaos in the lab. *Medical Laboratory Observer* .(mlo-online.com)
4. How hospitals can manage supply shortages as demand surges. *Harvard Business Review*. 2021. Available at: https://hbr.org/2020/04/how-hospitals-can-manage-supply-shortages-as-demand-surges. Accessed April 1, 2021.
5. MLO Seegene forum link March: MLO FORUM (swoogo.com)

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Multiplex detection, sequencing and assessment of anti-viral immunization for SARS-CoV-2

By Martin Conway, BSc

Creating severe challenges, an unprecedented worldwide spread of SARS-CoV-2 impacted healthcare facilities, medical infrastructure, and developments in precision medicine. The ongoing COVID-19 pandemic has had devastating effects on populations, social structures, and economic growth for many nations. These are further impacted by the increasing extent of global connectivity and geographical mobility, which expedite infection spread at an uncontrollable pace.

Advances in diagnostic tools, treatment strategies, vaccine developments and logistical rollouts all play a pivotal role in mitigating the control and spread of SARS-CoV-2. Effective control and containment of this pathogen requires reliable diagnostic assays and potent therapeutic agents that interlink with molecular techniques, as well as accelerated vaccine development efforts. Advanced methodologies can be used in tracking and monitoring SARS-CoV-2 genomic sequences and viral evolution and spread around the world, while measuring the efficacy of vaccines throughout the course of clinical trials.

Multiplex SARS-CoV-2 detection

Recognized as the gold standard, polymerase chain reaction (PCR) is one of the most powerful technologies in molecular biology.[1] Using PCR, specific sequences can be copied, or "amplified," many thousand- to million-fold using sequence-specific oligonucleotides. Current front-line PCR testing only determines the presence of the virus with most commercial assays identifying SARS-CoV-2 and using a confirmatory method. However, as the spread continues, molecular techniques have been criticized for not identifying the genetic sequence of the virus or any information about the patient's immune response.[2]

Image by Fernando Zhiminaicela from Pixabay

Antibody detection combined with RT-PCR expands the detection window of SARS-CoV-2 infection and minimizes false negative RT-PCR testing.

In addition, many diagnostic assays currently available and in development do not provide clarity in identifying patients who have co-infections with symptoms similar to COVID-19. This, in turn, provides a need for a multiplex approach for situations, in which testing only for SARS-CoV-2 isn't enough. As SARS-CoV-2 affects the respiratory tract, it's vital that a multiplex molecular-based assay is used to not only identify SARS-CoV-2, but differentiate it from other viral respiratory pathogens, such as MERS, Influenza A / B and RSV.

SARS-CoV-2: Sequencing for Mutations

Coronaviruses are a group of related RNA viruses known to cause respiratory tract infections in humans and other animals. Although all viruses mutate while replicating and infecting host cells, RNA viruses are particularly unstable; meaning, they are more prone to mutation during replication.

When viruses produce copies of their genomes inside host cells, mutations – changes in their genome sequence – can occur. Mutations can affect the way viruses infect cells and replicate within them. They can lead to subtle changes in viral proteins, which can prevent existing antibodies in the immune system from recognizing the virus. Mutations can also reduce the efficiency of antiviral treatments. It's important to identify and catalog mutations, to better understand how viruses – such as the SARS-CoV-2 coronavirus that causes COVID-19 – spread and evolve over time.

The majority of viral mutations are minor and have no impact on the virus or the disease it causes. However, multiple mutations can lead to a new variant of a virus emerging, and sometimes, it is possible these new variants are more transmissible or deadly, as they can better evade the immune system. Globally, this has raised concerns about the efficacy of current vaccine rollouts and halted clinical trials currently underway for SARS-CoV-2. The emergence of these variants has created concerns that the vaccines authorized for COVID-19 may not be the way out of the pandemic that the world had hoped for. Fortunately, next-generation vaccines are coming through the pipeline, which have been designed with potential COVID-19 mutations and variants specifically in mind.

Circulating globally, there are now a few concerning mutations: the B.1.1.7 and the B.1.525 lineages in the United Kingdom, the B.1.351 lineage in South Africa, the B.1.1.28 lineage in Brazil, and many more. Some of these emerging variants are thought to be more transmissible, cause more severe disease and/or reduce efficacy of treatments and vaccines. Furthermore, variants may impact the performance of current diagnostic approaches.

Of particular interest is a double deletion at position 69-70 of the spike protein gene (69-70del), observed in the B.1.1.7 and B.1.525 variants, which has been found to affect the performance of some diagnostic PCR assays that use an S gene target (S gene dropout).[3,4]

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SARS-CoV-2, like other known SARS-CoV and SARS-related coronaviruses, encodes several smaller open reading frames (ORFs) such as ORF1ab, ORF3a, ORF6, ORF7a, ORF7b, ORF8 and ORF10. These ORFs are predicted to encode for the replicase polyprotein, the spike (S) glycoprotein, envelope (E), membrane (M), nucleocapsid (N) proteins, accessory proteins, and other non-structural proteins (NSP).[5,6,7]

Virus sequencing has been widely adapted to confirm individuals with positive cases of SARS-CoV-2 to distinguish which variant that individual has been exposed to. Efforts across the globe are underway to confirm whether any of these mutations are contributing to increased transmission of infection. However, the B.1.1.7 and the B.1.525 lineages in the United Kingdom, the B.1.351 lineage in South Africa and the B.1.1.28 lineage in Brazil are the most concerning. Most of the attention is on mutations in the gene that encodes the spike protein, which is associated with viral entry into cells, because this is replicated in therapeutic agents and vaccine developments currently in progress.

Multiplex SARS-CoV-2 serology is a tool to assess anti-viral immunization.

Rapid and accurate antibody testing on a large scale is vital to addressing some of the challenges presented by the SARS-CoV-2 pandemic. It plays an important role in research at the precision-medicine level and in surveillance strategies.

Serology tests measure the presence of antibodies (Abs) in the blood that occur when the body is responding to a specific infection – in this case, SARS-CoV-2 – which causes individuals to be infected with COVID-19. Antibodies to COVID-19 are produced over days to weeks after infection with the virus. The presence of antibodies indicates that a person was infected with the SARS-CoV-2 virus, irrespective of whether the individual had severe or mild disease, or even asymptomatic infection.

The use of SARS-CoV-2 serology testing has been challenging for a variety of reasons, such as the realization that the humoral immune response to the natural infection was very variable between individuals, was not systematically correlated with the cellular immune response governing the long-term memory response and varied widely over time, with specific anti-viral antibodies waning rapidly after recovery.[8,9,10]

Establishing a universal serology assay, able to detect the SARS-CoV-2 antibodies in every subject exposed to the virus, therefore, requires exquisite sensitivity. By increasing the number of antigenic targets in a single test, the chances of detecting at least one of the targets at a significant level is one of the best ways to increase the clinical sensitivity of specific antibody detection. It can also be a useful indicator of the time of infection, based on the respective kinetic of the various Ab species.

With the massive vaccination effort in progress globally, it is also important to identify people with pre-existing SARS-CoV-2 antibodies (that would potentially be eligible to a single vaccinal injection), and to study the various antibody species after vaccination to potentially determine a protective Ab level. Obviously, the antigenic component of the vaccine will define immunological diversity. It is expected, that taking into account the contribution of each Ab fraction, rather than relying on a single one, may reflect more accurately the immune status of an individual. Also, with the likely migration from intramuscular to nasal vaccination, salivary immunological profiling will become increasingly dominant.[10]

Widely used by precision medicine, antibody testing provides benefits to validate the effectiveness of vaccine trials. When there is little or no access to molecular testing, serology tests provide a means to quickly triage suspected cases of COVID-19, enabling appropriate case management, and guiding public health measures, such as quarantine or self-isolation. It is recognised that conventional serological tests have a high-throughput advantage that can complement PCR molecular testing. Antibody detection combined with RT-PCR expands the detection window of SARS-CoV-2 infection and minimizes false negative results from RT-PCR testing. Widely noted for effectively discriminating vaccinated individuals from those who have been naturally infected, it can also be used to identify disease severity, enabling calculation of previse rates of infection and case fatality rates.

Vaccine efficacy itself is very carefully determined during clinical trials, with emphasis being placed on the amount of neutralizing Abs vs the total Ab response. At present, anti-S antibodies have been shown to be closely correlated with the anti-RBD neutralizing antibodies; however, little is known about the contribution of other Ab species to the total neutralization power of the immune response.[11,12] A multiplex approach should, therefore, be of interest to vaccine developers, because it will help refine their assessment of their product's efficacy at various time frames post injection.

REFERENCES

1. Wee SK, Paramalingam SS, Yap EPH. Rapid direct nucleic acid amplification test without RNA Extraction for SARS-CoV-2 using a portable PCR thermocycler. *Genes*. 2020; 11 (6): 664 doi: 10.3390/genes11060664.

2. Peiris JS. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet*. 2003;361:1319-1325. doi: 10.1016/s0140-6736(03)13077-2.

3. Korber B, Fischer WM, Gnanakaran S, Yoon H, Theiler J, Abfalterer W, Hengartner N, Giorgi EE, Bhattacharya T, and Foley B. (2020). Tracking changes in SARS-CoV-2 spike: evidence that D614G increases infectivity of the COVID-19 virus. *Cell* 182, 812–827. e819. doi: 10.1016/j.cell.2020.06.043.

4. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, Zhang Q, Shi X, Wang Q., Zhang L, et al. (2020). Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *Nature*. 581, 215–220. doi: 10.1038/s41586-020-2180-5.

5. Walls AC, et al. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell*. 180, 1–12 (2020). Walls, AC. et al. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell* 180, 1–12 (2020). doi: 10.1016/j.cell.2020.02.058.

6. Ahmed SF, Quadeer A A, McKay MR. Preliminary identification of potential vaccine targets for the COVID-19 coronavirus (SARS-CoV-2) based on SARS-CoV immunological studies. *Viruses*. 12(3), 254 (2020). doi: 10.3390/v12030254.

7. Phan T. Genetic diversity and evolution of SARS-CoV-2. *Infect. Genet. Evol.* 81, 104260 (2020). doi: 10.1016/j.meegid.2020.104260.

8. Liu W, Fontanet A, Zhang PH, Zhan L, Xin ZT, Baril L, et al. Two-year prospective study of the humoral immune response of patients with severe acute respiratory syndrome. *J Infect Dis* (2006) 193(6):792–5. doi: 10.1086/500469.

9. Gaebler C, Nussenzweig MC. All eyes on a hurdle race for a SARS-CoV-2 vaccine. *Nature* (2020) 586(7830):501–2. doi: 10.1038/d41586-020-02926-w.

10. Ng K, Faulkner N, Cornish G, Rosa A, Earl C, Wrobel A, et al. Pre-existing and de novo humoral immunity to SARS-CoV-2 in humans. bioRxiv (2020). 2020.05.14.095414. doi: 10.1101/2020.05.14.095414

11. Wong SK, Li W, Moore MJ, Choe H, Farzan MA. 193-amino acid fragment of the SARS coronavirus S protein efficiently binds angiotensin-converting enzyme 2. *J Biol Chem*. 2004; 279: 3197-3201.

12. Tai W, He L, Zhang X et al. Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine. *Cell Mol Immunol*. 2020; 17: 613-620. doi: 10.1038/s41423-020-0400-4.

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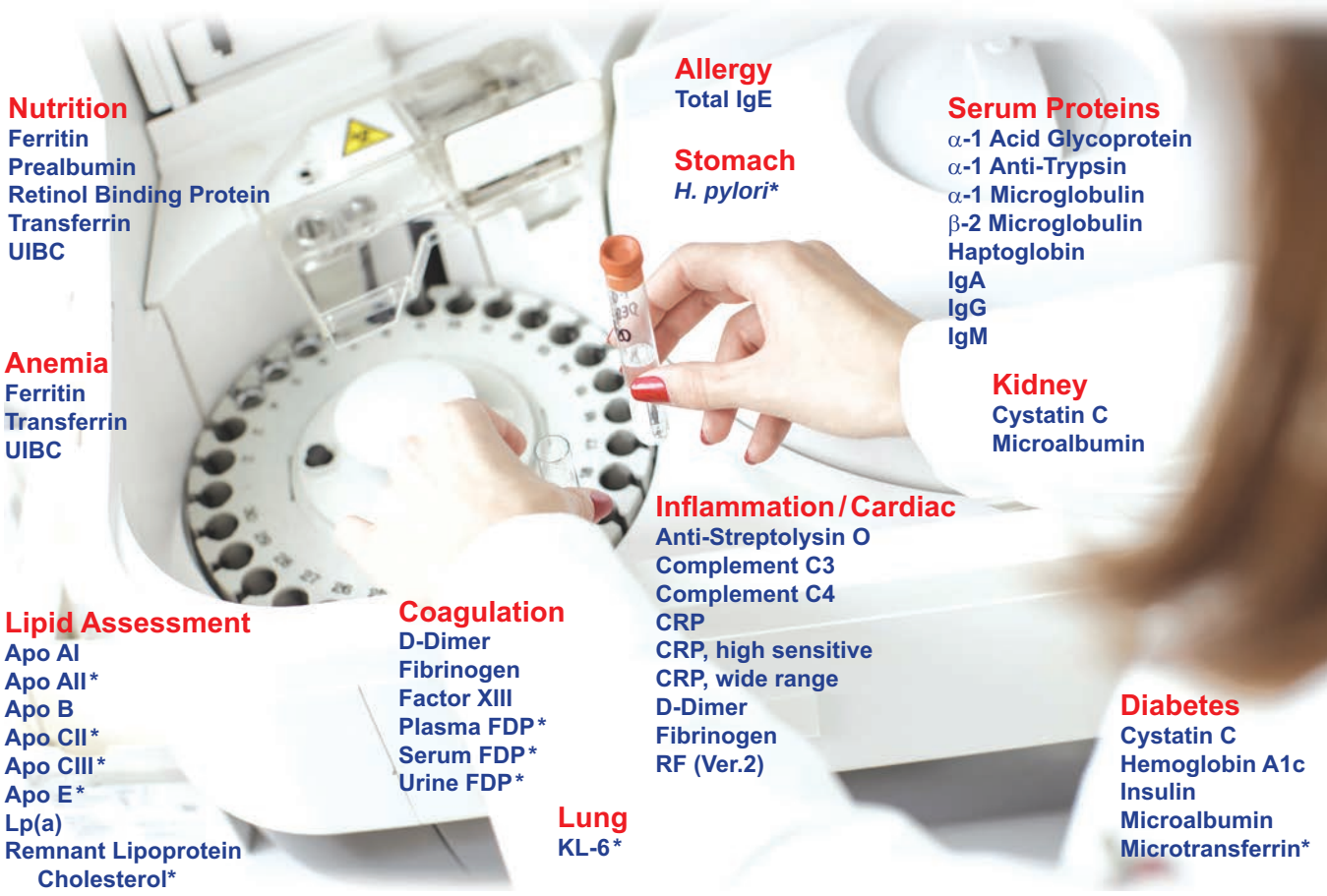

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Analysis of variants on COVID-19 testing

By Marisa L. Williams

People often confuse the terms variant, mutant and strain. A mutation is a single nucleotide change, which is introduced in the viral genome that leads to an amino acid change, while a variant is the viral genome that contains a particular set of mutations, and a strain is a variant that shows a differing phenotype, such as being more pathogenic or transmissible.[1]

For example, the UK variant, known as B1.1.7, has 23 mutations with 17 amino acid changes. Thus, it is considered a strain, as it has evidence of being more infectious. An amino acid change, a deletion or an insertion into the spike protein, can result in a mutation. Mutations take place throughout the viral genome, but it's not an equal occurrence, as there are "hotspots," such as the spike protein.

The Centers for Disease Control and Prevention (CDC) has been receiving samples from various state departments and agencies for sequencing since Nov. 2020. They provide further characterization, sequencing and evaluation. At the end of January 2021, the National SARS-CoV-2 Strain Surveillance (NS3) system was ramped up to 750 samples a week from across the country, as the CDC contracts with large commercial diagnostic labs to sequence 6,000 samples per week, with the capacity to increase if need be. [1]

Next-generation sequencing (NGS) and bioinformatics have been integrated into the public health system since 2014. Health departments apply for the resources during response to COVID-19, making genomic data available to public databases. In Dec. 2020, $15 million of COVID supplemental funds were released through the Epidemiology and Laboratory Capacity Program.

The CDC leads a national consortium of laboratories sequencing SARS-CoV-2 (SPHERES), which consists of more than 160 institutions, including academic centers, industry, non-governmental organizations, and public health agencies. This networking allows genomic data to be available through public databases for use by public health professionals and researchers. The FDA uses the health sequencing data to monitor mutations.

Sequencing and lab work

According to the FDA website, "the presence of mutations in the SARS-CoV-2 virus in a patient sample can potentially impact test performance. The impact of mutations on a test's performance is influenced by several factors, including the sequence of the variant, the design of the test, and the prevalence of the variant in the population."

With molecular tests, false negatives may occur if a mutation is in the part of the virus' genome that is being detected by a test. Since molecular tests use multiple genetic targets, final results are not as likely to be impacted by genetic variants. When viral genome changes viral proteins, it can impact an antigen or serology test.

Treat the whole patient. If there is a negative result, but clinical observations show additional signs, the patient has a worrisome history, or epidemiological information makes you think otherwise, consider retesting with a different test, perhaps targeting different genetics, if COVID-19 is still suspected.

Laboratories around the globe struggle to keep up with the number of emerging variants. "In terms of the variants, we have been following guidelines from different governments and institutions, using resources like the FDA, CDC and World Health Organization, for variants of concerns, and we target those regions," said Helen Roberts, PhD, President of Seegene Technologies, one of the many companies targeting variants for testing.

"Viruses often have mutations based on how prevalent a virus becomes. The more there is, the more likely there will be mutations, so mutations are not a surprise to the scientific community. It's more about discovering where the mutations are and how they affect, as they usually adapt to give an advantage to the virus, a selection. It's not surprising how fast the virus spreads. We have used an AI-based system to develop, and that's our key ability: to quickly adapt to make assays," explained Roberts.

There's a vast amount to learn about variants, from finding how far they have spread, to knowing the similarities and differences between strains, which helps to recommend the best therapies, tests and vaccines.

"If a nucleotide is missing, a sequencing is different from one to the next." Roberts shared how the differences impact an assay that can detect a deletion, as assays are designed to detect a specific protein sequence. If that sequence should change, "that change has a huge effect of how it hybridizes to find its target. We look for changes and deletions."

Through genomic sequencing, genes are decoded, a key to making new discoveries. The sections, or genes, are encoded to build the virus, and this is how the changes to variants can be monitored over time, knowing their characteristics.

Synthetic genomes can be used to generate viruses to test vaccines. "Synthetic genomes are a much more reliable and scalable source of viruses than clinical samples, since clinical samples, when propagated extensively, often result in a mixture of virus population with multiple genomic changes," explained Charlie Schmidt, Codex DNA Senior Director of Marketing. Synthetic genomes have also served as diagnostic controls in RT-PCR and NGS based assays.

"Codex DNA has harnessed its expertise in genome building to achieve one of the fastest design-build cycles in the industry. This is particularly important in the current scenario with the emerging SARS-CoV-2 variants. Researchers are able to use synthetic genomes of the emerging variants to quickly generate viral particles to test against existing or newly designed vaccines/therapeutics. Synthetic genomes will also be key in tracking the spread of the new and emerging variants across the globe through their use as diagnostic controls," said Schmidt.

Manoj Gandhi, MD, PhD, Senior Medical Director for Genetic Testing Solutions at Thermo Fisher Scientific suggested as the emphasis for SARS-CoV-2 strain identification increases, lab professionals will see an increased demand for surveillance testing.

"Conventional surveillance testing is performed by sequencing the viral genome. In some ways, sequencing can be considered as the 'classic' surveillance methodology. Since next generation sequencing (NGS) can provide the sequence of the entire viral genome, one can exactly know what the full sequence of the virus is. NGS is mostly useful if one would like to sequence the entire genome to discover 'new' or 'emerging' variants. In addition to NGS, one can also perform targeted sequencing of specific regions within the viral genome, such as the S-gene for example, using capillary electrophoresis, also commonly known as Sanger sequencing. Sanger sequencing can help rapidly verify and confirm the presence of specific mutations in the sample," said Gandhi.

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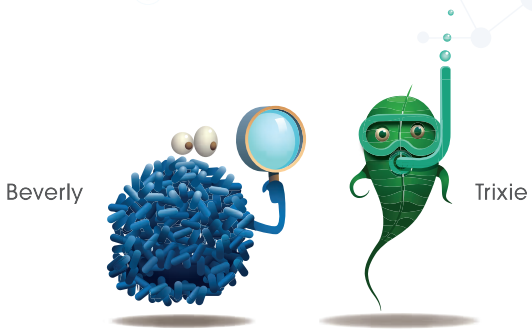

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James Gilmore, CCO of SeqOnce Biosciences, said, "RT-qPCR testing for Variants of Concern is faster and less expensive than sequencing. Additionally, more labs have access to qPCR instruments, compared to sequencers, so using qPCR makes sense for surveillance."

An assay is faster for labs to adopt than genomes. "It's just a workflow," Roberts explained. "The sample prep to read up is a longer workflow, and sequencing takes a few hours, so it's a longer workflow than the assays," which would be around two hours.

Government and private databases track variant impact on COVID-19 severity, as well as the effectiveness of vaccines and therapeutics. Researchers can track the variants' ability to spread, cause milder or more severe symptoms, and evade detection through some diagnostic tests. Many popular nucleic acid amplification tests use reverse transcription polymerase chain reaction (RT-PCR), where there are multiple detection targets. Thus, if a mutation impacts one of the targets, the other RT-PCR targets will still work, but in tests relying on only one target, mutations may not be detected.

Challenges

"From a laboratory perspective, the mutations in these variants may impact the way some of the diagnostic tests are able to detect the presence of the virus. For example, the 69-70 deletion in the S-gene in the B.1.1.7 variant can result in a S-gene target failure (SGTF), also called as a S-gene drop out, in the TaqPath COVID-19 Combo Kit. However, due to the built-in redundancy of the assay with two other targets available for result calling, the overall sensitivity of the test should not be impacted. Moreover, the S-gene drop out may be used as surveillance tool as an indicator for the presence of the B.1.1.7 variant of concern," said Gandhi.

"In light of the mutations that are occurring in different part of the viral genome, laboratory professionals need

Emerging COVID-19 variants

The first variant, D614G

The original Wuhan strain's first variant had a single amino acid change at position 614 in the S1 region, where a spike protein changed as aspartic acid to a glycine, known as D614G

The first genetic sequence was first identified in the United States as USA-WA1/2020.[3]

The United Kingdom (UK) variant, B.1.1.7

The B.1.1.7 Variant of Concern (VOC) is known as 201/501Y.V1.

Having a mutation in the receptor binding domain (RBD) at position 501 of the spike protein, the amino acid asparagine (N) has been replaced with tyrosine (Y), making shorthand notation of this mutation N501Y.

There is a 69/70 deletion that has occurred spontaneously often, which could lead to a conformational change in the spike protein.

Near the S1/S2 furin cleavage site, a site that varies a lot in coronaviruses, P681H mutation has emerged spontaneously a number of times.

The South Africa variant, B.1.351

Shares some mutations with B.1.1.7, such as the N501Y.

Other protein spikes include K417N and E484K, but it does not have the 69/70 deletion.

The E484K spike protein mutation may affect neutralization from some of the polyclonal and monoclonal antibodies.

The Brazilian variant, P.1

The Brazilian variant, P.1, also known as 20J/501Y.V3, is a branch of B1.1.28.[1]

It has three mutations in the spike protein receptor binding domain at K417T, E484K and N501Y.

The emergence of this variant in Manaus, where 75 percent of the population previously had been infected in October 2020, with 42 percent getting reinfected with the variant in December 2020.

ΔFVIspike

The Cluster 5 variant, or Δ*FVIspike*, mutations include 69-70deltaHV, which is a deletion of histidine and valine residues at 69th and 70th positions in the protein spike; Y453F, which is a change from tyrosine to phenylalanine at position 453; I692V, a change from isoleucine to valine at position 692; M1229I, methionine to isoleucine at position 1229; and a non-conservative substitution S1147L.

Spill-over from mink to humans can also spill-back from humans to minks, creating a concern about animal transmission of the virus, resulting in Denmark culling all farmed minks in attempt to rid the country of this strain.

B.1.427/B.1.429

Virologists found B.1.427/B.1.429[3] to have a spike protein mutation at position 452,[2] called L452R.

This mutation allows this variant to evade some vaccine antibodies, and the N501Y mutation speeds up transmission.

P.2

Characterized by a protein spike mutation at E484K.

S2

Named for its mutation in S2, called Q667P, it may enhance fusion of virus with the host cell.[1]

Mutations in S1-NTD and S2 could potentially present an immune escape adaptation.

Uganda strain, UG053

A sub-lineages A.23 and A.23.1.

In Uganda prison outbreaks, A.23 was spotted with three amino acid changes in S1 of the spike protein: F157L, V367F, and Q613H.

In A.23.1, the sequence encoded a few amino acid changes in the spike protein, such as open readings in frames 8 and 9 (ORF8 and ORF9) and nonstructural protein (snp3 and nsp6); it features E484K.

In the region, 39 percent of strains were of major B lineage, and 61 percent are within the A lineage. Of six lethal cases in the country, the genome sequences belonged to lineage A.25 and B.1.393.

Variant Under Investigation (VUI)

The variant VUI-202102/04 is a VUI, having a key mutation of E484K, which can "escape" antibodies of variants.

The VIU-202201/01 was first found, also with the E484K mutation.

Another UK variant known as B.1.1.318 has the E484K mutation, but it does not have the N501K mutation that other variants have.

B.1.525 is a VUI that is similar to B1.1.7 but with additional mutations, including E484K.[4]

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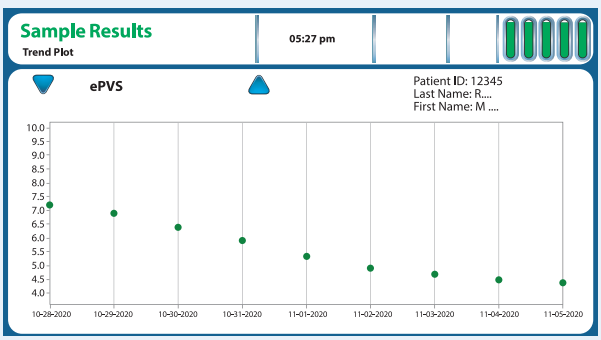
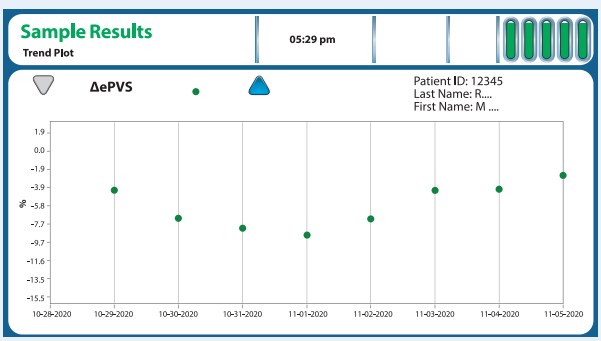


Prime Plus screen showing absoute values (ePVS)



Prime Plus screen showing percent change (ΔePVS)

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to make sure that these mutations are not impacting the PCR tests that have been deployed in their laboratory for SARS-CoV-2 detection. Laboratory professionals also need to evaluate tests as to which and how many targets does a specific test use for result calling. Multi target assays that target more than one region of the viral genome are generally preferable to single target assays, since it offers built-in redundancy in case one of the targets is impacted by a mutation."

When testing for B.1.427/B.1.429, he added,"due to the presence of the L452R mutation, it may be associated with poor response to antibody-based therapies."

Studies have shown spike-bearing viruses do not infect cells when soluble ACE2 is present, as it acts like a viral decoy, or with Camostate (Calu-3 cells), a TMPRSS2 inhibitor.1 A 13/14 sera from infected patients also produced potent neutralization of spike-driven entry into the host cell.

For molecular tests, the FDA noted the following molecular tests may be impacted by mutations:

- Accula SARS-CoV-2 test, Mesa Biotech, for a variant at position 28881 (GGG to AAC)
- Linea COVDI-19 Assay Kit, Applied DNA Sciences, impacted by B.1.1.7 mutations
- TaqPath COVID-19 Combo Kit, Thermo Fisher Scientific, reduced sensitivity to S-gene target
- Xpert Xpress SARS-CoV-2, Xpert Xpress SARS-CoV-2 DoD, and Xpert Omni SARS-CoV-2, Cepheid, which has sensitivity detecting the N2 target[3]

Most developing vaccines are either mRNA, adenoviral or recombinant protein, and all currently approved vaccines targets the spike protein; thus, a RBD-based assay has to be used when determining a vaccine antibody response when the nucleoprotein is not a part of it.

Studies of the mRNA-1273 vaccine against various variants[4] revealed a decrease in titers of neutralizing antibodies against B.1.351,[5] but it had no real effect on B.1.1.7. Levels of neutralization against D614 were similar to strains EU1, 20A. EU2, N439K-D614G and the cluster 5 variants.

The Janssen vaccine is based on older vaccine technology using a cold virus to deliver instructions to make the spike protein used by the COVID-19 virus, triggering an immune response and the development of antibodies. Similar technology was used to make the vaccine against Ebola. The Moderna and Pfizer vaccines differ, as they deliver mRNA instructions for the spike protein inside of a lipid ball that enters cells, creating the immune system.

With so many developments on a fast learning curve, it's tough for laboratories to keep up with the latest about variants and mutations. "There isn't really a resource like the FDA EUA website, so it's more challenging. Companies market themselves, because the FDA hasn't consolidated and authorized for clinical use yet. It's all for research use. The FDA is still recommending sequencing for variant typing, but not all laboratories have access to that," said Roberts.

Gilmore said, "from a pandemic standpoint, we seem to be in a game of 'whack-a-mole' for developing assays to detect the SARS-CoV-2 mutations. New mutations are being reported almost daily. This has made SeqOnce Biosciences re-think how to approach our assay development by making it more routine, ordering multiple probe/primer designs simultaneously (rather than sequentially), and streamlining the manufacturing process (e.g. conserving plasticware, maintaining consistent formulations and master mixes)." SeqOnce Biosciences has RT-qPCR assays for the CDC SARS-CoV-2 Variants of Concern (VOC), including: N501Y, E484K, and K417 wild type. They are also in the process of developing assays to detect variants E484Q, Q677H, and F888L.

"This is still very new," explained Roberts. "Most labs are not testing yet. Now, there's a few of us that have released tests, and it's important for researchers to know there are several now available as a tool for them."

Roberts stressed the important for surveillance and epidemiology to see if variants of concern are circulating in an area, as some are more resistant to vaccines."So, be aware of what is circulating in the client pool, and be aware assays are available as a tool for them. PCR's are easier than assays for labs to adopt if they are not already set up for sequencing."

Advice for labs

"Labs should be aware that variants of concern may have multiple mutations of interest. As an example, there are reports of 'double mutation,' where a variant in India was positive for both L452R and E484Q," said Gilmore.

"It's very important for labs to understand the assays they're using," Roberts stressed,"as a few have been noted to have performances changed, so it's important for labs to understand what assays they're using and what part of the gene they are detecting. So, if they see a weird pattern, is this a variant issue, or something else?"

For tracking lineages, sequencing is good for identifying new mutations; whereas, PCR-based mutation testing is good for known mutations.

"Viruses mutate and especially RNA viruses like the coronavirus are more prone to undergoing mutations. As we now move from a pandemic to an endemic state, more and more people will either have the natural infection or will be vaccinated. As the human body mounts an immune response in either of those situations, there is selective pressure on the virus to mutate at higher rates. Recent data shows that the SARS-CoV-2 virus may be mutating much more rapidly that we may have anticipated. Some of these variants have been shown to be more transmissible. Some may impact the disease severity, and some may even impact vaccine efficacy. As the virus evolves, lab workers can expect to see certain variants harboring specific mutations becoming dominant in the population, a phenomenon called as convergent evolution," explained Gandhi.

"Because there are so many mutations, labs really should consider their strategy to identify from strands," Roberts added. "Think about how they want to tackle that issue to identify and report to the CDC or state labs to stay on top of mutations. It's better for all of us Americans."

REFERENCES

1. Centers for Disease Control and Prevention. 2021. COVID-19 and your health. Available at: https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html. Accessed 1 April 2021.
2. COVID-19 variant first found in other countries and states now seen more frequently in California | UC San Francisco. 2021. *COVID-19 variant first found in other countries and states now seen more frequently in California.* Available at: https://www.ucsf.edu/news/2021/01/419656/covid-19-variant-first-found-other-countries-and-states-now-seen-more. Accessed 1 April 2021.
3. Center for Devices and Radiological Health. SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests. U.S. Food and Drug Administration. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests?. Accessed April 6, 2021.
4. New England Journal of Medicine. 2021. *Serum neutralizing activity elicited by mRNA-1273 vaccine | NEJM.* Available at: https://www.nejm.org/doi/full/10.1056/NEJMc2102179. Accessed 1 April 2021.
5. Tom Pilgrim, P., 2021. *New covid variant found in UK after 16 cases spark investigation.* Daily Record. Available at: https://www.dailyrecord.co.uk/news/scottish-news/new-covid-variant-found-uk-23610523. Accessed 1 April 2021.
6. Healthblog.uofmhealth.org. 2021. COVID Vaccines: *Does it matter which one You get?* Available at: https://healthblog.uofmhealth.org/wellness-prevention/covid-vaccines-does-it-matter-which-one-you-get. Accessed 1 April 2021.

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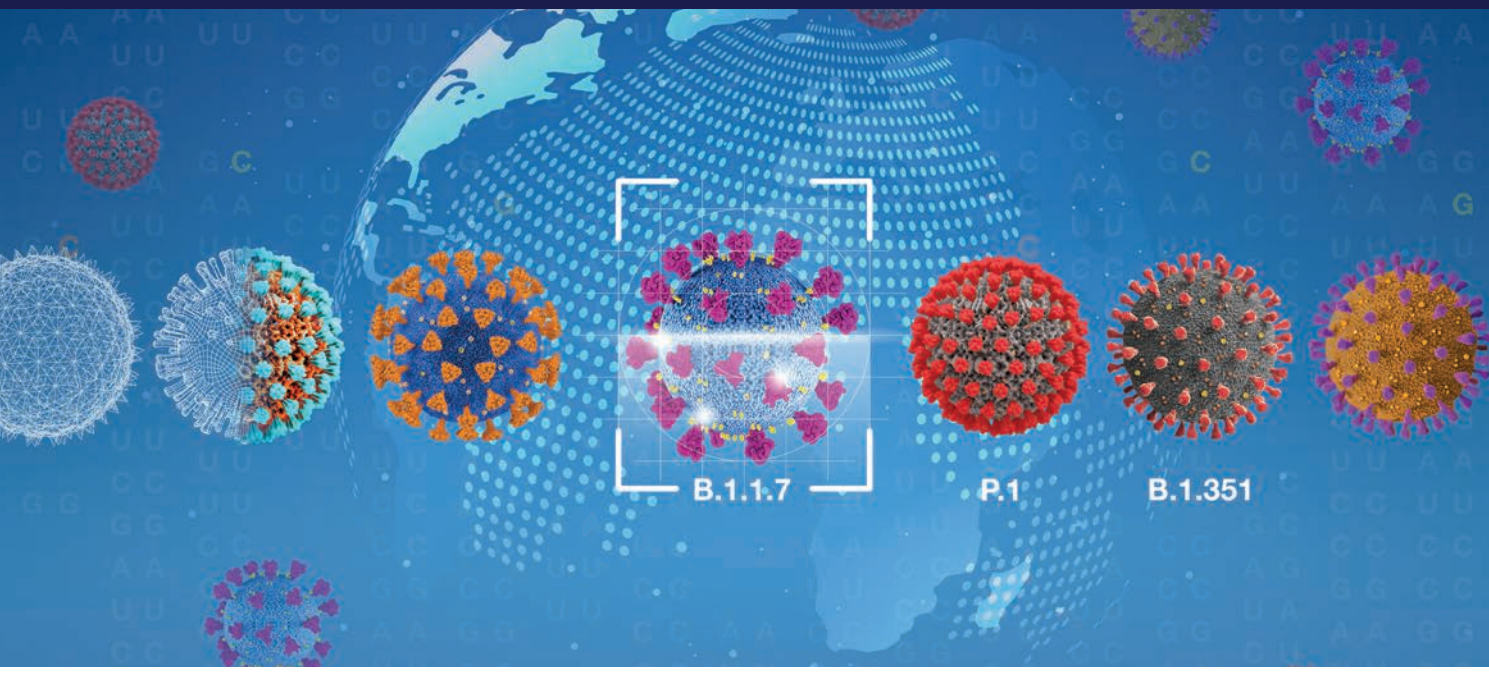

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Automating the steps in the revenue cycle process helps produce clean claims and fewer denials.

Automating denials management for lab reimbursement

By Linda Wilson

The rate of claims denials at health systems and laboratories has been increasing, which means that managing denials is becoming an important part of an organization's revenue cycle workflow.

The Change Healthcare 2020 Revenue Cycle Denials Index showed that the rate of denials for the healthcare industry increased steadily between 2017 and 2020, topping out at 11% of claims being denied in the third quarter of 2020. The analysis was based on more than 102 million claim remittances, reflecting more than $407 billion in total charges, processed by Change Healthcare between July 2019-June 2020 for 1,500 hospitals nationwide.[1]

Meanwhile, XIFIN, a vendor of revenue cycle management software, performed an analysis on its laboratory customers' claims data to uncover trends in denials. It found that the percentage of claims denied varied by type of lab (such as clinical, molecular, hospital or pathology) and payer (such as Blue Cross Blue Shield or Medicare). For example, molecular labs faced the highest denial rates for in-network claims, ranging from slightly more than 20% for commercial payers to nearly 45% for Medicaid. For clinical labs, denial rates ranged from less than 5% for Medicare to 22.5% for workers' compensation.[2]

Overall, XIFIN said denial rates averaged 15% for in-network claims and 30% for out-of-network claims.

Reasons for denials

XIFIN also analyzed the reasons for denials, finding that the most common reasons for denials are for tests deemed experimental, performed without prior authorization, medically unnecessary or not covered by an insurance plan.[2]

XIFIN's analysts also have seen an increase in denials associated with what are known as Medically Unlikely Edits, which are coding rules developed by the Centers for Medicare & Medicaid Services (CMS) to determine the maximum number of units of service allowed for a given date and patient. "We've recently begun to see payers denying all units associated with a procedure code that exceeds the MUE limit, instead of only the subsequent units that exceed the limit," said Clarisa Blattner, Senior Director, MDx Support Services at XIFIN.

Blattner said XIFIN also has seen an increase in denials for missing information (CO 16) and missing documentation (CO 252).

"Although, the claim itself may have a diagnosis code/ICD-10-CM code that supports medical necessity, some payers are performing post-payment audits, requesting medical records to confirm the ordering/treating physician has documented the patient's diagnosis, clinical justification for requesting the test, how the test will impact clinical decision making, and the treatment plan," Blattner said.

COVID-19 issues

Jim O'Neill, Business Development Manager for Laboratory Services at Advanced Data Systems Corporation, said denials have been particularly problematic for COVID-19 testing. However, this has been less of an issue in 2021 than it was in 2020. He most often sees claims denied because of

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missing or inaccurate information about insurance eligibility or diagnosis codes.

Suren Avunjian, Chief Executive Officer of LigoLab, said denials for COVID-19-related CPT codes often occur because of the fast pace of regulatory changes and updates about the use of add-on code U0005 for COVID-19 tests.

Effective January 1, 2021, CMS decreased its base payment rate for a high-throughput COVID-19 test from $100 to $75.

At the same time, it created add-on code U0005, which allows labs to bill Medicare an additional $25 for a molecular COVID-19 test run on high-throughput technology if two conditions are met:

- A turnaround time of two calendar days from the time the specimen is collected.
- The majority, which CMS defines as 51%, of high-throughput COVID-19 tests in the previous month also met the TAT requirement of two calendar days or less.[3]

Preventing denials

Whatever the reasons for denials, there are steps labs can take to both prevent them from happening in the first place or resolve them successfully when they do occur.

To prevent denials, which is the most cost-effective of the two options, labs should fix errors, before they submit claims to payers. "Clean claims are less likely to be rejected and more likely to be paid," Avunjian explained. "Any reworking of claims, even if successful, drives up costs, reduces employee productivity, and negatively impacts the customer experience."

> "Clean claims are less likely to be rejected and more likely to be paid. Any reworking of claims, even if successful, drives up costs, reduces employee productivity, and negatively impacts the customer experience."
> —Suren Avunjian,
> Chief Executive Officer of LigoLab

Automating the steps in the revenue cycle process helps produce clean claims and fewer denials.

On the front end of the process, it is important to ensure that accurate information is gathered from patients. Avunjian suggests that labs consider using automated tools to verify patients' address and insurance information, including eligibility verification.

Diana Richard, Director of the Anatomic Pathology Program at XIFIN, recommends that labs incorporate a direct interface with a service that specializes in prior authorization. "There are several very qualified vendors that offer this service, allowing laboratories to confirm prior authorization on the front end of the billing process; integrated, these services can establish an automated process for acquiring prior authorization numbers from the vendor electronically without requiring additional staff to manage."

Avunjian also recommends that labs consider automation designed to predict possible denial of claims based on an analysis of a payer's history. Specifically, labs should look for "billing patterns in rejections related to payer regulations and requirements," he said.

O'Neill added that tight integration between a laboratory information system (LIS) and revenue cycle software also is important. "If the LIS is sending over the appropriate information, a quality RCM company or quality laboratory billing software product should be able to catch – using a rules-based system – any type of error coming through."

O'Neill also said, "If there are any issues with regards to missing or invalid information, the billing company or RCM company should pick that up all almost immediately." At that point, any missing or inaccurate information should be reported back to the lab and referring physician within 24 to 48 hours to be corrected.

Avunjian said, "LIS and RCM integration gives labs a head start on the billing cycle. Integrated RCM adds transparency and automation to the process that begins at order origination and before testing."

Even with automation, labs still need to educate referring physicians about using the correct diagnosis codes and documenting the clinical indications for various tests in patients' medical records.

O'Neill noted that it is better to have a conversation with referring physicians upfront about the type of information needed for a clean claim. "And the problem is most laboratories are not doing that these days, and they're causing themselves a lot of issues with regards to accounts receivable building up."

Appealing denials

But even if front-end staff follows the steps before sending a claim to a payer, some denials still occur.

Then it is time to rework the claims. As is the case on the front end of the revenue cycle, automation in the process of reworking denials also increases efficiency. "The less manpower that's involved in correcting your claim and refiling a claim, the more profitable it is for the laboratory to get smaller claims paid," O'Neill said.

XIFIN's Blattner agrees. "Having an automated workflow and the ability to attach custom letters (driven by denial type, CPT code, and/or payer, and level 1, 2, and 3) to pathology reports, requisitions, clinical history and other key documents also increases your efficiency and likelihood of success."

Level one appeals typically require a cover letter, pathology report, and requisition, Blattner said.

For level two and three appeals, payers often have registered nurses or other qualified individuals reviewing them. "But they're likely not specialized in pathology coding and will follow AMA (American Medical Association) coding guidelines very closely. It's critical to use terminology consistent with the guidelines to explain your purposes for justifying the services performed. This way, the individual reviewing your claims can assess it with the consistency of the information they're referencing," Blattner said.

REFERENCES

1. What's driving your denials? Change Healthcare. https://info.changehealthcare.com/reduce-denials. Accessed April 5, 2021.
2. Richard D. The remaining 20%: the critical role denials play in lost revenue (Part 1). XIFIN. March 2021. https://www.xifin.com/resources/blog/202103/remaining-20-critical-role-denials-play-lost-revenue-part-1. Accessed April 5, 2021.
3. COVID-19 Frequently asked questions (FAQs)on Medicare fee-for-service (FFS) billing. Updated March 21, 2021. Centers for Medicare & Medicaid Services. https://www.cms.gov/files/document/03092020-covid-19-faqs-508.pdf. Accessed April 6, 2021.

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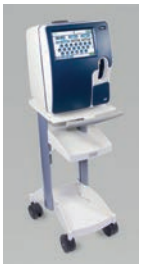

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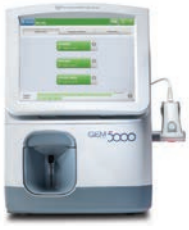

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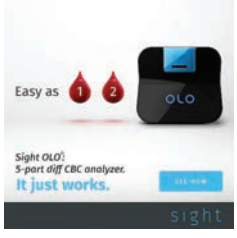

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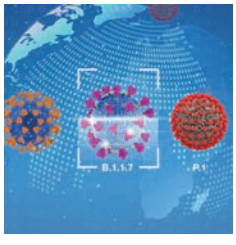

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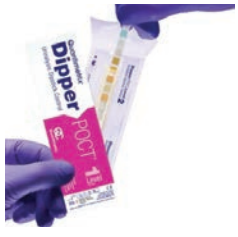

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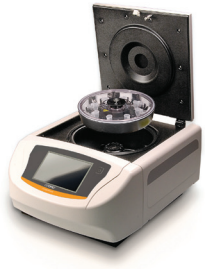

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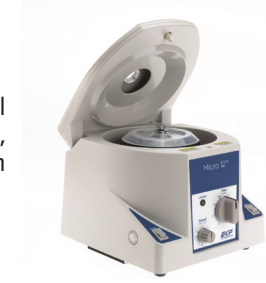

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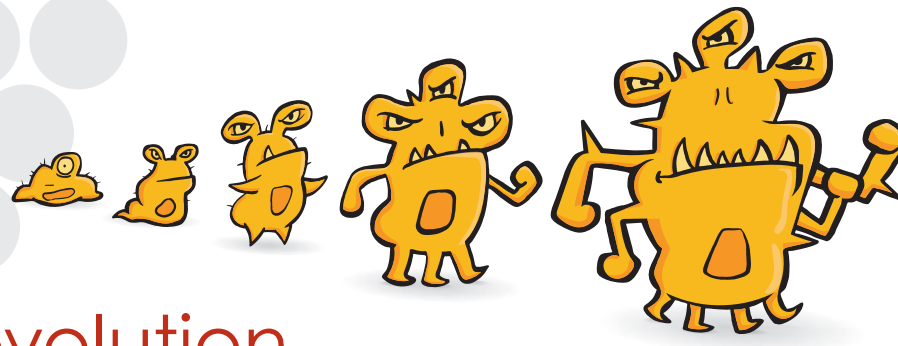

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LABORATORY INNOVATOR

A career combating AMR

By Linda Wilson

Jean B. Patel, PhD, D(ABMM) is the Principal in Scientific Affairs for Microbiology at **Beckman Coulter Diagnostics**. Before joining Beckman Coulter, Patel spent nearly 17 years at the Center for Disease Control and Prevention (CDC) in the Antimicrobial Resistance Reference Laboratory and the Office of Antimicrobial Resistance. Prior to that, she was the Assistant Professor of Pathology and Laboratory Medicine and the Assistant Director of Clinical Microbiology at the University of Pennsylvania.

Why did you decide to become a medical technologist and to specialize in molecular microbiology?

I loved the idea of working in a laboratory and using this interest to provide quality medical care seemed like a great idea. I thank my aunt for introducing me to the field of medical technology. Microbiology was my favorite specialty. Molecular microbiology was a growing field of study, and I wanted to learn how to use genetic tools to discover how bacteria work.

What accomplishment are you most proud of during the 17 years you spent at the Centers for Disease Control and Prevention (CDC)?

I am most proud of leading the CDC-FDA Antibiotic Resistant (AR) Isolate Bank and the CDC AR Laboratory Network. The bank provides medical laboratories, researchers, and industry with well-characterized resistant pathogens. This ensures new and existing laboratory tests can detect significant AR threats, and new drugs are active against the most resistant pathogens. The AR Lab Network creates a national capacity to detect and characterize resistant pathogens. This is a laboratory resource that healthcare systems can access for the testing needed to make infection prevention decisions and for outbreak response.

In your opinion, which pathogen(s) pose the greatest threat and why do they?

Carbapenem-resistant *Enterobacteriaceae* (CRE) keeps me up at night. There are few drugs for treating CRE infections, and there are not enough drugs in the pipeline. Right now, CRE primarily cause infections in healthcare settings; however, these bacteria have the potential to cause community-associated infections as well. Preventing infections in the community is much harder than in hospitals. We have already seen methicillin-resistant *Staphylococcus aureus* and ESBL-producing *Enterobacteriaceae* infections transition from healthcare settings to community settings. It seems like it is only a matter of time before this happens for CRE.

Will you describe colonization testing and what role it could play in combating the spread of antimicrobial resistant pathogens in hospital and community settings?

Diagnostic tests are typically aimed at detecting infections and the pathogens that cause infections. However, before a patient is infected, they are often colonized with a pathogen, and sometimes, these pathogens are resistant to antibiotics. For example, a person can become colonized with CRE in the gastrointestinal tract. This person is at greater risk for infection, and they can pass the pathogen to other people – especially in healthcare settings. Detecting colonization using laboratory tests is an essential tool for disrupting person to person transmission. The CDC recommends CRE colonization testing as a tool for infection prevention in healthcare settings. Colonization testing is recommended for CRE prevention, but some hospitals do not do this testing in house because it is not an everyday test.

What technical advances do you think will be incorporated into pathogen identification and antimicrobial susceptibility testing over the next three- to five-years?

Pathogen identification and antimicrobial susceptibility testing will get much faster in the next few years. Maldi-TOF technology has already had a considerable impact on rapid identification, changing this from an overnight test to a test that takes just a few minutes. Faster antimicrobial susceptibility testing from a positive blood culture is a reality too, but future rapid AST (antimicrobial susceptibility testing) systems are challenged with combining a simple laboratory workflow with increased instrument throughput and results that meet overnight AST accuracy. All of this needs to be done without adding costs that cannot be absorbed in today's healthcare environment. That is a big lift, and there are lots of tests in development, which truly makes this an exciting era of microbiology laboratory innovation.

Harnessing the data generated by infectious disease and AST systems requires software solutions that can integrate test results from multiple sources and generate reports that provide a comprehensive picture of AR infections within a healthcare setting and healthcare system. Data like these are essential for implementing the best antibiotic stewardship and infection control measures. I expect a lot of innovation in this area.

What is Beckman Coulter doing to help combat AMR?

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The DxM Trio solution has a proven track record of accurate organism identification and antimicrobial susceptibility testing in the laboratory. Together, this integrated solution of technologies streamlines processes to enhance efficiency and take strides in antibiotic stewardship.

- Combat emerging resistance with accurate detection
- Improve laboratory efficiency with a reliable instrument that offers award-winning system performance[2]
- Reduce ancillary testing and lower costs with the DxM Trio
- Fewest clinically significant limitations of any automated identification and antimicrobial susceptibility testing (ID/AST) system

See how your laboratory can benefit from the DxM Trio solution.
Learn more at www.beckmancoulter.com/dxmtrio

References

1 UN.org. UN, global health agencies sound alarm on drug-resistant infections; new recommendations to reduce 'staggering number' of future deaths. April 29, 2019 retrieved from https://news.un.org/en/story/2019/04/1037471

2 ServiceTrak™ Clinical Executive Summary Report for ID/AST Systems, 2019, 2018 and 2017

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SeqOnce Biosciences

AzureSeq

One Step Universal RT-qPCR Kit
SARS-CoV-2 Variant Assay v1.1

Single Reaction Assay for:
E484K, N501Y, K417

Easy to use RT-qPCR kit for reflex testing of SARS-CoV-2 Variants

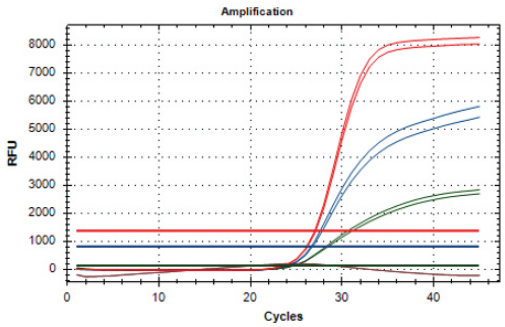
Faster, less expansive than sequencing

RNaseP (internal control)

Designed for ABI and BioRad qPCR Instruments

5ul sample input (100ng to 1pg using CDC extraction protocol, 20ul reaction size)

Made in America



WT K417, WT N501, E484K variant result. FAM (K417) and HEX (E484K) shows amplification while Quasar670 (Cy5 N501Y variant) shows no amplification.

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Coming Soon: AzureSeq SARS-CoV-2 Variant Assay v1.2 with N1 Gene

Research Use Only