MLO-online.com

MEDICAL LABORATORY OBSERVER

MLO®

FEBRUARY 2023 • Vol 55 • No 2

The Peer-Reviewed Management Source for Lab Professionals since 1969

CE:

Diagnosing upper and lower respiratory tract infections

Page 8

A system laboratories' experience with Hurricane Ian

Page 16

PLUS

Toxicology testing data magnifies America's misuse

Page 20

Importance of hemoglobin A1c testing post-COVID

Page 32

LAB INNOVATOR
Philip Cotter, PhD, FACMG, FFSC (RCPA)
Principal and Co-Founder, ResearchDx
A2LA Assessor

Optimize for **today**.

Are you ready to fully automate your molecular testing to meet rising demands?

Trust Hologic to deliver excellent lab automation with Panther® Trax. Combine the agility of the Panther® system with the power of lab automation to improve your lab's flexibility and capacity. Connect multiple Panther® instruments to manage unpredictable surges while utilizing existing resources and reducing complexities.

Scan to discover more

HOLOGIC®

Prepare for **tomorrow**.

Maximize your molecular assay menu today and meet your lab's growing needs of tomorrow.

WOMEN'S HEALTH

- CT/NG
- *Mycoplasma genitalium*
- *Trichomonas vaginalis*
- Bacterial vaginosis
- Candida vaginitis/*Trichomonas vaginalis*
- HSV 1 & 2
- HPV
- HPV 16 18/45
- Group B Strep
- Zika Virus†

INFECTIOUS DISEASE

- HIV-1 Quant Dx
- HCV Quant Dx
- HBV Quant
- CMV Quant
- Flu A/B/RSV
- Paraflu 1-4
- AdV/hMPV/RV
- SARS-CoV-2†
- SARS-CoV-2/Flu A/B†
- ☐ SARS-CoV-2/Flu A/B/RSV*
- ☐ EBV*
- ☐ BKV*
- ☐ GI Bacterial*
- ☐ GI Expanded Bacterial*
- ☐ GI Viral*
- ☐ GI Parasite*
- ☐ GBS*
- ☐ C. difficile*
- ☐ M. gen macrolide resistance*
- ☐ Mpox*

PANTHER®
TRAX

* In development and not for sale.

† The Aptima SARS-CoV-2, Aptima Zika Virus, Aptima SARS-CoV-2/Flu and Panther Fusion SARS-CoV-2 assays have not been FDA cleared or approved; These tests have been authorized by FDA under an EUA for use by authorized laboratories; The Aptima and Panther Fusion SARS-CoV-2 assays have been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; The Aptima Zika Virus assay has been authorized only for the detection of nucleic acid from Zika virus, not for any other viruses or pathogens; The Aptima SARS-CoV-2/Flu assay has been authorized only for the simultaneous qualitative detection and differentiation of nucleic acid from SARS-CoV-2, Flu A, Flu B, and not for any other viruses or pathogens. The Aptima SARS-CoV-2, Panther Fusion SARS-CoV-2, and Aptima SARS-CoV-2/Flu assays are only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner. The Aptima Zika assay is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

MEDICAL LABORATORY OBSERVER
MLO
The Peer Reviewed Management Source for Lab Professionals since 1969

8

Photo 163597947 © Kuprevich | Dreamstime.com

16

257964314 © Felix Mizioznikov | Dreamstime.com

24

Photo Courtesy of Orchard Software

32

Photo 48923286 © Sherry Young | Dreamstime.com

40

Photo courtesy of Philip D. Cotter, PhD, FACMG, FFSC (RCPA)

4 **From the editor**

6 **The observatory**

CONTINUING EDUCATION

8 **Diagnosing upper and lower respiratory tract infections**
By Rajasri Chandra

14 **CE test**
Tests can be taken online or by mail. See page 14 for testing and payment details.

SPECIAL FEATURE

16 **A healthcare system and its laboratories' experience with Hurricane Ian**
By Kara Nadeau

CLINICAL ISSUES

20 **A decade lost to the drug crisis: Toxicology testing magnifies America's misuse**
By Jeffrey Gudin, MD

LAB MANAGEMENT

24 **Leveraging LIS tools to keep your lab inspection-ready**
By Kim Futrell, MT(ASCP), MSHI

INFECTION DIAGNOSTICS

28 **Shifting HIV focus from at-risk populations to at-risk behavior**
By Tamar Tchelidze, MD, MPH and Benjamin LaBrot, MD

EDUCATION

32 **Importance of hemoglobin A1c testing for diabetes diagnosis and management post-COVID-19 infection**
By Thomas Kampfrath, PhD, DABCC, NRCC and Jeanne Rhea-McManus, PhD, MBA, DABCC, NRCC

BEST PRACTICES

36 **Optimal testing methods for early prostate cancer detection**
By John Sylvester, MD

Q&A

38 **Readers' questions answered**

PRODUCT FOCUS

39 **Antibody Tests**

MARKETPLACE

39 **Advertisers index**

LAB INNOVATOR

40 **A leader in clinical laboratory consulting**
By Christina Wichmann

COVER IMAGE: jitendrajadhav/ iStock / Getty Images Plus

RALS™

PAIN RELIEF
AT THE POINT-OF-CARE

When it comes to managing point-of-care testing (POCT), if you're like most POCCs, you probably have lots of pain points, including:

Managing Operators

Can you auto-recertify?

Managing Devices

Where are they? Who is using them?

Being Inspection Ready

Inspectors are coming... are you prepared?

Measuring POCT Performance

Is my program what it should be?

RALS connectivity can help reduce your workflow pain points and provide long-lasting relief with everything from a range of operator management tools, personalized dashboards for monitoring key performance indicators, and custom saved views for quick and efficient data review.

TO SEE ALL THE WAYS RALS CAN HELP VISIT WWW.RALS.COM

Abbott

2023 Outlook

By Christina Wichmann
Senior Editor

According to the results of a new survey conducted by the Deloitte Center for Health Solutions, hospital and health system leaders are preparing to navigate a possibly turbulent 2023.[1] The majority of healthcare leaders (85%) said staffing challenges would have a major impact on their strategy for 2023, and 76% said inflation is a significant factor in organizational strategies. Staffing challenges, including burnout, shortages, and turnover are prompting many hospital and health system leaders to pay closer attention to the mental health and well-being of their employees. Nearly all of the Deloitte survey respondents (95%) said investing in their workforce in 2023 was "important" or "very important."

Clinical laboratories produce more than 652,000 jobs nationwide according to recent analysis from the American Clinical Laboratory Association (ACLA).[2] And there is no shortage of jobs out there in the field. For example, LinkedIn has listings for 15,363 medical laboratory scientists and 19,650 medical laboratory technologists.

To address staffing challenges, I have seen the following in recent literature and laboratory job announcements:

- 2:1 retirement savings match
- Addressing compensation disparities between temporary and permanent staff
- Job sharing (splitting a full-time position between two people)
- No-cost continuing education
- Optimizing workflows through automation
- Sign-on bonuses
- Student loan assistance
- Work/life balance, including flexible work shifts, no third-shift, one weekend requirement a month, minimal holidays

Hopefully, staffing challenges start to improve in 2023 versus the opposite.

As for healthcare leaders' concerns about inflation this year, the "Fiscal Year 2023 Omnibus Appropriations Bill" was recently signed into law. This will help some as it provides a one-year reprieve from Medicare cuts of up to 15 percent for over 800 laboratory services that would have gone into effect January 2023 through the Protecting Access to Medicare Act (PAMA). Perhaps the long-term fix to PAMA, the Saving Access to Laboratory Services Act (SALSA), will move forward this year.

I welcome your comments and questions — please send them to me at cwichmann@mlo-online.com.

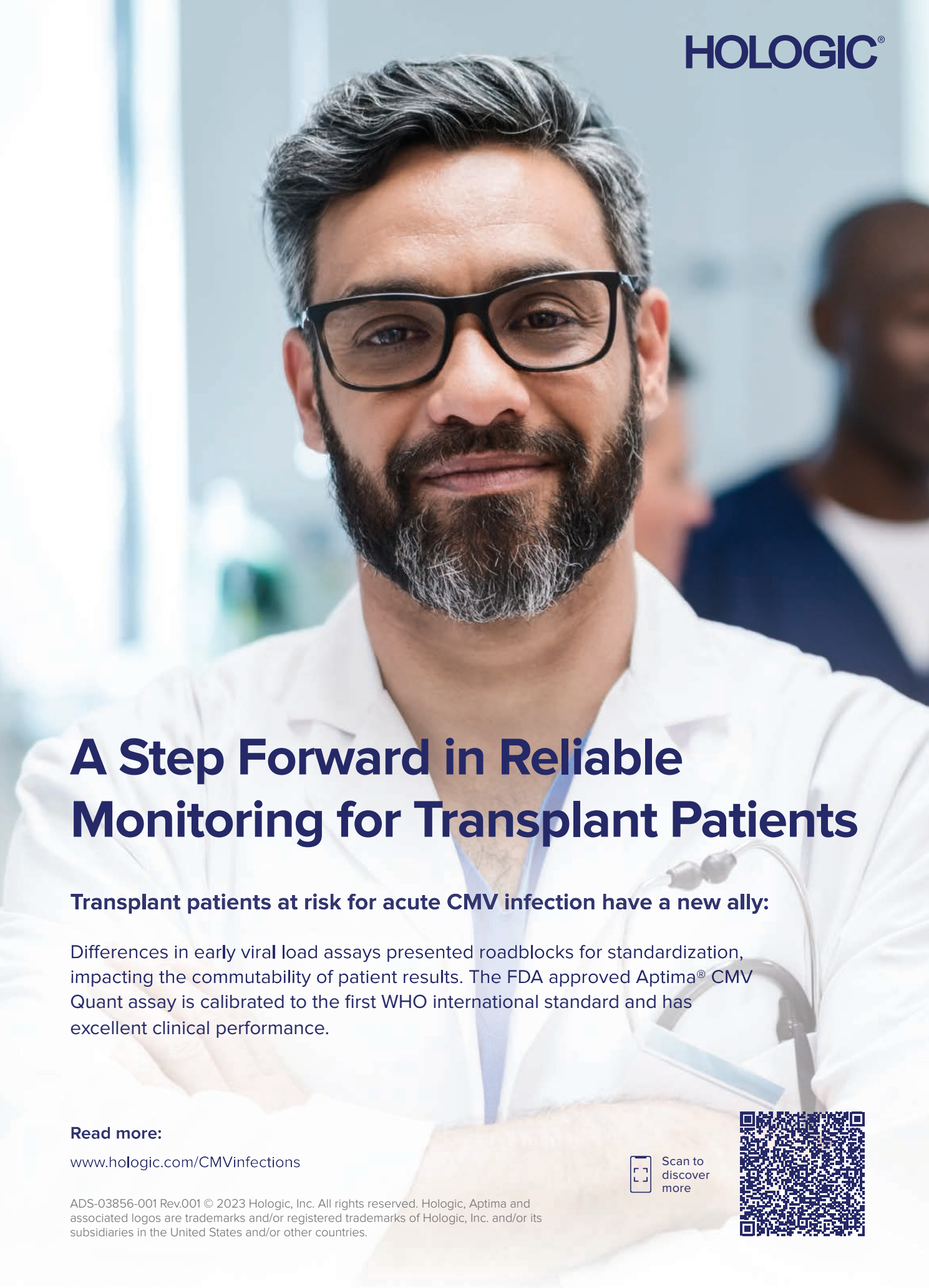
REFERENCES

1. 2023 outlook for health care. Deloitte United States. Accessed January 10, 2023. https://www2.deloitte.com/us/en/blog/health-care-blog/2022/2023-outlook-for-health-care-could-margins-staffing-stall-progress-to-future-of-health.html.

2. New analysis shows value of clinical laboratories to the U.S. economy. American Clinical Laboratory Association. Published November 28, 2022. Accessed January 10, 2023. https://www.acla.com/%ef%bf%bcnew-analysis-shows-value-of-clinical-laboratories-to-the-u-s-economy/.

MEDICAL LABORATORY OBSERVER Vol.55, No. 2

Medical Laboratory Observer USPS Permit 60930, ISSN 0580-7247 print, ISSN 2771-6759 online is published 12 times annually (Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Sep CLR, Oct, Nov, Dec), with an additional issue in September, by Endeavor Business Media, LLC. 1233 Janesville Ave., Fort Atkinson, WI 53538. Periodical postage paid at Fort Atkinson, WI, and additional mailing offices. POSTMASTER: Send address changes to Medical Laboratory Observer, PO Box 3257, Northbrook, IL 60065-3257. SUBSCRIPTIONS: Publisher reserves the right to reject non-qualified subscriptions. Subscription prices: U.S. $160.00 per year; Canada/Mexico $193.75 per year; All other countries $276.25 per year. All subscriptions are payable in U.S. funds. Send subscription inquiries to Medical Laboratory Observer, PO Box 3257, Northbrook, IL 60065-3257. Customer service can be reached toll-free at 877-382-9187 or at MLO@omeda.com for magazine subscription assistance or questions.



HOLOGIC®

A Step Forward in Reliable Monitoring for Transplant Patients

Transplant patients at risk for acute CMV infection have a new ally:

Differences in early viral load assays presented roadblocks for standardization, impacting the commutability of patient results. The FDA approved Aptima® CMV Quant assay is calibrated to the first WHO international standard and has excellent clinical performance.

Read more:

www.hologic.com/CMVinfections

Scan to discover more

Fast Facts

The U.S. Department of Health and Human Services' (HHS) Substance Abuse and Mental Health Services Administration (SAMHSA) released the results of its annual National Survey on Drug Use and Health (NSDUH), which shows how people living in America reported about their experience with mental health conditions, substance use, and pursuit of treatment in 2021. The 2021 NSDUH national report includes selected estimates by race, ethnicity, and age group. It is the most comprehensive report on substance use and mental health indicators that SAMHSA has released to date.

Key findings from the 2021 NSDUH include:

61.2 million

people aged 12 or older (or 21.9 percent of the population) used illicit drugs in the past year.

52.5 million

people used marijuana, the most used illicit drug.

9.2 million

people 12 and older misused opioids in the past year.

94%

of people aged 12 or older with a substance use disorder did not receive any treatment in 2021.

1 in 5

adolescents had a major depressive episode in the past year.

13.5 percent

of young adults aged 18 to 25 had both a substance use disorder and any mental illness in the past year.

Source: https://www.hhs.gov/about/news/2023/01/04/samhsa-announces-national-survey-drug-use-health-results-detailing-mental-illness-substance-use-levels-2021.html

The Joint Commission retires select accreditation requirements

The Joint Commission previously announced that it would review accreditation requirements that are above and beyond the Centers for Medicare & Medicaid Services (CMS) Conditions of Participation (CoPs). This initiative aims to help their customers address the many challenges that healthcare is facing by eliminating requirements that do not add value to accreditation surveys so that healthcare organizations and surveyors can focus on other strategies and structures that support quality and safety.

The review began with hospital elements of performance (EPs) that met all of the following criteria:

- The EP does not support a CMS CoP or state regulation.
- The EP has been in effect for at least three years.
- The EP has been scored five times or less during full triennial surveys between 2017 and 2019 (the three years prior to the COVID-19 public health emergency).

Staff across multiple divisions reviewed each of the selected EPs and reported the possible reasons why scoring was low, including organizations are compliant with the requirement because they have adopted it as a standardized practice, the EP is redundant to another requirement, and the EP is difficult to assess compliance objectively and consistently during surveys. As a result of this review, 56 hospital EPs were identified for deletion, and 4 EPs needed minor revisions to make them more effective. Many of these EPs were also accreditation requirements for other programs, and these were deleted or revised from those programs as well.

WHO updates recommendations on HPV vaccination schedule

In a new position paper published, the World Health Organization has updated its recommendations for the human papillomavirus (HPV) vaccine. Of note, the paper states that a single-dose schedule, referred to as an alternative, off-label single–dose schedule can provide a comparable efficacy and durability of protection to a two-dose regimen. The recommendation for alternative single-dose scheduling was initially made by WHO's independent expert advisory group, SAGE in April 2022.

The position paper is timely in the context of a deeply concerning decline in HPV vaccination coverage globally. Between 2019 and 2021, coverage of the first dose of HPV vaccination fell by 25% to 15%. This means 3.5 million more girls missed out on HPV vaccination in 2021 compared to 2019.

The optimization of the HPV schedule is expected to improve access to the vaccine, offering countries the opportunity to expand the number of girls who can be vaccinated and alleviating the burden of the often complicated and costly follow-up required to complete the vaccination series. It's vital that countries strengthen their HPV vaccination programs, expedite implementation and reverse the declines in coverage.

WHO now recommends:

- **A one or two-dose schedule** for girls aged **9-14 years**
- **A one or two-dose schedule** for girls and women aged **15-20 years**
- Two doses with a 6-month interval for women **older than 21 years**

WHO meets with Chinese officials on current COVID-19 situation

A high-level meeting took place on December 30 between the World Health Organization and China about the current surge in COVID-19 cases, to seek further information on the situation, and to offer WHO's expertise and further support.

High-level officials from China's National Health Commission and the National Disease Control and Prevention Administration briefed WHO on China's evolving strategy and actions in the areas of epidemiology, monitoring of variants, vaccination, clinical care, communication and R&D.

WHO asked for regular sharing of specific and real-time data on the epidemiological situation — including more genetic sequencing data, data on disease impact including hospitalizations, intensive care unit (ICU) admissions and deaths — and data on vaccinations delivered and vaccination status, especially in vulnerable people and those over 60 years old. WHO reiterated the importance of vaccination and boosters to protect against severe disease and death for people at higher risk.

WHO called on China to strengthen viral sequencing, clinical management and impact assessment, and expressed willingness to provide support on these areas, as well as on risk communications on vaccination to counter hesitancy. Chinese scientists are invited to engage more closely in WHO-led COVID-19 expert networks including the COVID-19 clinical management network. WHO has invited Chinese scientists to present detailed data on

viral sequencing at a meeting of the Technical Advisory Group on SARS-CoV-2 Virus Evolution on January 3.

WHO stressed the importance of monitoring and the timely publication of data to help China and the global community to formulate accurate risk assessments and to inform effective responses.

COVID-19 vaccine for children after MIS-C appears safe

A study of children and adolescents who received a COVID-19 vaccination following multisystem inflammatory syndrome (MIS-C) found that there were no reports of serious complications including myocarditis or MIS-C reoccurrence.

About half of participants experienced mild and typical reactions, including arm soreness and fatigue. The study, funded by the National Institutes of Health, demonstrates that it is safe to get a vaccine after having MIS-C. The findings will be published in *JAMA Network Open*.

The multicenter, observational study helps resolve a lingering question about whether the COVID vaccine can increase the risk of health problems in young people who have had MIS-C, a rare and potentially fatal immunological reaction that can occur following infection with SARS-CoV-2, the virus that causes COVID-19.

The cross-sectional study included 22 medical centers (21 in the United States and 1 in Canada) participating in the NHLBI's Long-Term Outcomes After the Multisystem Inflammatory Syndrome in Children (MUSIC) study. It enrolled 385 patients aged 5 years or older with prior MIS-C who were eligible for COVID-19 vaccination. Of this group,185 (48.1%) received at least one vaccine dose. The median age was 12.2 years and 73.5% were male. The participants were racially diverse – 24.3% were Black, 31.9% were Hispanic, and 28.6% were white. The median length of time from their MIS-C diagnosis to their first vaccine dose was 9 months.

Of those who received a COVID vaccination following MIS-C, mild adverse reactions – mostly arm soreness and fatigue – occurred in 49% of them, similar to the general population. There were no reports of serious complications, including myocarditis or recurrence of MIS-C, the researchers said.

UTSW researchers map activity of inherited gene variants linked to prostate cancer

UT Southwestern researchers have identified the molecular function of 87 inherited genetic variants that affect the risk of prostate cancer, and the majority appear to control the activity of genes located far away from the risk variants themselves. The findings, published in *Cancer Discovery*, could lead to better ways to assess cancer risk and new targets for anti-cancer drugs, the study authors say.

Researchers used several approaches to identify which genes serve as targets for the risk alleles. A three-dimensional mapping technique using data from 565 prostate cancer tumors showed that 87 of these risk alleles affected the activity of hundreds of genes.

Although malignant tumors typically arise in the prostate's epithelial cells, researchers found that the affected genes were often in other tissue types, including stromal cells and smooth muscle cells that support the epithelial cells. Most of the risk alleles appeared to alter the activity of these genes, which produced proteins known to be involved in molecular pathways for development, apoptosis (programmed cell death), and metabolism, among other cellular processes.

Study leader Ram Mani, Ph.D., said some alleles had opposing activity on the multiple genes they control. For example, one allele known as rs8102476 simultaneously increased the activity of one gene while decreasing the activity of a neighboring gene. The risk alleles also had significant interaction with genes that acquired nonheritable mutations associated with prostate cancer; these interactions appeared to predict how aggressive a patient's disease became.

COVID-19 vaccine acceptance increased globally in 2022

Global willingness to accept a COVID-19 vaccine increased from 75.2% in 2021 to 79.1% in 2022, according to a new survey of 23 countries that represent more than 60% of the world's population, published in *Nature Medicine.* Vaccine acceptance decreased in eight countries however, and nearly one in eight vaccinated respondents were hesitant about receiving a booster dose.

Of the 23,000 respondents (1000 per country surveyed), 79.1% were willing to accept vaccination, up 5.2% from June 2021. The willingness of parents to vaccinate their children also increased slightly, from 67.6% in 2021 to 69.5% in 2022. However, eight countries saw an increase in hesitancy (from 1.0% in the U.K. to 21.1% in South Africa). Worryingly, almost one in eight (12.1%) vaccinated respondents were hesitant about booster doses, and booster hesitancy was higher among the younger age groups (18-29).

FDA updates safety communication on bacterial contamination of platelets

The Food and Drug Administration issued a second update to its April 2019 safety communication related to the investigation of bacterial contamination of platelets for transfusion with Acinetobacter species and certain other bacterial species in combination, according to a release from AABB.

The implicated components were subject to various bacterial risk mitigation strategies, including bacterial culture and/or secondary rapid testing prior to release or processing with an FDA-approved pathogen-reduction device prior to transfusion. The agency also received additional reports of positive bacterial cultures during routine testing of units that were not transfused where the same organisms were also identified. Several of these isolates showed a genetic match to isolates from the clinical cases of septic reactions.

Among the septic reaction cases that were genetically matched, the platelet components were all manufactured using blood collection and storage systems and solutions from a single manufacturer. FDA continues to conduct inspections of the manufacturer to ensure control of the manufacturing process and to maintain sterility of the collection sets and solutions. At this time, the strategies to assure the bacterial safety of platelet components recommended in FDA guidance remain acceptable.

Photo 163597947 © Kuprevich | Dreamstime.com

Diagnosing upper and lower respiratory tract infections

By Rajasri Chandra

Respiratory tract infections (RTIs) are among the most common reasons why patients visit their physicians. These infections can range from mild, self-limiting, or life-threatening requiring hospitalization. Though the majority of respiratory tract infections are caused by viruses, some bacteria and fungi can also cause respiratory tract infections. RTIs can be classified as upper and lower respiratory tract infections depending on the site of the infection in the respiratory system. However, in many cases, viruses may enter the upper respiratory tract and subsequently reach the lower respiratory tract. Organisms gain entry to the respiratory tract by inhalation of droplets or contact with contaminated

Earning CEUs

See test on page 14 or online at www.mlo-online.com under the CE Tests tab. Passing scores of 70 percent or higher are eligible for 1 contact hour of P.A.C.E. credit.

LEARNING OBJECTIVES

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

1. Discuss healthcare statistics of various respiratory tract infections (RTIs) in the United States.
2. List the causative agents of RTIs.
3. Describe the serotypes of various viruses causing RTIs and their complications.
4. List and describe the benefits and limitations of laboratory diagnosis of RTIs.

Depending on which part of the upper respiratory tract is infected, symptoms can be as follows:
• Cough
• Sore throat
• Runny nose
• Nasal congestion
• Headache
• Low-grade fever
• Facial pressure
• Sneezing
• Malaise
• Myalgias
Symptoms usually appear one to three days after exposure and last 7–10 days, but can persist up to 3 weeks.

Table 1. Possible symptoms of upper respiratory tract infections.[2]

LRIs can be mild exhibiting the following symptoms:
• Stuffy or runny nose
• Dry cough
• Low fever
• Mild sore throat
• Dull headache
LRIs can be severe exhibiting the following symptoms:
• Severe cough that may produce phlegm
• Fever
• Difficulty breathing
• Blue tint to the skin
• Rapid breathing
• Chest pain
• Wheezing
Patients with pneumonia may also exhibit non-respiratory symptoms such as confusion, headache, myalgia, abdominal pain, nausea, vomiting, and diarrhea.

Table 2. Possible symptoms of lower respiratory tract infections.[1,7]

fomites.[1,2] They then invade the mucosa, followed by epithelial destruction, along with redness, edema, hemorrhage, and sometimes an exudate.[1]

Upper respiratory tract infections (URIs) affect the respiratory tract above the lungs including the nose, throat, nasopharynx, sinus, larynx, epiglottis, or trachea causing rhinitis, pharyngitis, nasopharyngitis, sinusitis, laryngitis, epiglottitis or tracheitis respectively. They account for an estimated 10 million outpatient appointments annually.[3] Though anyone can get affected by URIs, children are at a higher risk. URIs are caused by viruses in approximately 90 to 98 percent of cases.[4] That said, a few bacteria and fungi can also cause URIs. **Table 1** shows the probable symptoms of URIs.

Lower respiratory tract infections (LRIs) are infections in the lungs or below the larynx, a major killer globally. These include pneumonia, bronchitis, and tuberculosis. According to the Global Burden of Disease report of 2019, 489 million LRI episodes occurred, leading to a total of 2.5 million deaths.[5] LRIs can be caused by viruses, bacteria, and fungi.[1,6] **Table 2** shows the probable symptoms of LRIs.

Respiratory tract infections caused by viruses

Human rhinovirus and human enterovirus: Human rhinoviruses (HRVs) and respiratory enteroviruses (HEVs) are leading causes of upper respiratory tract infections and among the most frequent infectious agents in humans worldwide.[8] Both are classified in the enterovirus genus within the *Picornaviridae* family, and they have been assigned to seven distinct species, RV-A, B, C and EV-A, B, C, D.[8] HRV was first identified in the 1950s and known to cause over 50% of cases of "common cold."[9,10] The common cold is the most frequently occurring URI. Each year in the United States there are millions of cases of the common cold. Colds are the main reason that children miss school and adults miss work. Adults have an average of two to three colds per year.[11] A preschool-aged child has an average of 6 to 10 episodes per year, and 10% to 15% of school-aged children have at least 12 infections per year.[10] The common cold is self-limited and does not cause serious health issues. Symptoms of common cold include sore throat, runny nose, coughing, sneezing, headache, and body ache.[11]

Initial research suggested that HRV is a benign virus restricted to growth within the upper airways of humans. However, recent research shows that HRV is not only able to effectively reach, penetrate, and replicate within the lower airway epithelium of individuals in vivo, but also causes histologic changes of the lung interstitium and alveoli. Moreover, HRVs have now been shown to be an important cause of superinfection, with bacteria like Streptococcus pneumoniae and Staphylococcus aureus.[9]

Recent clinical studies in pediatrics have also shown the association of HRVs with lower respiratory tract infections including bronchiolitis and pneumonia. However, it is still not totally understood if HRVs can cause LRIs on their own. It has also been shown that both HRVs and HEVs shed in the nasopharynx of children following acute infection for up to 6 weeks and 3 weeks, respectively.[12]

HEV infections with non-polio enteroviruses are common in the United States during summer and fall. A mix of enteroviruses circulates every year, and different types can be common in different years.[13] HEVs are found to have 4 genotypes: A, B, C, and D. Three better-known, non-polio enteroviruses are enterovirus D68 (EV-D68), enterovirus A71 (EV-A71), and coxsackie virus A6 (CV-A6). EV-D68 usually causes respiratory illness. EV-A71and CV-A6 are known to cause hand, foot, and mouth disease. Most people who get infected with non-polio enteroviruses do not get sick, or they only have mild illness, like the common cold. Symptoms of mild illness can include fever, runny nose, sneezing, cough, skin rash, mouth blisters, and body and muscle aches.[13] EV-D68 can cause mild to severe respiratory illness or no symptoms at all. Mild symptoms may include runny nose, sneezing, cough, body aches, and muscle aches. Severe symptoms may include wheezing and difficulty breathing. It can also cause acute flaccid myelitis (AFM), an uncommon but serious neurologic condition that mostly affects children and causes the muscles and reflexes in the body to become weak.[14]

Influenza viruses: These are the next common viruses causing upper respiratory tract infection with symptoms similar to that of common cold. There are four types of influenza viruses: A, B, C, and D. Influenza A and B viruses cause seasonal flu epidemics almost every winter in the United States. Influenza A viruses are capable of causing flu pandemics. Influenza C viruses generally cause mild illness and are not thought to cause human epidemics. Influenza D viruses primarily affect cattle and are not known to infect or cause illness in people. Influenza A viruses are further divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes (H1 through H18 and N1 through N11, respectively). Currently influenza A (H1N1) and influenza A (H3N2) subtypes are found in infected individuals. Influenza B viruses are not divided into subtypes, but various strains/lineages are found. Vaccines are available for influenza viruses A and B.[15]

The burden of influenza (flu) disease in the United States varies widely and is determined by the characteristics of circulating viruses, the timing of the season, how well the vaccine is working to protect against illness, and how many people got vaccinated. Influenza can cause mild to severe illness, and at times can lead to death.[16] Flu symptoms usually come on suddenly. People who have the flu often feel some or all of these symptoms: fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue, vomiting, and diarrhea in some, though more common in children than adults.

Bacteria	Site of infection	Respiratory infection
Group A β-hemolytic Streptococcus	Throat, pharynx	Sore throat, pharyngitis
Group C β-hemolytic Streptococcus	Throat, pharynx	Severe acute pharyngitis
Corynebacterium diphtheria	Throat, pharynx	Diphtheria
Neisseria gonorrhea	Oropharynx	Tonsilitis, pharyngitis
Neisseria meningitis	Larynx	Epiglottitis
Arcanobacterium haemolyticum	Pharynx	Pharyngitis
Mycoplasma pneumoniae	Throat, pharynx	Sore throat, pharyngitis, sinusitis, otitis media
Chlamydophila pneumoniae	Throat, pharynx	Sore throat, pharyngitis, sinusitis, otitis media
Hemophilus influenza	Nasopharynx	URTI, meningitis, epiglottitis
Moraxella Catarrhalis	Nasopharynx	Sinusitis, otitis media
Bordetella pertussis	Human respiratory mucosa	Whooping cough
Bordetella Para pertussis	Human respiratory mucosa	Whooping cough (milder)

Table 3. Bacteria causing upper respiratory tract infections.

Most people recover in a few days to less than two weeks, but some people may develop complications. Sinus and ear infections are examples of moderate complications from flu, while pneumonia is a serious flu complication that can result from either flu virus infection alone or from co-infection of flu virus and bacteria. Other possible serious complications triggered by flu can include inflammation of the heart (myocarditis), brain (encephalitis) or muscle tissues (myositis, rhabdomyolysis), and multi-organ failure (for example, respiratory and kidney failure). Flu virus infection of the respiratory tract can trigger an extreme inflammatory response in the body and can lead to sepsis, the body's life-threatening response to infection. The Centers for Disease Control and Prevention (CDC) estimates that flu has resulted in 9 million – 41 million illnesses, 140,000 – 710,000 hospitalizations, and 12,000 – 52,000 deaths annually between 2010 and 2020.[17]

Human respiratory syncytial virus (RSV): RSV is an enveloped single-stranded RNA virus of the genus Orthopneumovirus, family Pneumoviridae. It has a single serotype with two major antigenic subgroups, A and B.[18] The clinical manifestations range from mild upper respiratory tract illness or otitis media to severe and potentially life-threatening lower respiratory tract involvement (LRI). The most common form of LRI in RSV-infected infants is bronchiolitis, but pneumonia and croup are also seen.[18] Most people recover in a week or two, but it can also be serious, especially for infants and older adults. It is the most common cause of bronchiolitis and pneumonia in children younger than one year of age in the United States.[19]

Bacteria	Site of infection	Respiratory infection
Streptococcus pneumoniae	Lung	Pneumonia
Hemophilus influenza	Lung	Pneumonia
Klebsiella pneumoniae	Lung	Pneumonia
Staphylococcus aureus	Lung	Pneumonia
Legionella pneumophila	Lung	Pneumonia
Chlamydophila pneumoniae	Lung	Pneumonia
Mycoplasma pneumoniae	Lung	Pneumonia
Chlamydia psittaci	Lung	Pneumonia

Table 4. Bacteria causing lower respiratory tract infections, i.e., pneumonia.

Human coronavirus and SARS-CoV-2: There are six human pathogenic coronaviruses (CoV) that primarily cause respiratory infections in humans. Four of them, 229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus), and HKU1 (beta coronavirus) occur worldwide and are very common. These viruses usually cause mild to moderate upper respiratory tract infections after 2–10 days of incubation with the typical symptoms of a cold or flu-like infection, i.e., runny nose, cough, sore throat, headache, and fever or feverishness. Severe cases are rare and are most likely to occur in immunosuppressed patients. Two other types are rare but responsible for severe viral pneumonia: MERS (Middle East respiratory syndrome) and SARS-CoV (severe acute respiratory syndrome). While SARS-CoV has not been found in humans since 2004, infections with MERS-CoV have been continuously detected since 2012.[20]

SARS-CoV-2 is a coronavirus discovered in 2019 that caused the COVID-19 pandemic. Per World Health Organization (WHO) data, as of December 13, 2022, it caused 652 million cases with 6.6 million deaths worldwide and 99.6 million cases with 1.1 million deaths in the United States.[21] The virus keeps mutating resulting in eight variants so far — Alpha, Beta, Gamma, Delta, Omicron, Lambda, Mu, and BA.2. The virus spreads mainly from person to person through respiratory droplets produced when an infected person coughs, sneezes, or talks. Some people who are infected may not have symptoms. For people who have symptoms, illness can range from mild to severe. Adults 65 years and older and people of any age with underlying medical conditions are at higher risk for severe illness.[22] Main symptoms are fever, cough, shortness of breath, trouble breathing, fatigue, chills, body aches, headache, sore throat, congestion/runny nose, loss of smell or taste, nausea, diarrhea. The virus can lead to pneumonia, respiratory failure, heart problems, liver problems, septic shock, and death.[23]

Human adenovirus: A DNA virus that most commonly causes respiratory illness. The illnesses can range from the common cold to pneumonia, croup, and bronchitis. People with weakened immune systems are at high risk for developing severe illness caused by adenovirus infection.[24]

Human parainfluenza viruses (HPIV): Commonly cause respiratory infections in infants and young children. Patients

Quidel has developed an innovative line of respiratory products for decades.

So whatever respiratory season may bring, we're ready.

1979 Quidel founded

1996 First company to receive CLIA waiver for Strep A with QuickVue In-Line Strep A Test

1999 Receives FDA clearance for world's first rapid diagnostic flu test QuickVue Influenza Test (A/B)

2011 Quidel launches Sofia automated analyzer FIA

2015 Introduction of Solana assays

2018 Receives FDA clearance for QuickVue Influenza A+B which meets FDA's Class II RIDT requirements

2020 Receives FDA EUA for Sofia 2 SARS Antigen FIA, Sofia 2 Flu+SARS FIA (ABC), QuickVue SARS Antigen Test, and Solana SARS-CoV-2

QUIDEL®

QuickVue®
Influenza A+B, RSV, SARS* Antigen Assays

Solana®
Influenza A+B, RSV + hMPV, SARS-CoV-2*, Bordetella Complete Assays

Sofia®/Sofia 2
Influenza A+B, RSV, SARS* Antigen, Flu + SARS* Antigen Assays

To get the right RIDT for your patient, contact a Quidel Inside Sales at **858.431.5814** or visit **quidel.com**

*THESE TESTS ARE AVAILABLE FOR SALE IN THE USA UNDER EMERGENCY USE AUTHORIZATION. These SARS tests have not been FDA cleared or approved, but have been authorized by the FDA under an Emergency Use Authorization (EUA) for use by authorized laboratories for the detection of proteins (QuickVue and Sofia) or nucleic acids (Solana) from SARS-CoV-2, not for any other viruses or pathogens. These tests are only authorized for the duration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless terminated or revoked sooner.

AD10183600EN00 (06/22)

Fungi	Possible symptoms	Diagnostic test
Aspergillus fumigatus	Shortness of breath, wheezing, cough, headache, pneumonia, can lead to pulmonary or brain hemorrhage causing death	Chest x-ray, microscopic observation of sputum sample
Blastomyces dermatitidis	Fever, chills, cough, chest pain, body aches. Can spread from lungs and cause chronic, crusted lesions in face and hands with permanent scarring. Can be fatal.	Microscopic observation of sputum sample, urine antigen test, enzyme immunoassay
Coccidioides immitis	Granulomatous lesions on face and nose, may spread to other organs and brain, causing fatal meningitis	Culture in BSL-3 lab, serological antibody tests
Cryptococcus neoformans	Fever, cough, shortness of breath if disseminated to brain causing meningitis	Microscopic examination of lung tissue or cerebral spinal fluid
Histoplasma capsulatum	Fever, headache, chest pain, lesions on lungs	Chest x-ray, direct fluorescence antibody staining, complement fixation assay, histoplasmin sensitivity test
Mucormycetes	Headache, fever, facial swelling, congestion, black lesions in oral cavity, cough, chest pain, often fatal	Microscopic examination of tissue biopsy specimens
Pneumocystis jirovecii	Fever, cough, shortness of breath, can be fatal if untreated	Microscopic examination of lung tissue and fluid, PCR test

Table 5. Respiratory tract infections caused by fungi.

usually recover on their own. However, HPIVs can also cause more severe illness, such as croup or pneumonia.[25]

Human metapneumovirus (HMPV): Can cause upper and lower respiratory disease in people of all ages, especially among young children, older adults, and people with weakened immune systems. Symptoms commonly associated with HMPV include cough, fever, nasal congestion, and shortness of breath. Clinical symptoms of HMPV infection may progress to bronchitis or pneumonia.[26]

Human bocavirus (HBoV1): Small, nonenveloped linear single-stranded DNA virus of the Parvoviridae family that was discovered in 2005 in nasopharyngeal aspirates of children with respiratory tract infections. HBoV1 causes both upper and lower respiratory tract infections of diverse severity and affects most children before age seven. After primary infection, HBoV1 can, despite a vigorous antibody response, persist in the respiratory tract for at least up to 12 months.[27]

Respiratory tract infections caused by bacteria

Though viruses are known to cause more cases of respiratory tract infections, some bacteria can cause upper and lower respiratory tract infections.[1] Co-infection with a virus and bacteria may contribute to severe disease and increased mortality in patients.[28] **Table 3** lists the common bacteria causing upper respiratory tract infections and **Table 4** lists the bacteria that cause lower respiratory tract infections, mostly pneumonia.

Laboratory diagnosis of respiratory viruses and bacteria

Proper diagnosis to determine the causative organism is very important for proper patient management. There are several methods for detecting and identifying respiratory viruses and bacteria and every method has its pros and cons, which are listed below.[29]

Electron microscopy: Though electron microscopy had been used in the past to identify novel viral strains, its use is limited in diagnosis as it is expensive, laborious, time-consuming, and is not as sensitive compared to many other diagnostic methods.

Culture: Culture has been considered the gold standard for both viruses and bacteria for decades. There have been several improvements in the viral culture process over time. That said, some viruses, including rhinovirus and coronavirus, are difficult to grow and repeated freeze thaw of samples can lower the viral titer affecting growth of the viral culture.

Viral cultures are time consuming, laborious, and can result in false negatives. Bacterial cultures are easier to grow, but testing takes 48 to 96 hours when the culture is followed by drug susceptibility testing. Also, if the sample is collected after antimicrobial treatment, false negative results may be seen.

Rapid immunoassays: Rapid immunoassays (RIAs) can deliver test results in less than 30 minutes even when the patient is at the doctor's office, enabling early patient management and treatment. Knowing the causative agent early helps to check spread of the disease. RIAs are relatively inexpensive, easy to perform, and most are CLIA-waived, thereby making them invaluable in outpatient, primary care, emergency, and low-resource settings. In spite of these benefits, RIA tests vary greatly in sensitivity, and RIA may not be available for all types of respiratory viruses and bacteria.

Direct fluorescent antibody tests: Direct fluorescent antibody (DFA) testing of nasopharyngeal wash specimens is considered a rapid and reliable method for detecting respiratory viral infections. Many commercial DFA kits have high sensitivity and specificity, but the results can be subjective and require technical expertise for accurate interpretation.

Serological tests: Pathogen-specific antibodies generally appear about two weeks after the initial infection and can be detected by serological tests. Serological tests can successfully identify antibodies to most respiratory pathogens such as RSV, adenovirus, influenza A and B, parainfluenza 1-3 virus, etc. These tests can also detect mixed infections from hospitalized children suffering from acute respiratory infections. That said, antibody response in infants is not well detected and serological tests against all viruses and bacteria may not be very sensitive.

Nucleic acid amplification tests: A wide variety of nucleic acid amplification tests (NAATs) for the detection of respira-

tory pathogens are commercially available. NAAT tests are highly specific and have high sensitivity. However, they are generally more expensive than immunoassays and some require high technical skill. The tests are of varying complexity, including:

- Rapid, CLIA-waived tests that detects one or a few pathogens
- Moderately complex test that detects a few pathogens
- Highly complex multiplex assays detecting several pathogens simultaneously

Respiratory tract infections caused by fungi

Respiratory tract infections caused by fungi have been reported in immunocompromised patients. **Table 5** lists some fungi that cause respiratory infections, along with symptoms and diagnostic tests.[30]

Conclusion

As respiratory tract infections exhibiting similar symptoms may be caused by different pathogens with varying prognosis, it is necessary to accurately identify the causative pathogen at the earliest point possible.

Benefits of early detection and initiation of appropriate patient management are as follows:

- Rapid recovery of the patient;
- Check transmission of the infectious agent especially in case of highly infectious viruses;
- Curtail unnecessary use of antibiotics and prevent antibiotic resistance when the infection is found to be of viral origin, as antibiotics are known to be ineffective against viruses.

REFERENCES

1. Dasaraju PV, Liu C. Infections of the Respiratory System. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 93. Available from: https://www.ncbi.nlm.nih.gov/books/NBK8142/.

2. Charlton CL, Babady E, Ginocchio CC, Hatchette TF, et al. Practical Guidance for Clinical Microbiology Laboratories: Viruses Causing Acute Respiratory Tract Infections. *Clin Microbiol Rev*. 2018;12;32(1):e00042-18. doi:10.1128/CMR.00042-18.

3. Thomas M, Bomar PA. Upper Respiratory Tract Infection. [Updated 2022 Jun 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532961/.

4. Chow AW, Benninger MS, Brook I, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012;54(8):e72-e112. doi:10.1093/cid/cir1043.

5. GBD 2019 LRI Collaborators. Age-sex differences in the global burden of lower respiratory infections and risk factors, 1990-2019: results from the Global Burden of Disease Study 2019. *Lancet Infect Dis*. 2022;22(11):1626-1647. doi:10.1016/S1473-3099(22)00510-2.

6. Chowdhary A, Agarwal K, Meis JF. Filamentous Fungi in Respiratory Infections. What Lies Beyond Aspergillosis and Mucormycosis? *PLoS Pathog*. 2016;28;12(4):e1005491. doi:10.1371/journal.ppat.1005491.

7. Fletcher J. Lower respiratory tract infection: Symptoms, diagnosis, and treatment. Medicalnewstoday.com. Published February 11, 2019. Accessed December 20, 2022. https://www.medicalnewstoday.com/articles/324413.

8. Royston L, Tapparel C. Rhinoviruses and Respiratory Enteroviruses: Not as Simple as ABC. *Viruses*. 2016; 11;8(1):16. doi:10.3390/v8010016.

9. Smith ME, Wilson PT. Human Rhinovirus/Enterovirus in Pediatric Acute Respiratory Distress Syndrome. *J Pediatr Intensive Care*. 2020;9(2):81-86. doi:10.1055/s-0039-3400466.

10. Loo M. Upper Respiratory Tract Infection. *Integrative Medicine for Children*. Published online 2009:450-455.

11. CDC. Common colds: Protect yourself and others. Centers for Disease Control and Prevention. Published November 29, 2021. Accessed December 20, 2022. https://www.cdc.gov/features/rhinoviruses/index.html.

12. Jartti T, Lehtinen P, Vuorinen T, Koskenvuo M, Ruuskanen O. Persistence of rhinovirus and enterovirus RNA after acute respiratory illness in children. *J Med Virol*. 2004;72(4):695-9. doi:10.1002/jmv.20027.

13. CDC. Enteroviruses. Centers for Disease Control and Prevention. Published November 14, 2022. Accessed December 22, 2022. https://www.cdc.gov/dotw/enteroviruses/index.html.

14. Enterovirus D68. Cdc.gov. Published September 9, 2022. Accessed December 22, 2022. https://www.cdc.gov/non-polio-enterovirus/about/ev-d68.html.

15. CDC. Types of influenza viruses. Centers for Disease Control and Prevention. Published December 2, 2022. Accessed December 22, 2022. https://www.cdc.gov/flu/about/viruses/types.htm.

16. CDC. Flu symptoms & complications. Centers for Disease Control and Prevention. Published November 30, 2022. Accessed December 22, 2022. https://www.cdc.gov/flu/symptoms/symptoms.htm.

17. CDC. Disease burden of flu. Centers for Disease Control and Prevention. Published December 1, 2022. Accessed December 22, 2022. https://www.cdc.gov/flu/about/burden/index.html.

18. Borchers AT, Chang C, Gershwin ME, Gershwin LJ. Respiratory syncytial virus--a comprehensive review. *Clin Rev Allergy Immunol*. 2013;45(3):331-79. doi:10.1007/s12016-013-8368-9.

19. CDC. Learn about respiratory syncytial virus infection (RSV). Centers for Disease Control and Prevention. Published November 9, 2022. Accessed December 22, 2022. https://www.cdc.gov/rsv/index.html.

20. Corman VM, Lienau J, Witzenrath M. Coronaviren als Ursache respiratorischer Infektionen [Coronaviruses as the cause of respiratory infections]. *Internist (Berl)*. 2019;60(11):1136-1145. German. doi:10.1007/s00108-019-00671-5.

21. WHO Coronavirus (COVID-19) dashboard. Who.int. Accessed December 22, 2022. https://covid19.who.int/.

22. CDC. Coronavirus disease 2019 (COVID-19). Centers for Disease Control and Prevention. Published December 19, 2022. Accessed December 22, 2022. https://www.cdc.gov/dotw/covid-19/index.html.

23. Coronavirus (COVID-19) overview. WebMD. Accessed December 22, 2022. https://www.webmd.com/covid/coronavirus.

24. Clinical overview. Cdc.gov. Published November 23, 2022. Accessed December 22, 2022. https://www.cdc.gov/adenovirus/hcp/clinical-overview.html.

25. Human Parainfluenza viruses (HPIVs). Cdc.gov. Published November 18, 2022. Accessed December 22, 2022. https://www.cdc.gov/parainfluenza/index.html.

26. Human metapneumovirus clinical features - NREVSS. Cdc.gov. Published November 29, 2022. Accessed December 22, 2022. https://www.cdc.gov/surveillance/nrevss/hmpv/clinical.html.

27. Xu M, Perdomo MF, Mattola S, et al. Persistence of Human Bocavirus 1 in tonsillar germinal centers and antibody-dependent enhancement of infection. *MBio*. 2021;12(1). doi:10.1128/mBio.03132-20.

28. Liu Y, Ling L, Wong SH, Wang MH, et al. Outcomes of respiratory viral-bacterial co-infection in adult hospitalized patients. *EClinicalMedicine. 2021;10;37:100955. doi:10.1016/j.eclinm.2021.100955.*

29. Das S, Dunbar S, Tang YW. Laboratory diagnosis of respiratory tract infections in children - the state of the art. *Front Microbiol*. 2018;9:2478. doi:10.3389/fmicb.2018.02478.

30. *Fungal Infections of the Respiratory Tract: Geoff's Essential Microbiology*. 2019.

Rajasri Chandra, MS, MBA is a global marketing leader with expertise in managing upstream, downstream, strategic, tactical, traditional, and digital marketing in biotech, in vitro diagnostics, life sciences, and pharmaceutical industries. Raj is an orchestrator of go-to-market strategies driving complete product life cycle from ideation to commercialization.

Diagnosing upper and lower respiratory tract infections

FEBRUARY 2023 *[This form may be photocopied. It is no longer valid for CEUs after JULY 31, 2025.]*

Passing scores of 70 percent or higher are eligible for 1 contact hour of P.A.C.E. credit.

TEST QUESTIONS

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

1. What is the most common reason why patient visit their physicians?
- A. Urinary tract infections
- B. Ear infections
- C. Respiratory tract infections
- D. Skin infections

2. Upper respiratory tract infections (URIs) have accounted for an estimated _____ outpatient appointments annually.
- A. 1 million
- B. 10 million
- C. 100 million
- D. 10 billion

3. Most cases of URIs are caused by bacteria.
- A. True
- B. False

4. Lower respiratory tract infections (LRIs) include
- A. Tuberculosis
- B. Tuberculosis and pneumonia
- C. Pneumonia, sinusitis, and laryngitis
- D. Pneumonia, tuberculosis, and bronchitis

5. In 2019, LRIs accounted for a total of _____ deaths.
- A. 1.8 million
- B. 2.5 million
- C. 4.2 million
- D. 6.6 million

6. What is/are the cause(s) of LRIs
- A. Bacteria
- B. Fungi
- C. Viruses
- D. All of the above

7. What is the leading cause(s) of upper respiratory tract infections?
- A. Human rhinoviruses
- B. Human enteroviruses
- C. Both A and B
- D. None of the above

8. The common cold accounts for _____ episodes per year in preschool-aged children.
- A. 1 to 3
- B. 3 to 5
- C. 6 to 10
- D. 12 to 15

9. Human rhinoviruses have been shown to be an important cause of superinfections in humans.
- A. True
- B. False

10. In an acute infection in children, human rhinoviruses and human enteroviruses can shed in the nasopharynx for _____ and _____, respectively.
- A. 3 weeks and 6 weeks
- B. 1 week and 4 weeks
- C. 4 weeks and 1 week
- D. 6 weeks and 3 weeks

11. Which serotypes of enterovirus and coxsackie viruses cause hand, foot, and mouth disease?
- A. EV-A71 and CV-A6
- B. EV-D68 and CV-A6
- C. EV-D68 and CV-C26
- D. EV-A71 and CV-A2

12. Acute flaccid myelitis is an uncommon but severe complication that can develop from influenza infection.
- A. True
- B. False

13. Which influenza viruses cause seasonal flu epidemics almost every winter in the United States?
- A. Influenza A and D
- B. Influenza B and C
- C. Influenza C and D
- D. Influenza A and B

14. Which influenza serotype is primarily found in cattle?
- A. A
- B. B
- C. C
- D. D

15. What virus is the most common cause of bronchiolitis and pneumonia in children younger than 1 year of age in the United States?
- A. SARS-CoV-2
- B. RSV
- C. Influenza A
- D. Rhinovirus

16. The variants 229E, NL63, OC43, and HKU1 are the most common worldwide _____.
- A. Influenza viruses
- B. Rhinoviruses
- C. Coronaviruses
- D. Adenoviruses

17. The current SARS-CoV-2 variants include
- A. Alpha, Beta and Gamma
- B. Delta, Omicron and Lambda
- C. Mu and BA.2
- D. All of the above

18. Other respiratory viruses that typically cause mild infection in healthy individuals include
- A. Human adenovirus and Human parainfluenza virus
- B. Human metapneumovirus and Human bocavirus
- C. Both A and B
- D. None of the above

19. There are a number of methods to detect respiratory infections that include
- A. RIA and DFA
- B. Electron microscopy and serological tests
- C. Culture and NAAT
- D. All of the above

20. There are some bacteria that can cause upper and lower respiratory tracts infections and some fungi have been reported in the immunocompromised population.
- A. True
- B. False

Tests can be taken online or by mail. Easy registration and payment options are available through NIU by following the links found at www.mlo-online.com/ce. The certificate is automatically awarded with a passing online test score.

PLEASE PRINT CLEARLY

NAME _____ MAILING ADDRESS _____ ☐ HOME ☐ WORK

CITY _____ STATE _____ ZIP _____ INSTITUTION/FACILITY _____

PHONE _____ E-MAIL ADDRESS _____

Send your $20 check payable to Northern Illinois University with this form to: University Outreach Services, Northern Illinois University, DeKalb, IL 60115-2860
email: outreach_helpdesk@niu.edu. FEE NOT REFUNDABLE OR TRANSFERABLE

P = Poor; E = Excellent

1. **To what extent did the article focus on or clarify the objectives?** P ① ② ③ ④ ⑤ E
2. **To what extent was the article well-organized and readable?** P ① ② ③ ④ ⑤ E
3. **How will you use the CE units?** ☐ state license ☐ employment ☐ recertification ☐ other

CE Licensure Information for FL and CA:

FL: Your FL license number: _____ ***(required for CE credit)***

CA: Accrediting Agency: 0001 ***(for use in submitting your CE credits to CA)***

MLO and Northern Illinois University (NIU), DeKalb, IL, are co-sponsors in offering continuing education units (CEUs) for this issue's CE article. CEUs or contact hours are granted by the College of Health and Human Sciences at Northern Illinois University, which has been approved as a provider of continuing education programs in the clinical laboratory sciences by the ASCLS P.A.C.E.® program. Approval as a provider of continuing education programs has been granted by the state of Florida (Provider No. JP0000496). Continuing education credits awarded for successful completion of this test are acceptable for the ASCP Board of Registry Continuing Competence Recognition Program. Readers who pass the test successfully (scoring 70% or higher) will receive a certificate for 1 contact hour of P.A.C.E.® credit. Participants should allow three to five weeks for receipt of certificate. The fee for this continuing education test is $20. **This test was prepared by Amanda Voelker, MPH, MT(ASCP), MLS, Clinical Education Coordinator, School of Health Studies, Northern Illinois University, DeKalb, IL**

Acute Care Diagnostics

Integrative solutions at the speed of life

When care can't wait, hospitals rely on **Acute Care Diagnostics** from Werfen, a synergistic testing portfolio in point-of-care settings. Our integrative Blood Gas, Whole Blood Hemostasis and Patient Blood Management cartridge-based systems with quality management and connectivity solutions deliver fast, actionable results—simply and efficiently—so you can remain focused on patient care.

Emergency Department | Intensive Care Unit | Cardiac Catheterization Laboratory | Cardiovascular Operating Room

For more information, contact your local Werfen representative or distributor.

werfen.com

*Not Health Canada-licensed. Not available in all countries.

werfen

A healthcare system and its laboratories' experience with Hurricane Ian

By Kara Nadeau

The same week that Category 4 Hurricane Ian made landfall in Florida, researchers from the Center for Climate, Health and the Global Environment, Harvard T.H. Chan School of Public Health in Boston published their systematic assessment of hurricane risk to United States hospital-based healthcare delivery. Published in the October 2022 edition of GeoHealth, the study revealed:[1]

- A total 25 of 78 metropolitan statistical areas (MSAs) on the U.S. Atlantic and Gulf Coasts have half or more of their hospitals at risk of flooding from relatively weak hurricanes.
- The 0.82 m of sea level rise expected within this century from climate change increases the odds of hospital flooding 22%.
- In 18 MSAs, at least half of the roads within 1.6 km of hospitals were at risk of flooding from a Category 2 cyclone.

In their conclusion, they state:"Many cities and healthcare systems in the United States are shoring up resilience to extreme events, but more work is needed…The prospect of more probable and severe hurricane strikes in regions lesser experienced with hurricanes, such as the Northeast, underscores the importance of sharing best practices and standardized approaches to hurricane preparedness and response."

Hurricane Ian, which was the deadliest hurricane to strike Florida since 1935, made landfall on the west coast of the state on September 28, 2022. This was followed by Hurricane Nicole, the first hurricane in 40 years to hit the United States during the month of November, striking Florida's east coast on November 10, 2022. Both caused significant flooding and damage.

All U.S. healthcare organizations have some level of emergency planning procedures required through federal regulations and accreditors, such as The Joint Commission. But were existing procedures adequate for responding to Hurricane Ian, and are hospitals rethinking their preparedness strategies given the devastating impact of Ian?

MLO interviewed Lynn Gott, MHA, MT(ASCP), System Director, Laboratory Services for Lee Health in Southwest Florida, which was in the direct path of Hurricane Ian, on the organization's emergency preparedness plan, which elements were most helpful during the devastating Category 4 storm, and her advice to other lab leaders on both preparing for an emergency and maintaining operations during one.

Preparing for continuous lab coverage

Patients continue to require medical care and lab testing regardless of what is happening outside the four walls of a hospital; therefore, a continuity plan for lab operations is an emergency plan essential.

"Our Lab Hurricane Plan is structured around the Lee Health System Hurricane Response Plan," said Gott. "An Incident Command System is set up for the entire health system to coordinate efforts. Disaster management training is provided for the leadership team and a needs assessment is conducted."

Lee Health's laboratory hurricane plan defines essential staff (those who perform critical patient care and operations functions) as either Team A or Team B (primarily in the acute care settings).

When the Code Brown Hurricane Warning is called by the health system in coordination with the Lee County Emergency Operations Center (EOC), Team A members must report on site at a designated time and remain until the storm has passed and the "all clear" is called.

"Team A is told that they could be deployed as long as 5 days," Gott explained. "They are paid for all hours they are on site, including sleep time (excluding shift differential).

Those individuals assigned to Team B are expected to maintain lab operations prior to the arrival of Team A to allow Team A members to leave work and prepare for the storm (e.g., secure their homes, gather necessary supplies to bring with them such as bedding, snacks, water, etc.). After the "all clear" is called and it is safe to travel, Team B is expected to report into the facility to relieve Team A (preferably within 3 hours).

"Assignment to hurricane teams is voluntary (A or B) whenever possible unless there is not a balance to provide continuous coverage of the lab 24/7 before, during, and after the storm," Gott explained. "This is the responsibility of the lab leaders at each respective location."

Lee Health's Laboratory Hurricane Plan also includes a section to address lab relocation if the lab must evacuate to a safer part of the facility due to flooding or wind. In the event this happens, certain equipment and supplies would be moved to the new temporary lab location in accordance with the Hurricane Relocation Checklist document that is an addendum to the Hurricane Plan. During relocation, lab staff would offer a limited test menu until they return to the lab.

Weathering Hurricane Ian

Lee County, Florida, where Lee Health is based, took a direct hit from Hurricane Ian, resulting in widespread evacuations, more than 50 deaths, and destruction of critical community infrastructure.

"All facilities were placed on lockdown during the storm and all individuals in the facility had to be registered and wear a wristband to keep track of who was in the building," said Gott. "There were frequent department huddles and leadership meetings held during the storm and afterwards to keep everyone informed of what was happening in the facility and across the system."

Severe damage to Lee County's utilities occurred because the storm surge shifted buried water pipes, causing them to crack and develop leaks. The community was without running water because of a water main break, and the extensive work to fix the system and flush it of contaminants meant weeks with low water pressure.

"The evacuation efforts were quite impressive for the facilities that lost water pressure due to a community infrastructure failure from the hurricane," said Gott. "When it came to our response, all efforts were made to ensure continuity of care for our patients during and after the evacuation process.

"We continued to upload the patient's electronic medical record (EMR) with lab results that were still being generated or coming in from reference labs," Gott continued." And in instances when the receiving facility did not use the same EMR, we would fax them the information to continue to provide our patients with high-quality care."

Gott noted how outpatient locations were reopened as soon as possible following the storm to minimize the impact to the community and to keep the emergency departments from becoming overwhelmed.

Lynn Gott, MHA, MT(ASCP). Photo Courtesy of Lee Health.

Supporting staff members

Lee Health leaders prioritized staff member safety and well-being during and after the storm. Team A members were paid continuously, even when sleeping (minus shift differential). In addition, free meals were provided to all staff during the storm, and for a period after the storm from food trucks stationed at each facility.

Gott described how the system provided support to staff who suffered catastrophic loss in multiple ways:

"For example, for Team A staff whose cars were flooded at HealthPark Medical Center and Golisano Children's Hospital and others whose vehicles were damaged while at work during the storm, Lee Health reimbursed them for their out-of-pocket insurance deductible. Leaders were also instructed to identify staff who suffered serious loss so that all resources would be made available to help provide additional support financially and emotionally."

Transportation arrangements were made for staff who had lost their vehicles or were unable to get to work for other reasons. For staff whose departments were shut down temporarily because of the hurricane and for those who couldn't come to work due to hurricane clean-up or other recovery efforts, Lee Health offered continuation pay for a two-week period.

Offering advice to other labs

When asked if Lee Health has made any changes to its emergency plan since the devastation of Ian, Gott stated:

"A deep dive/debrief is still in the works to determine what changes/updates need to be made, if any, to the existing policy/processes," she explained. "That is standard protocol following a storm and it can take a significant amount of time to make sure everything is carefully reviewed and assessed."

When asked for her advice to other lab leaders when preparing for an emergency or maintaining operations during one, Gott offered the following:

- Work closely with the county EOC to coordinate efforts and keep information flowing. There can never be too much communication internally and externally.
- Expect the unexpected. No one anticipated that this storm was going to be as bad as it was.
- Come up with a plan for communication when all traditional means of communication are down. This happens a lot during these storms when LAN lines and cell towers are down and there is no TV or radio to receive news and get messages about what is happening in the area.
- Be as cognizant of the emotional needs of the leaders, staff, and patients as you are of the physical needs, maybe even more so.
- Always debrief and make adjustments in the policies as you gain more experience and encounter new challenges.
- Have resources readily available to employees to help them get through a very difficult and traumatizing event.

Emergency preparedness resources

Hospitals must comply with all applicable federal, state and local emergency preparedness requirements. Here are just some of the resources available to laboratory leaders for information and guidance.

The Clinical and Laboratory Standards Institute (CLSI) GP36, Planning for Laboratory Operations During a Disaster, 1st Edition. Free for a limited time, this electronic document "provides guidance for laboratory and health care leadership for development, implementation, and sustainment of effective emergency preparedness plans (all hazards) supporting nonanalytical components of clinical and public health laboratory services that may pertain to various natural and manmade disasters." https://clsi.org/standards/products/general-laboratory/documents/gp36/

The Joint Commission Emergency Management Standards
These standards apply to all Joint Commission–accredited hospitals and critical access hospitals. They can be accessed through The Joint Commission Emergency Management website, along with webinars offering recommendations for implementing the standards, and answers to frequently asked questions (FAQ). https://www.jointcommission.org/resources/patient-safety-topics/emergency-management/

The "Medicare and Medicaid Programs; Emergency Preparedness Requirements for Medicare and Medicaid Participating Providers and Suppliers" Final Rule (81 FR 63860). This Centers for Medicare & Medicaid Services (CMS) final rule "establishes national emergency preparedness requirements for participating providers and certified suppliers to plan adequately for both natural and man-made disasters, and coordinate with federal, state, tribal, regional and local emergency preparedness systems." It also "assists providers and suppliers to adequately prepare to meet the needs of patients, clients, residents, and participants during disasters and emergency situations, striving to provide consistent requirements across provider and supplier-types, with some variations." som107ap_z_emergprep.pdf (cms.gov)

The Occupational Safety and Health Administration (OSHA) Directorate of Technical Support and Emergency Management (DTSEM)
DTSEM provides "special expertise in a number of areas to ensure that OSHA's capabilities are state-of-the-art with regard to occupational safety and health," including emergency preparedness. Its Emergency Preparedness and Response pages "provide information on how to prepare and train for emergencies and the hazards to be aware of when an emergency occurs," for both employers and workers across industries, as well as workers who will be responding to the emergency. https://www.osha.gov/contactus/byoffice/dtsem

The U.S. Department of Health & Human Services (HHS) Administration for Strategic Preparedness and Response (ASPR) Hospital Preparedness Program (HPP)
HPP "provides leadership and funding through cooperative agreements to states, territories, and eligible major metropolitan areas to increase the ability of HPP funding recipients to plan for and respond to large-scale emergencies and disasters." Its TRACIE Healthcare Emergency Preparedness Information Gateway offers technical assistance and resources for those responsible for health system preparedness. https://aspr.hhs.gov/HealthCareReadiness/HPP/Pages/default.aspx

REFERENCES

1. Tarabochia-Gast AT, Michanowicz DR, Bernstein AS. Flood risk to hospitals on the United States Atlantic and Gulf Coasts from hurricanes and sea level rise. GeoHealth. 2022;6(10):e2022GH000651. doi:10.1029/2022GH000651.

Kara Nadeau, has 20+ years of experience as a healthcare/medical/technology writer, having served medical device and pharmaceutical manufacturers, healthcare facilities, software and service providers, non-profit organizations and industry associations.

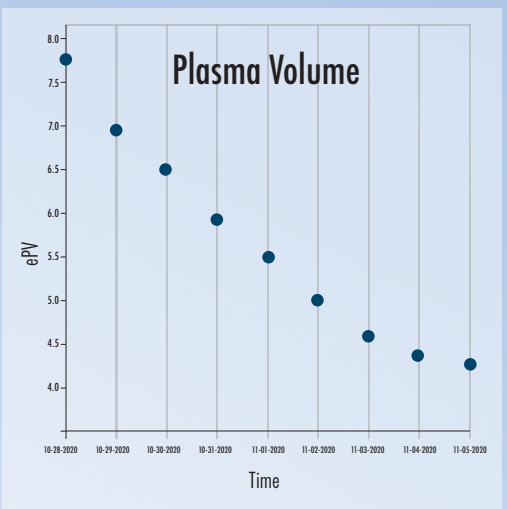
STAT PROFILE Prime+®

Offer Your Clinicians One of the Most Important Critical Care Assays

PLASMA VOLUME

Test Menu:

- pH
- pCO_2
- pO_2
- $SO_2\%$
- Hct
- Hb
- MCHC
- Na
- K
- Cl
- TCO_2
- iCa
- iMg
- GLU
- Lac
- Urea
- Creat
- CO-Ox
- ePV
  Estimated Plasma Volume



Prime Plus screen showing ePV values

Plasma volume status is vital in testing critically ill patients but is extremely difficult and costly to obtain, particularly as a POC test. Plasma volume assessment affects almost every aspect of a patient's care, including giving IV fluids, diuresing, starting vasopressors, initiating renal replacement therapy, deciding on transfusion requirements and intubation and extubation.[1,2]

Nova's Prime Plus® blood gas analyzer automatically calculates patient plasma volume status using the Strauss formula, which requires measured hemoglobin (Hb) and measured hematocrit (Hct) in order to calculate ePV (estimated plasma volume). Prime Plus reports ePV as part of a comprehensive panel including tests for kidney function, electrolytes, metabolites, gases, and acid/base. It also stores prior ePV values and displays them as a patient trend (ΔePV) graph.

1. Kalantari, I et al. Assessment of intravascular volume status and volume responsiveness in critically ill patients. Kidney Int, 2013.83(6): 1017-28.
2. Kobayashi M, Girerd M et al. Estimated plasma volume status in heart failure: clinical implications and future directions. Clinical Research in Cardiology 2021. 110(8):1159-1172.

nova® biomedical
novabiomedical.com

A decade lost to the drug crisis: Toxicology testing magnifies America's misuse

By Jeffrey Gudin, MD

Ten years ago, drug overdoses claimed nearly 42,000 lives annually in the United States.[1] By the end of 2021, that number climbed to nearly 108,000.[2] Today, the drug crisis shows no signs of abating, and remains largely fueled by increased access to illicit drugs as well as barriers to healthcare access exacerbated by the COVID-19 pandemic.

For the last decade, Quest Diagnostics, through its Health Trends program, has examined insights gleaned from results of our large volume of clinical drug tests, with a goal of empowering better patient care, population health management and informing public health policy. Our annual scientific report on prescription drug misuse sadly shows that drug misuse — including potentially dangerous drug mixing — remains prevalent, with patients of all ages and both sexes at risk.[3]

The findings of this year's report, based on a cohort of 20 million deidentified clinical drug tests, reveal the persistence of the prescription and illicit drug crisis. While illicit fentanyl drives most overdose deaths, the misuse of opioids, benzodiazepines, amphetamines and other controlled substances prescribed by a physician is a pressing medical and social concern. In fact, nearly

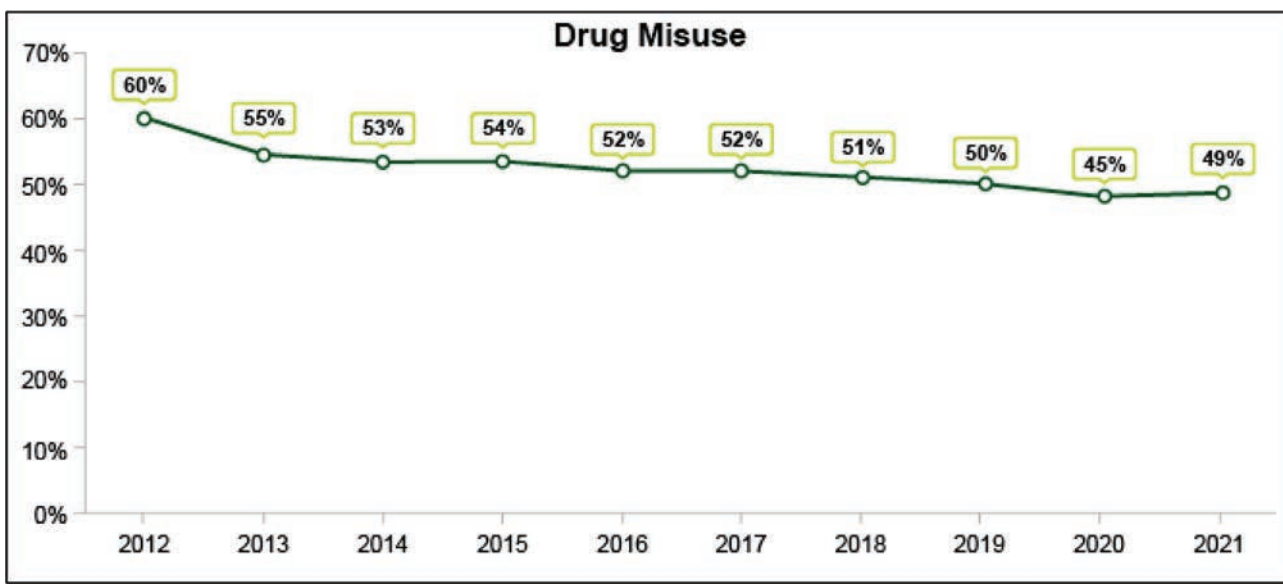


Figure 1. Rate of drug misuse among patients tested by Quest Diagnostics over 10 years.

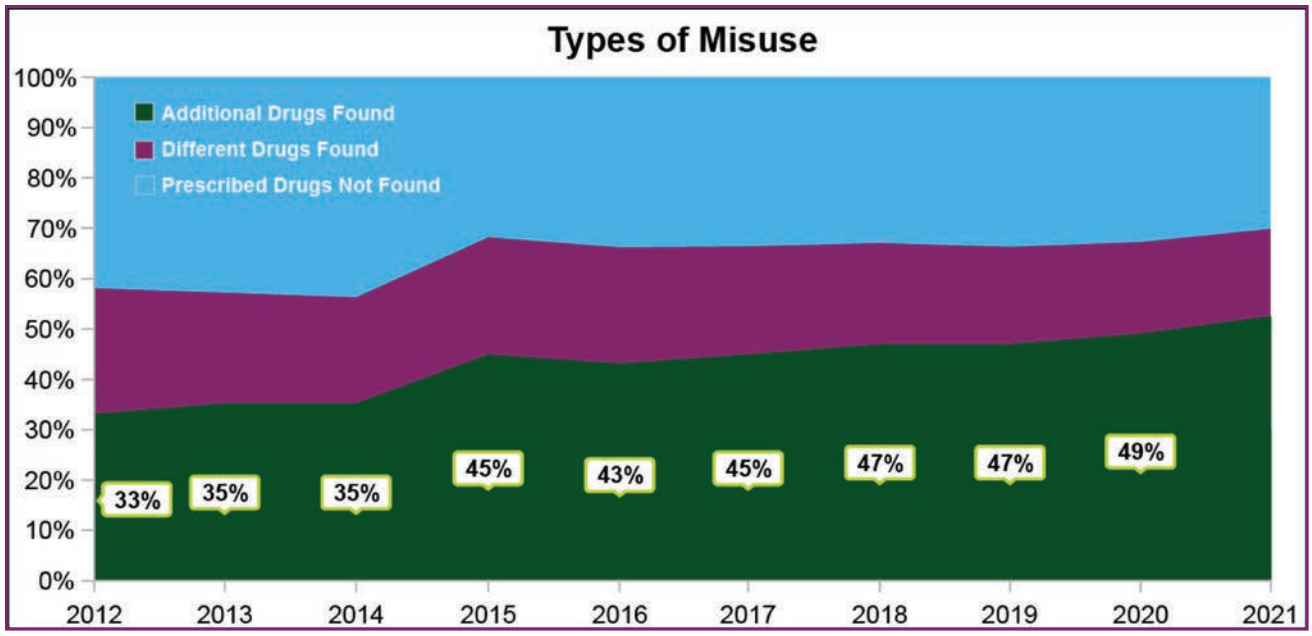


Figure 2. Types of misuse reported by Quest Diagnostics over 10 years.

1 in 4 opioid overdose deaths in 2020 were due to prescription opioids, a 16% increase from 2019.[2]

Data from testing shows a decline of misuse, but an increase in dangerous drug mixing

Throughout the last decade, though recent years have seen a decline in overall misuse, the rate of patients tested by Quest Diagnostics with signs of drug misuse has remained exceedingly high **(Figure 1)**. As of 2021, roughly 1 in 2 patients (49%) generated test results suggesting misuse, i.e., either a) additional drugs were found with the patient's prescribed medication(s); b) different drugs were found than the prescribed medication; or c) no drugs were found (indicating possible diversion).[6]

These data are even more concerning given some test results suggested an increase in the mixing of synthetic fentanyl with other drugs, often without the user's knowledge.[7] Fentanyl is a highly potent synthetic opioid that can depress respiration when combined with other drugs, leading to overdose and death. In 2020, Quest reported a surge in drug combining involving nonprescribed fentanyl with amphetamines, opiates (which also includes opioids), and other drugs during the early months of the pandemic **(Figure 2)**.[8]

The costs of the drug misuse epidemic

While substance use disorder (SUD) creates substantial costs for hospitals and payers ($13.2 billion annually), few hospital patients receive SUD treatment services.[9] But access to these services may abate the need for further treatment down the line, ultimately leading to savings in the overall cost of care. In fact, according to the Centers for Medicare & Medicaid Services, there is "strong evidence that treatment and management of substance use disorders provides substantial cost savings."

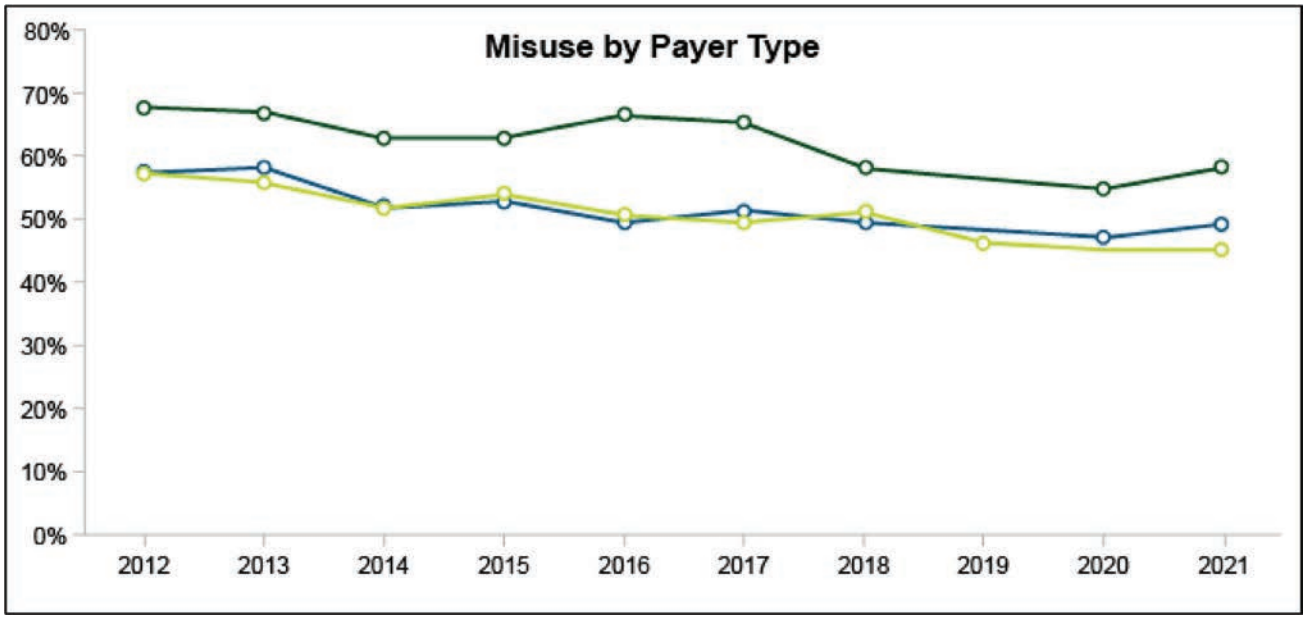


Figure 3. Misuse by payer type, reported by Quest Diagnostics over 10 years.

Drug monitoring's and clinical guidelines' role in the nation's misuse crisis

Over the years, there has been much discussion on whether physicians should employ toxicology testing as part of opioid treatment therapies. Guidelines could be better defined, so understanding physician attitudes towards the role of clinical drug testing in safely prescribing opioids has been critical.

A recent Harris Poll survey of over 500 treating primary care physicians showed, that physicians largely believe clinical drug testing is critical for managing opioids and other prescribed controlled medications, but feel clearer guidelines are needed to help optimize its use. In fact, most (85%) physicians surveyed expressed confidence that testing aids in prescribing safely, and a similar majority (88%) believe better guidelines would help ensure testing is used equitably.

The role of guidelines impacting drug monitoring, and drug monitoring's subsequent role in combatting the nation's drug misuse crisis, is particularly relevant as the U.S. Centers for Disease Control and Prevention (CDC) recently updated its opioid prescribing guidelines to improve the safety and effectiveness of pain care, including with prescription opioids. Among other recommendations, the guidance states that clinicians should consider clinical drug testing (toxicology testing) before starting opioids and periodically (at least annually) during opioid therapy when there is risk of overdose due to mixing with other controlled substances.[4]

In addition, the use of clinical drug testing in chronic opioid therapy is recommended uniformly by medical guidelines, including from the American Pain Society (APS), American Academy of Pain Medicine (AAPM), American Society of Interventional Pain Physicians (ASIPP), American Association for Clinical Chemistry (AACC), and the Federation of State Medical Boards (FSMB). In fact, current clinical practice guidelines from AACC recommend that, in addition to baseline drug testing, testing should be performed throughout the year for patients prescribed controlled substances.[5]

For instance, methadone treatment has been found to generate $4 to $5 in returns on healthcare expenditures for every $1 invested.[10] By an estimate outlined in 2017, the economic costs of the U.S. opioid epidemic, due to healthcare expenses, criminal justice, lost productivity and reduced quality of life, top $1 trillion annually.[11]

Though the drug misuse crisis touches individuals at all walks of life, Quest's data shows patients covered by Medicaid consistently had higher rates of misuse than patients with commercial insurance or enrolled in Medicare **(Figure 3)**. Other research suggests that individuals in Medicaid are comparatively more likely to have risk factors for substance use disorders, such as mental illness and economic disadvantage.[2] Given this data, broadly testing all patients, regardless of individual demographics, may help to reduce bias and diminish stigma around drug monitoring. In fact, in its recently released guidelines, the CDC recommends that "clinicians, practices, and health systems should aim to minimize bias in testing and should not apply this recommendation differentially on the basis of assumptions about patients."[4]

Finally, there has been significant discussion over the years about the need to minimize the use of definitive testing to limit costs, mostly due to a few bad actors in the industry seeking to improperly utilize testing for financial gain. While reducing costs of toxicology testing is a worthwhile goal, and not all patients will require a definitive test, clinical drug testing fits in a larger landscape of patient care, from treatment for substance use disorders to emergency department visits for overdose — some of which toxicology testing may help to avert, as mentioned above.

Though presumptive point-of-care tests are an important tool for clinicians, they are often less sensitive and can miss drugs that definitive lab tests will detect. Recent data shows point-of-care presumptive urine tests may miss about 74% of specimens with fentanyl, as determined by sensitive definitive laboratory tests. These same point-of-care tests were also shown to have missed large percentages of other drugs, including marijuana, amphetamine, methamphetamine, oxycodone, and cocaine.[12] Yet, presumptive tests still have an important role to play, such as for low-risk patients.

Conclusion: Toxicology screening remains an important tool in prevention

It is difficult not to feel hopeless when examining the results of a decade of drug monitoring and the conclusion drawn by the data: that the crisis of prescription and illicit drug use is unlikely to end soon. According to the Quest data, about half of all patients tested showed signs of drug misuse in 2021, roughly the same proportion as ten years ago. On top of this, potentially dangerous drug combining actually rose during the same period.

Much of today's national discourse on the drug crisis focuses on reducing harm in individuals who have already developed a dependency and are at heightened risk of drug combining and overdose, particularly from illicit fentanyl. Policies to encourage early detection and reduce harm in individuals with an established dependency are urgently needed. Yet, in some ways, these measures address the problem too late, after a substance use disorder has already led to serious harm or tragedy.

For many other conditions, such as cancer and heart disease, a preventative care model is widely accepted. Yet, when it comes to preventing drug misuse and substance use disorder, treatment often begins in the back of an ambulance, illustrating just how vital greater attention on the earliest stages of risk is. Data shows a majority of physicians agree: clinical drug testing is the only objective source of insight into a patient's drug use behaviors. These tests act as screenings to provide unbiased insight into potential risk, inform clinical decisions, and preempt the worst outcomes from drug misuse.

But screening for drug misuse is only one part of the solution. Policies must also address the underlying dynamics that

drive some individuals to misuse, like mental health conditions, including anxiety and depression, or social disparities of health, including poverty. Lack of access to healthcare, including mental healthcare, further limits opportunities for intervention.

If the nation wants to mitigate the drug misuse crisis, physicians and policy makers should implement measures to reduce stigma and prevent bias, including with respect to lab testing. Standardization of care may be one way to help reduce physician bias in patient monitoring, clinical drug testing, and treatment decisions — and hopefully, it won't take another ten years of data to convince the country to act.

REFERENCES

1. Multiple cause of death data on CDC WONDER. Cdc.gov. Accessed January 3, 2023. https://wonder.cdc.gov/mcd.html.
2. Saunders H, Rudowitz R. Demographics and health insurance coverage of nonelderly adults with mental illness and substance use disorders in 2020. KFF. Published June 6, 2022. Accessed January 3, 2023. https://www.kff.org/medicaid/issue-brief/demographics-and-health-insurance-coverage-of-nonelderly-adults-with-mental-illness-and-substance-use-disorders-in-2020/.
3. Drug Misuse in America, 2021: Physician Perspectives and Diagnostic Insights on the Drug Crisis and COVID-19. Quest Diagnostics. Published November 2021. Accessed January 3, 2023. https://filecache.mediaroom.com/mr5mr_questdiagnostics/203277/PRUS.COCM.CL.006259_001_Quest_Hazel_PDMSurveyReport_W27.pdf.
4. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95. DOI: http://dx.doi.org/10.15585/mmwr.rr7103a1.
5. Langman LJ, Jannetto PJ. Using Clinical Laboratory Tests to Monitor Drug Therapy in Pain Management Patients at 7. AACC Academy, Laboratory Practice Guidelines. American Association for Clinical Chemistry; 2018.
6. Quest Diagnostics internal drug monitoring data.
7. NIDA. Fentanyl DrugFacts. National Institute on Drug Abuse website. https://nida.nih.gov/publications/drugfacts/fentanyl. June 1, 2021 Accessed January 3, 2023.
8. Niles JK, Gudin J, Radcliff J, Kaufman HW. The Opioid Epidemic Within the COVID-19 Pandemic: Drug Testing in 2020. *Popul Health Manag*. 2021;24(S1):S43-S51. doi:10.1089/pop.2020.0230.
9. Peterson C, Li M, Xu L, Mikosz CA, Luo F. Assessment of Annual Cost of Substance Use Disorder in US Hospitals. *JAMA Netw Open*. 2021;1;4(3):e210242. doi:10.1001/jamanetworkopen.2021.0242.
10. Substance Use Disorders. Medicaid.gov. Accessed January 3, 2023. https://www.medicaid.gov/medicaid/benefits/behavioral-health-services/substance-use-disorders/index.html.
11. Kuehn BM. Massive Costs of the US Opioid Epidemic in Lives and Dollars. *JAMA*. 2021;25;325(20):2040. doi:10.1001/jama.2021.7464.
12. Gudin K, Hilborne E. Edinboro: *PAINWeek Poster Number 30 - Presumptive Versus Definitive Drug Testing: What Are We Missing?*

Jeffrey Gudin, MD, is a senior medical advisor to **Quest Diagnostics** and its Drug Monitoring and Toxicology services arm and faculty member at the University of Miami Miller School of Medicine in the Department of Anesthesiology, Perioperative Medicine and Pain Management. Board certified in pain medicine, anesthesiology, addiction medicine and hospice/palliative medicine, Dr. Gudin is a renowned expert in pain management and opioid and prescription drug misuse and use disorders.

Photo Courtesy of Orchard Software

Leveraging LIS tools to keep your lab inspection-ready

By Kim Futrell, MT(ASCP), MSHI

Though often dreaded, laboratory inspections are an essential process to ensure compliance with state and federal regulations and accreditation requirements. In fact, laboratory professionals and managers spend a significant amount of time ensuring that regulatory requirements are met to achieve accreditation.

The most valuable tool a laboratory has to help with complex accreditation requirements is its laboratory information system (LIS). Today's laboratories require a strong LIS to function efficiently and breeze through the inspection process, as the LIS can track process steps and maintain required records such as operator certifications, quality control, and other documentation required for accreditation surveys.

Importance of documentation to accrediting organizations

Laboratory inspections are overseen by the Centers for Medicare & Medicaid Services' (CMS) against the Clinical Laboratory Improvement Amendments (CLIA), which are regulations that establish quality standards for laboratory testing performed on specimens from humans. Even laboratories classified as waived must comply with applicable CLIA requirements. Laboratories are either inspected by CMS or by an accrediting organization that has been given inspection authority by CMS. There are several CMS-approved accreditation organizations:

- Accreditation Commission for Health Care (ACHC)
- American Association for Laboratory Accreditation (A2LA)
- American Osteopathic Association (AOA)
- American Society of Histocompatibility and Immunogenetics (ASHI)
- Association for the Advancement of Blood & Biotherapies (AABB)
- COLA Inc.
- College of American Pathology (CAP)
- The Joint Commission

Preparing for an inspection is an ongoing process. If your laboratory is documenting properly day to day and leveraging its LIS tools, your lab should sit inspection-ready at all times with no need to rush around at the last minute collecting paperwork for an inspection.

> "Often, the most commonly cited deficiencies involve documentation of activities that can be tracked in some way within the LIS."

Required documentation

Laboratories are required to provide all information and data necessary for CMS (or its accrediting representatives) to determine the laboratory's compliance. All records and data must be accessible and retrievable within a reasonable amount of time during the inspection. A plethora of documentation must be available for an inspector, including:

- Personnel records (education, job descriptions)
- Proficiency testing records
- Training and ongoing competency evaluations
- Procedure manuals
- Reagent, quality control, calibrator storage, and tracking of reagent lot numbers
- Quality control records and Individualized Quality Control Plans (IQCPs)
- Quality assessment activities (corrective actions, annual QA review)
- Instrument calibration, maintenance, and function check records
- Temperature and humidity records
- Test requisitions and report forms
- Incident management plan and reports
- Instrument validation studies (precision, accuracy, linearity, correlations, normal range verification)
- Patient records/test results (critical values, audit trail)

Common deficiencies

Often, the most commonly cited deficiencies involve documentation of activities that can be tracked in some way within the LIS. For example, in 2021, the top cited deficiencies were as follows:

1. Missing documentation of employee competencies (493.1235 - Personnel Competency Assessment)
2. Incomplete monitoring of essential conditions for reagent and specimen storage, accurate and reliable test system operation, and test result reporting (493.1252 - Analytic Systems)
3. Missing verification and documentation (twice annually) of the accuracy of any test or procedure it performs that is not included in subpart I or this part (493.1236 - General Lab Systems)[1]

Each of these requirements can be supported by your LIS. Many commercial LISs today offer personnel competency assessment tracking, documenting and reporting reagent and testing conditions, and documenting test accuracy verification studies.

How the LIS can help

All LISs are not created equal; however, many offer the ability to create and store records and reports for inspection. Below are examples of inspection requirements that your LIS should be able to track and document.

Administrative reports

Data mining tools within the LIS can be tapped to mine patient data and create reports required for inspection (for example, test completion reports, turnaround times, utilization reports, and auto-approval reports). These reports can be set to auto-print at the desired time, pulling data for the specific dates desired.

Audit logs

LIS audit logs can track errors and user actions within the system, including any changes made and who made them. This is important to demonstrate that each step of the testing process is performed per defined procedures and to document which technologist performed each step.

> "Before LISs were commonplace in laboratories, reams of paper were printed every month to comply with inspection requirements, and you had to save all these records for two years."

Quality control

The LIS contains advanced quality control features that track qualitative and quantitative quality control (QC) across testing locations. Quantitative QC can be monitored via Levey-Jennings graphs and Westgard Rules. Integrated logic within the LIS can be used to auto-order QC at the desired frequency and to deny result approval if QC results are not present or are outside of acceptable ranges. Intuitive filters can allow users and inspectors to review numerous QC graphs and accompanying comments without the need for paper printouts. Rules can be established to set up a weekly QC review to meet inspection criteria.

Reagent lot tracking

When lot numbers of QC and testing reagents change, this must be clearly documented so that you can track for each patient sample which lot numbers were in use when that test was run. For some specialties, parallel correlation studies between QC lots are required. An LIS can be used to track usage of reagent lot numbers and document parallel QC lot studies.

Quality assessment

Quality assessment refers to different processes in each laboratory. However, the LIS has many tools that can help with whatever your lab selects for its ongoing QA tracking. For example, the LIS can track and document result discrepancies, incident reports, remedial actions, complaint investigations, analyzer comparisons, and pre-analytical, analytical, and post-analytical errors.

Operator certifications

Some LISs can track personnel competencies and restrict operators who are not up to date on their certification. The LIS can track the due dates so that training and six-month/annual competency dates are not missed. It can be configured to send automated emails to operators when their certification is near expiration. Once certification is complete, the documentation can be scanned and linked to the operator. Some LISs can also link to a learning management system or allow the creation of quizzes, their auto-assignment to operators, and auto-recertification of operators based on lab-defined criteria. With these tools, your competency evaluation process becomes much more automated, which is especially important when you have a large number of end users for point-of-care testing.

Proficiency test reporting and tracking

Handling of proficiency testing (PT) is also reviewed in detail by inspectors. It is extremely important that PT samples are managed exactly the same as patient samples so that they actually "test" the process and operator competency. By using the LIS to track PT samples, you can set up PT just like you set up a patient so there is no question that the PT samples are handled as required. The entire testing process is clearly documented in the LIS. Over time, you can pull up historical PT results just like you would for a patient. And you can ensure that each

lab employee takes their turn performing PT because the LIS automatically documents who does the testing.

Workflow tracking

Inspectors often will ask to "follow" a specimen through your laboratory's processes to verify that each step along the way is properly performed and documented. If your LIS offers a workflow tracking tool or process engine, this tool can allow laboratories to track the status of their testing as it progresses through the analytical phase. Within the tracking tool, transitions between testing statuses can be triggered manually or automatically via various events. This allows the testing for each order to stay on the proper workflow process and ensures real-time status assignment with automated transition triggers.

Sample tracking

Sample tracking in the LIS is helpful for inspection purposes as well. Sample tracking allows laboratories to track the movement of samples through the pre-analytical phase, as well as the storage and disposal of samples in the post-analytical phase. It may include a sample inquiry log that displays the history of the sample as it progresses through its life cycle. Sample tracking features bring overall transparency to the movement of samples through your laboratory's various checkpoints.

Decision-support rules

Configurable decision-support rules are a powerful component of the LIS that allows users to automate processes and reduce errors associated with manual processes. Many areas within the lab can use rules to aid with inspection readiness and ensure consistent execution of procedures. For example, order entry rules can be used to manage test orders, such as splitting an order based on sample handling requirements.

Users can also create sequential test protocols or reflex testing that allows rule conditions to be based on results from previous tests. Additional rules that may be available can allow labs to automate label printing, update CPT codes, automate QC, autoverify "normal" results, and schedule messages that improve communication and workflow.

Lab analyzer and EHR integration

Having interfaces between the LIS and your lab equipment and with your EHRs and reference labs provides a tremendous amount of automation and documentation of test orders and results delivery. In your LIS, inspectors can easily see incoming orders and outgoing results, verify that proper processes are being followed, and ensure that all required information is included on the test reports.

Test report setup

Per CLIA guidelines, the test report must contain the necessary information for positive patient identification, which includes the patient's name and an identification number, the name and address of the laboratory where the test was performed, and a few other requirements specified in 493.1291(c): Post Analytic Systems.[2] These requirements can be automated within your EHR–LIS interfaces.

Record & document retention

Before LISs were commonplace in laboratories, reams of paper were printed every month to comply with inspection requirements, and you had to save all these records for two years. Now, the LIS can basically save an unlimited amount of patient data and laboratory records so that paper is reduced and record retention requirements are easily met.

Summary

To make your lab inspection less stressful, make sure you are using your LIS to its full capabilities. Its role is to make your job easier and less error prone. Consider asking your LIS vendor for a checklist of the features and functionality that your LIS includes that can support your accreditation efforts.

In addition, there may be functionality that the LIS has that your lab team is unaware of, or your LIS vendor may release new features that can improve your inspection readiness, so be sure and take any opportunity available for additional LIS training and learn all that you can about leveraging your LIS's tools to stay inspection ready.

REFERENCES

1. Division of Clinical Laboratory Improvement and Quality Centers for Medicare & Medicaid Services. Year 2021. Top 10 Deficiencies in the Nation – CMS Surveys. Accessed December 22, 2022. https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/cliatopten.pdf.

2. Code of Federal Regulations. § 493.1291 Standard: Test report. Accessed December 22, 2022. https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-G/part-493/subpart-K/subject-group-ECFR9482366886d579f/section-493.1291.

Kim Futrell, MT(ASCP), MSHI is the Senior Strategic Marketing Manager at **Orchard Software.** Prior to joining Orchard in 2012, Futrell, who has a Master of Science in health informatics, worked as a lab manager for more than 20 years.

NEW! Choyce Urine Collection and Transport Containers

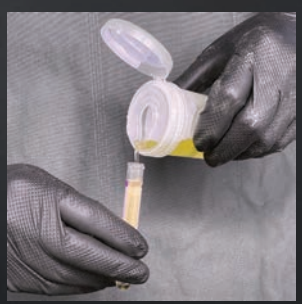
The ultimate innovation for safety and product efficacy!

Choyce **Easy-Hold** Handles and leak resistant containers makes it easier to urinate into the cup and not over your fingers, hands, and floor!

Choyce's unique urine collection and transport container with **recessed needle** and infection control safety lid.

(compatible with BD and Greiner tubes)

Choyce's new **Easy-Pour** offers you a secure, leak-proof container with infection-control lid that allows the lab to easily obtain a sample without removing the cap, consequentially less propensity for spilling urine, and safer diagnosis.



CHOYCE PRODUCTS

For further information and samples, please call or write.

info@choyce-products.com
1 - 8 0 0 - 8 0 3 - 5 9 3 9
www.choyce-products.com

Shifting HIV focus from at-risk populations to at-risk behavior

By Tamar Tchelidze, MD, MPH and Benjamin LaBrot, MD

Since 2015, only about 1.2 million people have been considered 'at risk' of HIV and potentially able to benefit from pre-exposure prophylaxis, also known as PrEP, according to medical literature. These numbers were gleaned by focusing on identifiable populations, such as men who have sex with men and drug users who use needles.

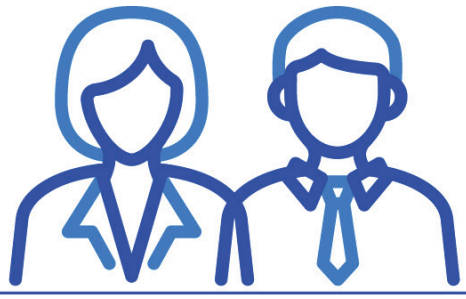
However, the focus on groups of people, rather than on specific behaviors that put people at risk, may cause clinicians considering who might be eligible for HIV screening and PrEP to focus on a particularly narrow population. It could also create a false sense of security to people outside the narrowly defined 'at risk' groups. Additionally, this may perpetuate stigmas against certain groups, and perhaps most alarmingly, may result in a gross underestimation of the number of people who could significantly benefit from HIV screening and protection by PrEP.

Sharing needles is a clear and obvious behavior that creates risk of HIV through direct blood-to-blood contact, of course. But it seems like, 'risk' gets trickier when it comes to sex and risk. The hard reality is that *everyone* of any gender or orientation who has vaginal or anal sex even once is at risk for HIV. Even protected sex carries at least some risk for HIV.

In 1991, a survey found that about 40% of young people considered oral sex to be 'sex,' but by 2007 and again in 2017, similar surveys found that only about 20% viewed oral sex as 'sex.'[1] And when it comes to risk, not all kinds of sex are created equal: the risk of HIV from *receptive* vaginal sex — receiving the penis in the vagina — is almost exactly twice as high as the risk for insertive vaginal sex - inserting the penis in the vagina. The risk of receptive anal sex is almost 13 times greater than receptive vaginal sex, and although insertive anal sex is about 10 times less risky than receptive anal sex, the risk for uncircumcised insertive anal sex is six times greater than for circumcised insertive anal sex.[2]

People who have unprotected receptive vaginal or anal sex are generally at the highest risk of contracting HIV and other sexually transmitted diseases, and unprotected receptive anal sex is the riskiest type of sex overall.[3] However, this example of the complexity of individual risk illustrates how the complex algorithms currently in use for diagnosis and monitoring can further cloud

> "The hard reality is that everyone of any gender or orientation who has vaginal or anal sex even once is at risk for HIV."



Anal Sex Between Women and Men

	2015 - 2017		2017 - 2019	
	Women	Men	Women	Men
Percentage of men and women 15-49 years of age who have ever had anal sex with an opposite-sex partner	32.6%	38.5%	35.1%	38.1%

Source: Special tabulation by National Center for Health Statistics based on Audio Computer-Assisted Self-Interview questions.

a clinician's assessment of what management strategy to pursue.[4]

Heterosexual anal intercourse increases

For a long time, and still today, anal sex was associated most strongly with men who have sex with men. However, heterosexual anal intercourse (HAI) has become much more common with more than three in ten people reporting having HAI. A survey question from the Centers for Disease Control and Prevention's (CDC) National Survey of Family Growth showed that about 38% of women reported they had anal sex with a different sex partner in 2017–2019, compared to 33% in 2015–2017. Men stayed consistent at about 38%. See **Figure 1**.

Women aged 25–29 reported in 2015 to be the population most actively engaging in anal receptive sex in the past month, according to the most recent data available from the 2015 Sexual Exploration in America Study survey.

There are many potential reasons for changes in sexual habits, including more people being open to sexual experimentation, partners seeking to simultaneously avoid pregnancy without contraception, and culturally, some people may feel they are retaining their virginity by engaging in anal sex.

These factors influence the risk paradigm as anal sex is the riskiest type of sex for getting or transmitting HIV.[3] All of this could mean that a sexually abstinent drug user who always uses clean needles and a long-time monogamous gay couple who consistently practice safe sex has less risk of HIV than a heterosexual person who has occasional unprotected casual sex. Assigning risk based on membership in an 'at-risk group' could easily be both inaccurate and stigmatizing.

So, this begs the question—is it the GROUP that is 'at risk?' Or is it specific behaviors that may or may not be practiced by a member of any group, that create a person's individual risk profile?

> "We should encourage broader use of HIV screening and use of the preventative, PrEP, not just for specific populations or 'at risk groups' but for individual patients who engage in specific behaviors that put them at increased risk."

HIV transmission

By HIV transmission category, the annual number of HIV infections in 2019, compared with 2015, decreased among males when transmission was attributed to male-to-male sexual contact, but remained stable among all other transmission categories.[6]

In 2019, the largest percentages of HIV infections were attributed to male-to-male sexual contact, 66% overall and 81% among males. In 2019, among females, the largest percentage of HIV infection was attributed to heterosexual contact at 83%.[6]

Impact on PrEP use

Pre-exposure prophylaxis can reduce the chance of getting HIV from sex or injection drug use. Unfortunately, routinely used diagnostic tests fail to detect early infection, leading to adverse health outcomes, including delayed antiretroviral treatment, the emergence of INSTI resistance, and on-going HIV transmission.[7] Based on this new evidence, the CDC updated the PrEP guidelines to include testing with antigen/antibody (Ag/Ab) and nucleic acid amplification test at every PrEP monitoring visit.[4]

While strides have been made in the use of PrEP, especially from 2015 to 2020,[8] noticeable gaps exist in race, ethnicity and in sex. Black and Hispanic/Latino people account for the majority of people for whom PrEP is recommended, but have the lowest rates of PrEP use among all racial/ethnic groups. PrEP coverage was about three times as high in 2020 among males as among females. Young people ages 16–24 are the least likely to be using PrEP, however, 20% of the new HIV cases are youths 13–24.[9]

The pool of 1.2 million people who, historically, have been eligible for PrEP is quickly dwarfed when you consider the following:

- 1 in 5 HIV-negative (inferred from HCV study) persons who inject drugs has indications for PrEP.[10]
- 1 in 200 HIV-negative heterosexually active adults have indications for PrEP, which seem low as statistically half of them are not using condoms.[11]
- 1 in 4 sexually active HIV-negative adult men who have sex with men have indications for PrEP, which seems low with 70% condomless encounters.[11]
- 1.3 million incarcerated men in the United States.[12]
- 3.6 million people inject drugs.[13]

Perhaps 5 million men between 15–75 would identify as only or predominantly attracted to men, based on an extrapolation of the percentage of men who identify as gay, according to recent Gallup polls, and population estimates.[14,15]


Photo 161495544 © Stepan Khadzhi | Dreamstime.com

What can we do?

To be serious about ending the HIV epidemic, it's critical that everyone who is sexually active know their HIV status, everyone with HIV receive high-quality care and treatment—including an accurate and individualized assessment of their risk profile and counseling about available strategies for protection, including PrEP—and that we end the stigma around HIV and AIDS. These recommendations are similar to those in the National HIV/AIDS Strategy 2022–2025, which has the aim of reducing new HIV transmission by 90% in 2030.[16]

The CDC recommends that everyone between the ages of 13 and 64 get tested for HIV at least once as part of routine healthcare[17] and that anyone who asks for PrEP receives it. Under the *Affordable Care Act*, most new commercial health insurance plans must cover certain recommended preventive services, including HIV testing for everyone 15 to 65 and other ages at increased risk without additional cost-sharing, such as copays or deductibles.[18]

We should encourage broader use of HIV screening and use of the preventative, PrEP, not just for specific populations or `at risk groups' but for individual patients who engage in specific behaviors that put them at increased risk. Healthcare providers need to be willing to engage patients in conversations that really explore risk behaviors, so they can effectively counsel patients on the best ways to protect themselves.

As people who are passionate about public health, we all have a unique role and responsibility, given how vital early and accurate diagnoses are to effectively treating HIV. Ultimately, however, ending the epidemic is not just the job of the doctor, or the government, or nongovernmental organizations…it is everyone's job.

As laboratorians and clinicians, we must also be advocates for changing the paradigm of 'at risk group' to 'at risk patient' and make sure that the people who can actually benefit from PreP are identified and supported.

We agree that HIV should become a forgotten disease. Forgotten because we manage to get it onto the rare diseases list, not because we have failed to maintain enough focus and attention to eradicate the epidemic once and for all.

REFERENCES

1. Miller K. Most young adults: Oral sex is not sex. WebMD. Published April 8, 2010. Accessed December 22, 2022. https://www.webmd.com/sex-relationships/news/20100408/most-young-adults-oral-sex-is-not-sex.

2. Risk of exposure to HIV/AIDS. Stanfordhealthcare.org. Published 2017. Accessed December 22, 2022. https://stanfordhealthcare.org/medical-conditions/sexual-and-reproductive-health/hiv-aids/causes/risk-of-exposure.html.

3. Ways HIV can be transmitted. Cdc.gov. Published March 30, 2022. Accessed December 22, 2022. https://www.cdc.gov/hiv/basics/hiv-transmission/ways-people-get-hiv.html.

4. Cdc.gov. Accessed December 29, 2022. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

5. Herbenick D, Bowling J, Fu TJ, Dodge B, et al. Sexual diversity in the United States: Results from a nationally representative probability sample of adult women and men. *PLoS One*. 2017;20;12(7):e0181198. doi:10.1371/journal.pone.0181198.

6. U.S. Statistics. Hiv.gov. Accessed December 22, 2022. https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics.Eshleman SH, Fogel JM, Halvas EK, Piwowar-Manning E, et al. HIV RNA Screening Reduces Integrase Strand Transfer Inhibitor Resistance Risk in Persons Receiving Long-Acting Cabotegravir for HIV Prevention. *J Infect Dis*. 2022;13;226(12):2170-2180. doi:10.1093/infdis/jiac415.

7. PrEP for HIV Prevention in the U.S. Cdc.gov. Published November 23, 2021. Accessed December 22, 2022. https://www.cdc.gov/nchhstp/newsroom/

fact-sheets/hiv/PrEP-for-hiv-prevention-in-the-US-factsheet.html.

8. Basic statistics. Cdc.gov. Published June 21, 2022. Accessed December 22, 2022. https://www.cdc.gov/hiv/basics/statistics.html.

9. Tassiopoulos K, Bernstein J, Bernstein E. Age and sharing of needle injection equipment in a cohort of Massachusetts injection drug users: an observational study. *Addict Sci Clin Pract.* 2013;13;8(1):20. doi:10.1186/1940-0640-8-20.

10. German D, Nguyen TQ, Ogbue CP, Flynn C. Condomless Anal Intercourse Among Males and Females at High Risk for Heterosexual HIV Infection. *Sex Transm Dis.* 2015;42(6):317-23. doi:10.1097/OLQ.0000000000000275.

11. Correctional populations in the United States, 2013. Bureau of Justice Statistics. Accessed December 22, 2022. https://bjs.ojp.gov/library/publications/correctional-populations-united-states-2013.

12. Bradley H, Hall E, Asher A, Furukawa N, et al. Estimated number of people who inject drugs in the United States. *Clin Infect Dis.* 2022;6:ciac543. doi:10.1093/cid/ciac543.

13. Population of the U.S. by sex and age 2021. Statista. Accessed December 22, 2022. https://www.statista.com/statistics/241488/population-of-the-us-by-sex-and-age/.

14. Newport F. In U.S., estimate of LGBT population rises to 4.5%. Gallup. Published May 22, 2018. Accessed December 22, 2022. https://news.gallup.com/poll/234863/estimate-lgbt-population-rises.aspx.

15. National HIV/AIDS Strategy (2022-2025). Hiv.gov. Accessed December 22, 2022. https://www.hiv.gov/federal-response/national-hiv-aids-strategy/national-hiv-aids-strategy-2022-2025.

16. HIV testing. Cdc.gov. Published June 9, 2022. Accessed December 22, 2022. https://www.cdc.gov/hiv/testing/index.html.

17. The Affordable Care Act and HIV/AIDS. Hiv.gov. Accessed December 22, 2022. https://www.hiv.gov/federal-response/policies-issues/the-affordable-care-act-and-hiv-aids.

Tamar Tchelidze, MD, MPH, is a disease area partner at **Roche Diagnostics.** She has more than 20 years of experience in global health, managing change and transformation and demonstrated agility in academic, private and government environments.

Benjamin LaBrot, MD, is a global medical affairs manager for infection and immunity at **Roche Molecular Diagnostics.** He is a primary care physician who attended the Royal College of Surgeons, Ireland and worked as a hospitalist until founding the Floating Doctors humanitarian medical aid organization in 2009, subsequently practicing for more than 10 years in remote, rural underserved settings in Haiti, Honduras, and Panama.

Importance of hemoglobin A1c testing for diabetes diagnosis and management post-COVID-19 infection

By Thomas Kampfrath, PhD, DABCC, NRCC and Jeanne Rhea-McManus, PhD, MBA, DABCC, NRCC

How does hemoglobin A1c (HbA1c) testing support diabetes care?

The number of people affected by diabetes is expected to grow and may be further increased by the COVID-19 pandemic, as people <18 years of age were shown to be 2.5 times more likely to be diagnosed with diabetes following infection with COVID-19 compared to those without infection.[1] Diabetes mellitus, a group of metabolic disorders affecting glucose metabolism, is derived from the Greek word diabetes (to pass through) and the Latin word *mellitus* (sweet). Approximately one-third of Americans are prediabetic (defined by an HbA1c between 5.7% and 6.4%, fasting plasma glucose [FPG] of 100–125 mg/dL, or a 2-hour plasma glucose of 140–199 mg/dL during an oral glucose tolerance test [OGTT]), and more than 80% are unaware of their increased risk of progressing to diabetes.[2] In 2019, an estimated 11% of the total U.S. population (more than 37 million people) was living with diabetes, while an additional 8.5 million were estimated to have undiagnosed diabetes.[3] On a global scale, these numbers are even more concerning, with 50% of the 500 million people living with diabetes unaware they have the disease.

Diabetes is classified as either diabetes mellitus type 1 (DMT1) or diabetes mellitus type 2 (DMT2). DMT1 accounts for approximately 10% of those who have been diagnosed with diabetes and occurs when autoimmune reactions destroy the insulin-producing beta cells and impair the body's ability to make insulin. In DMT2, formerly known as adult-onset diabetes, the body is unable to use insulin efficiently. Of those diagnosed with diabetes, 90% are classified as having DMT2. Regardless of whether a person has DMT1 or DMT2, glycemic control is critical to avoiding complications of the disease; an estimated 74% of total diabetes expenditures are due to complications such as nephropathy, retinopathy, cardiovascular disease, stroke, peripheral artery disease, etc. Thus, early identification and treatment of the disease can improve health outcomes by avoiding or delaying long-term diabetic complications **(Figure 1)**.[4]

Earlier screening for diabetes and prediabetes now recommended for all adults

In 2022, the American Diabetes Association (ADA) lowered the recommended screening age for prediabetes and dia-

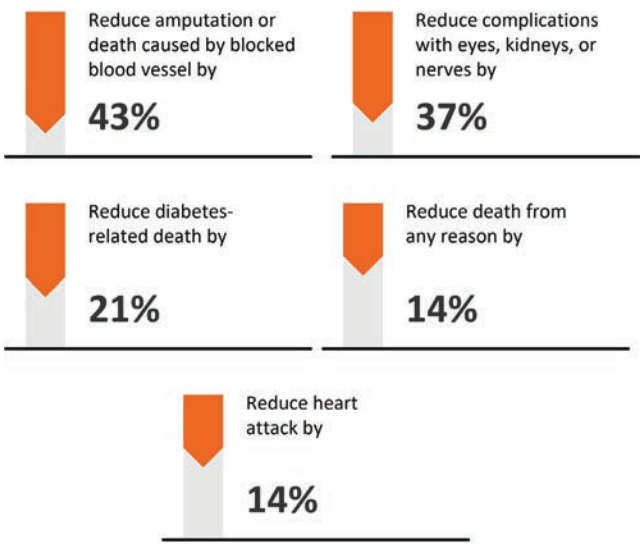


Figure 1. Reducing Hb_{A1c} by just 1% (absolute units) can prevent complications due to diabetes.[4]

betes for all people from 45 years to 35 years.[5] Screening using HbA1c has several advantages over FPG and OGTT, including no requirement to fast, increased analyte stability compared to glucose, and fewer variations due to stress, diet, or illness.[5] While both laboratory and point-of-care–based HbA1c assays can be used in monitoring glycemic control, the ADA recommends that testing for HbA1c should be performed using a method certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay.[5]

The ADA has defined risk-based screening recommendations for DMT2 and prediabetes in both asymptomatic adults and children. In overweight or obese adults (BMI ≥25 kg/m2) who have one or more additional risk factors as defined in **Table 1**, the ADA recommends testing for prediabetes and/or DMT2 regardless of age. The ADA recommends screening for prediabetes and/or type 2 diabetes in all adults beginning at 35 years of age and continuing at 3-year intervals as long as the test results are normal.[5] The importance of screening and potential downstream benefits of improved clinical and other health outcomes have also been recognized in studies where workplace screening programs that include HbA1c have been implemented.[6-8]

Screening should also be considered in children who are overweight (≥85th percentile) and who have one or more additional risk factors as defined in **Table 1**. Children with additional risk factors should be screened and testing repeated at a minimum of 3-year intervals when results are normal. Depending on the initial screening results and risk status of the patient, more frequent testing should be considered.[5]

Why is the COVID-19 pandemic also a risk factor for diabetes?

Diabetes is now known to be one of the major risk factors for the development of severe coronavirus disease 2019 (COVID-19).[9] Not only did the COVID-19 pandemic create challenges for the routine management of diabetic patients, it also made many populations more susceptible to developing diabetes, likely due to a variety of behavioral and lifestyle changes that affected dietary habits and exercise regimens. These include increased consumption of alcohol and sugary foods and decreased access to fresh food. Additionally, many studies have shown that the number of meals, snacking, and unhealthy dietary habits also increased during the pandemic. Furthermore, the closure of gyms and sporting clubs coupled with increased opportunities to work from home led to an overall more sedentary lifestyle due to reduced physical activity.[10]

Beyond lifestyle changes, the effects of the pandemic on diabetes care and management are well-documented, though the full extent of their impact is currently unknown. Lockdowns, social distancing, and quarantines led to a change in healthcare and a dramatic reduction in outpatient visits and laboratory testing.

Asymptomatic Adults
1. Testing should be considered in adults who are overweight or obese (BMI ≥25 kg/m2 or ≥23 kg/m2 in Asian Americans) who have one or more of the following risk factors:
• First-degree relative with diabetes
• High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
• History of cardiovascular disease
• Hypertension (≥140/90 mmHg or on therapy for hypertension)
• HDL cholesterol level <35 mg/dL [0.90 mmol/L] and/or a triglyceride level >250 mg/dL [2.82 mmol/L]
• Individuals with polycystic ovary syndrome
• Physical inactivity
• Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. People with prediabetes (HbA1c ≥5.7% [39 mmol/mol], impaired glucose test or impaired fasting glucose should be tested yearly.
3. People who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other people, testing should begin at age 35 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
6. People with HIV.
Asymptomatic Children and Adolescents
Screening should be considered in youth (defined as after onset of puberty or after 10 years of age, whichever occurs first) who are overweight (≥85th percentile) or obese (≥95th percentile) and who have one or more of the following risk factors:
• Maternal history of diabetes or GDM during the child's gestation
• Family history of DMT2 in a first- or second-degree relative
• Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander)
• Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)

Table 1. Criteria for screening for diabetes or prediabetes (adapted from ADA's Standards of Care in Diabetes).

> "Clinical studies suggest that COVID-19 is not only a lung disease, but also affects other organs such as the brain, heart, kidneys, gastrointestinal tract, and endocrine organs."

These factors contributed to gaps in diabetes management, such as significant reductions in testing for HbA1c, ultimately leading to missed or delayed diagnosis of diabetes and poor glucose control.[9]

Clinical studies suggest that COVID-19 is not only a lung disease, but also affects other organs such as the brain, heart, kidneys, gastrointestinal tract, and endocrine organs.[11] Another link between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and diabetes is suggested by the ability of the virus to infect cells of the human exocrine and endocrine pancreas.[11] The pancreatic localization of SARS-CoV-2 may lead to a dysregulation of cytokines and a proinflammatory environment that promotes an abnormal glucose metabolism.[12]

In summary, individual behavioral changes during the pandemic coupled with prior COVID-19 infections may have made many in the general population more prone to developing prediabetes and diabetes; many in this scenario likely remained undiagnosed. Therefore, it is critical to enhance access to diabetes screening and care by delivering a public health message that emphasizes the importance of diabetes diagnosis and management, with a focus on the younger adult population.[9]

Strengthening HbA1c surveillance programs increases population health

Diabetes is an important public health threat and one of the most common illnesses worldwide, with more than 500 million people affected, and its prevalence continues to rise. Use of available screening tests that detect the disorder in early asymptomatic stages enables the initiation of treatment and prevention efforts to improve long-term outcomes. HbA1c testing is an effective approach to identify asymptomatic patients with ongoing hyperglycemia. Patients often perceive HbA1c testing as more convenient than fasting blood glucose analysis, with no timing or dietary restrictions to be considered. A variety of automated laboratory-based methods are available for the large-scale analysis of HbA1c in patient samples using different analytical methodologies. Point-of-care HbA1c assays have also been shown to increase patient compliance for monitoring glycemic control, as they provide timely results and can be conveniently performed during a doctor visit.[13] In addition, point-of-care HbA1c testing provides the opportunity for informed decision making regarding treatment plans and/or changes while the patient is still in the physician's office.[14] Together, both traditional and point-of-care HbA1c testing are important tools for effective and reliable diagnosis, monitoring, and management of diabetes, with the long-term goal of preventing serious and costly diabetes-related complications.

REFERENCES

1. Barrett CE, Koyama AK, Alvarez P, et al. Risk for Newly Diagnosed Diabetes >30 Days After SARS-CoV-2 Infection Among Persons Aged <18 Years - United States, March 1, 2020-June 28, 2021. *MMWR Morb Mortal Wkly Rep.* Jan 14 2022;71(2):59-65. doi:10.15585/mmwr.mm7102e2.

2. CDC. Prediabetes - your chance to prevent type 2 diabetes. Centers for Disease Control and Prevention. Published March 2, 2022. Accessed December 21, 2022. https://www.cdc.gov/diabetes/basics/prediabetes.html.

3. Prevalence of both diagnosed and undiagnosed diabetes. Cdc.gov. Published September 21, 2022. Accessed December 21, 2022. https://www.cdc.gov/diabetes/data/statistics-report/diagnosed-undiagnosed-diabetes.html.

4. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 2000;12;321(7258):405-12. doi:10.1136/bmj.321.7258.405.

5. American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022;1;45(Suppl 1):S17-S38. doi:10.2337/dc22-S002.

6. Bali V, Yermilov I, Koyama A, Legorreta AP. Secondary prevention of diabetes through workplace health screening. *Occup Med (Lond).* 2018;26;68(9):610-616. doi:10.1093/occmed/kqy138.

7. Tarride JE, Smofsky A, Nykoliation P, et al. Effectiveness of a Type 2 Diabetes Screening Intervention in the Canadian Workplace. *Can J Diabetes.* 2018;42(5):493-499 e1. doi:10.1016/j.jcjd.2017.12.008.

8. Wang Y, Buchholz SW, Murphy M, Moss AM. A Diabetes Screening and Education Program for Chinese American Food Service Employees Delivered in Chinese. *Workplace Health Saf.* 2019;67(5):209-217. doi:10.1177/2165079918823218.

9. Czeisler ME, Barrett CE, Siegel KR, et al. Health Care Access and Use Among Adults with Diabetes During the COVID-19 Pandemic - United States, February-March 2021. *MMWR Morb Mortal Wkly Rep.* 2021;19;70(46):1597-1602. doi:10.15585/mmwr.mm7046a2.

10. Bennett G, Young E, Butler I, Coe S. The Impact of Lockdown During the COVID-19 Outbreak on Dietary Habits in Various Population Groups: A Scoping Review. *Front Nutr.* 2021;4;8:626432. doi:10.3389/fnut.2021.626432.

11. Muller JA, Gross R, Conzelmann C, et al. SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. *Nat Metab.* 2021;3(2):149-165. doi:10.1038/s42255-021-00347-1.

12. Ben Nasr M, D'Addio F, Montefusco L, et al. Indirect and Direct Effects of SARS-CoV-2 on Human Pancreatic Islets. *Diabetes.* 2022;1 ;71(7):1579-1590. doi:10.2337/db21-0926.

13. Whitley HP, Hanson C, Parton JM. Systematic Diabetes Screening Using Point-of-Care HbA(1c) Testing Facilitates Identification of Prediabetes. *Ann Fam Med.* 2017;15(2):162-164. doi:10.1370/afm.2035.

14. Schnell O, Crocker JB, Weng J. Impact of HbA1c Testing at Point of Care on Diabetes Management. *J Diabetes Sci Technol.* 2017;11(3):611-617. doi:10.1177/1932296816678263.

Dr. Thomas Kampfrath, PhD, DABCC, NRCC is a board-certified clinical chemist and medical officer for **Siemens Healthineers.**

Jeanne Rhea-McManus, PhD, MBA, DABCC, NRCC has been with **Siemens Healthineers** for eight years, previously as a Medical Officer and currently as the Sr Director of Medical Science Information and Communication.

MEDICAL LABORATORY OBSERVER

MLO Continuing Education Made Simple

COMPLETE YOUR CONTINUING EDUCATION HOURS ONLINE!

Take the monthly test online for immediate certification or download the printable test from www.mlo-online.com/ce

(Mail-in tests may take up to 6 weeks to score.)

The CE articles and accompanying CE tests remain online until the indicated deadlines have passed.

Completed tests and fees go directly to Northern Illinois University (NIU), and scores of 70% and higher qualify for one contact hour of P.A.C.E. credit.

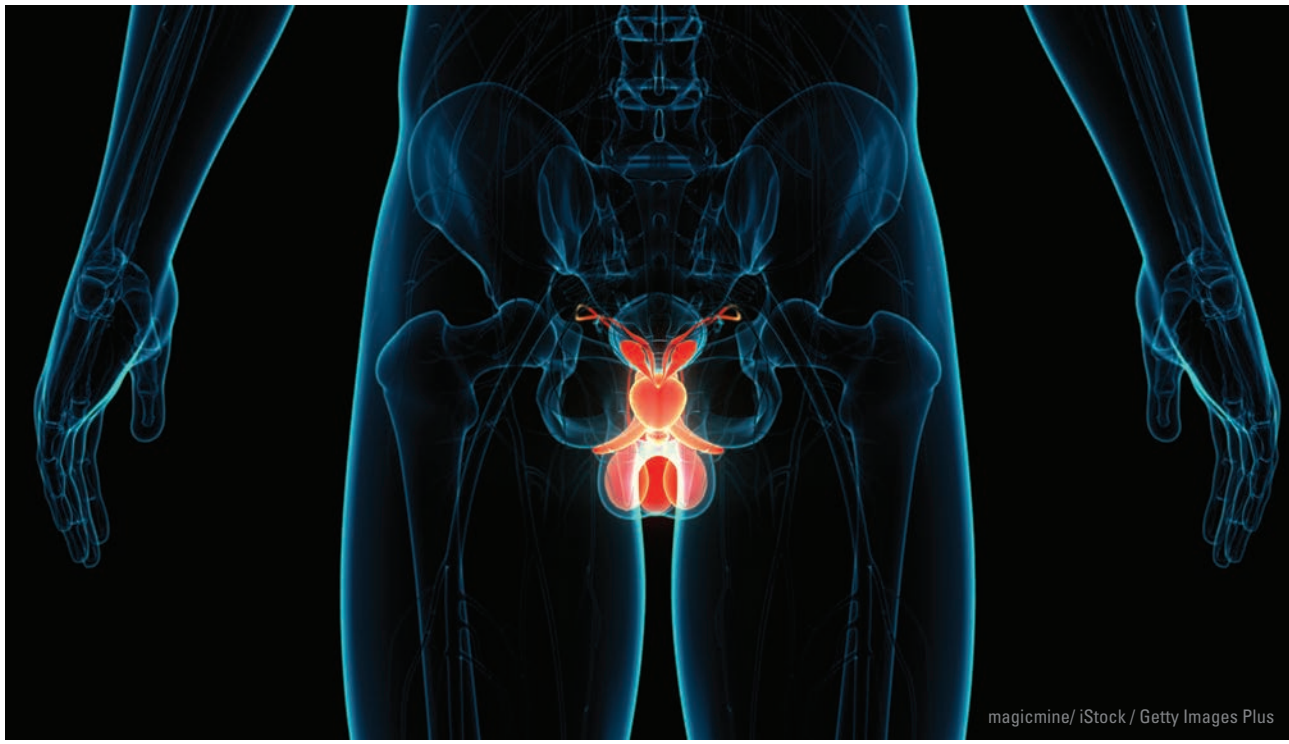
Easy registration and payment options are available through NIU by following the link found at www.mlo-online.com/ce

MLO and NIU DeKalb, IL, are co-sponsors in offering continuing education units (CEUs) for each issue's CE article. CEUs or contact hours are granted by the College of Health and Human Sciences at Northern Illinois University, which has been approved as a provider of continuing education programs in the clinical laboratory sciences by the ASCLS P.A.C.E.® program. Approval as a provider of continuing education programs has been granted by the state of Florida (Provider No. JP0000496). Continuing education credits awarded for successful completion of this test are acceptable for the ASCP Board of Registry Continuing Competence Recognition Program.

NIU

NORTHERN ILLINOIS UNIVERSITY

College of Health and Human Sciences



magicmine/ iStock / Getty Images Plus

Optimal testing methods for early prostate cancer detection

By John Sylvester, MD

Prostate cancer is one of the most common forms of cancer. According to estimates by the American Cancer Society, there will be 268,490 new cases of prostate cancer in 2022 along with 34,500 deaths.[1] These are staggering numbers that show just how common the disease is among American men.

While these numbers are concerning, there is a silver lining: the 15-year relative survival rate is 95 percent.[2] This is due in large part to an uptick in early detection and new treatment options.

How early detection works in practice

The number one way to detect prostate cancer in its early stages is a prostate-specific antigen (PSA) blood test. It is no coincidence that the prostate cancer death rate began to decline when the PSA test was introduced in the mid-1980s and early 1990s.[3]

Conversely, when the number of screenings declined during the COVID-19 pandemic, the number of patients diagnosed with high-risk or metastatic disease increased significantly. There has been some debate over this, but recent data seems to show at least a correlation between the decline in the PSA screening rates and an increase in advanced-stage prostate cancer diagnoses.[4]

Just recently, prostate-specific membrane antigen (PSMA) PET imaging emerged as the most effective and precise method for localizing metastatic prostate cancer. This PET imaging measures PSA levels as well but does so in a highly targeted manner that significantly improves how prostate cancer is detected and treated. Although these scans require machinery not yet available across the country, PSMA PET imaging is the best option to detect areas of suspected metastasis for initial therapy and suspected recurrence.

Holding off on a PSA screening or rectal examination can be a big mistake. Typically, this occurs because a patient isn't experiencing symptoms like urinary problems, obstruction, and/or bleeding. As a general rule of thumb, patients should start with an annual PSA screening at the age of 50. But if a patient has risk factors, such as a family history of prostate cancer or is of African American heritage, it is best to start regular screenings by age 40 at the latest.

Diagnosis and the importance of a second opinion

A prostate cancer diagnosis is sure to turn a person's life upside down. With so many questions and concerns, one of the biggest challenges faced is information overload.

In most cases, prostate cancer is diagnosed by a urologist, and in many cases, surgery is offered as the first option. While a diagnosis allows a patient to immediately proceed with treatment, it's all too common for patients to get ahead of themselves.

For newly diagnosed patients, a second opinion is recommended. While a urologist may suggest the prostate be removed as soon as possible, that is not always the best approach. Data shows patients are more likely to experience serious side effects from a surgical procedure, but a radiation oncologist who specializes in prostate cancer may be able to provide treatment other than surgery depending on the patient's unique circumstances. In fact, a randomized trial

> "Genetic (genomic) testing paired with a holistic view of a patient's lifestyleand health history can reduce the uncertainty of initial treatment decisions."

focused on early-stage disease concluded that radiation is equally effective while having significantly fewer serious side effects compared to surgery.[5] Furthermore, patients may end up needing radiation to address any cells that were left behind post-surgery anyways.

Thus, external beam radiation can be effective on its own, as a study published in *JAMA* concluded that in very high-risk patients combining it with brachytherapy provides a 30% better chance of preventing localized cancer from metastasizing.[6]

Prostate cancer testing

A prostate cancer diagnosis is serious, but doctors should not scare patients into making a rushed decision before additional tests are scheduled. For example, genetic testing on the biopsy specimen will determine how aggressive the disease is and help the patient's medical team determine the most appropriate treatment program. This contrasts with the more widely employed process of viewing tissue samples from the prostate biopsy under a microscope for cell abnormalities that are a sign of prostate cancer. If cell abnormalities are present, judgment calls are made on how likely the cancer will progress and the best treatment options.

The most exciting advancement happening right now regarding the treatment of prostate cancer is individualized therapy, with genetic testing at the forefront of this process. Genetic (genomic) testing paired with a holistic view of a patient's lifestyle and health history can reduce the uncertainty of initial treatment decisions. By taking more of the individual's genetic and lifestyle factors into account, a more aggressive treatment may be deemed necessary, which could result in a higher chance of survival.

Conversely, some patients may believe they have an aggressive form of prostate cancer but learn through genetic testing this isn't the case. This helps prevent overtreatment and ensures the highest quality of life possible for patients.

In closing

Patients should get an opinion from both a surgeon and a radiation oncologist before making a decision on how to treat newly diagnosed prostate cancer. It is worth noting that once the prostate is removed, treatment options become far more limited.

New tests for genomic evaluation of the cancer cells and high-quality imaging such as T3 MRI and PSMA pet scans are making a real positive impact in treatment outcomes and men's lives. Prostate cancer treatment is rapidly changing, so staying up to date on the latest research and collaborating with other physicians is the best way to facilitate a positive outcome for your patients. That is something we can all get behind.

REFERENCES

1. Key statistics for prostate cancer. Cancer.org. Accessed January 3, 2023. https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html.
2. Prostate cancer prognosis. Hopkinsmedicine.org. Published August 8, 2021. Accessed January 3, 2023. https://www.hopkinsmedicine.org/health/conditions-and-diseases/prostate-cancer/prostate-cancer-prognosis.
3. Zhou CK, Check DP, Lortet-Tieulent J, et al. Prostate cancer incidence in 43 populations worldwide: An analysis of time trends overall and by age group. *Int J Cancer.* 2016;138(6):1388-1400. doi:10.1002/ijc.29894.
4. Norton A. Did the Decline in PSA Testing Lead to More Cases of Advanced Prostate Cancer? U.S. News & World Report. Published October 28, 2022. Accessed January 3, 2023. https://www.usnews.com/news/health-news/articles/2022-10-28/did-the-decline-in-psa-testing-lead-to-more-cases-of-advanced-prostate-cancer.
5. Donovan JL, Hamdy FC, Lane JA, et al. Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. *N Engl J Med.* 2016;375(15):1425-1437. doi:10.1056/nejmoa1606221.
6. Kishan AU, Steigler A, Denham JW, et al. Interplay Between Duration of Androgen Deprivation Therapy and External Beam Radiotherapy with or Without a Brachytherapy Boost for Optimal Treatment of High-risk Prostate Cancer: A Patient-Level Data Analysis of 3 Cohorts. *JAMA Oncol.* 2022;8(3):e216871. doi:10.1001/jamaoncol.2021.6871.

John Sylvester, MD, Radiation Oncologist for **GenesisCare** has performed over 6,000 prostate brachytherapy procedures. He has developed multiple technical improvements in the procedure, by improving visualization of the urethra during the procedure, optimally utilizing R.A.P.I.D. strand, and co-developed THINStrand. He has published numerous articles and medical textbook chapters on prostate brachytherapy and co-authored and edited The Prostate Cancer Treatment Book. He publishes prostate cancer research papers every year and regularly lectures at the National Radiation Oncology Society Medical Conferences.

Charles K. Cooper, MD
Chief Medical Officer
Siemens Healthcare Diagnostics,
Siemens Healthineers

Readers' questions answered

Do you know if there are criteria for acceptable analytical performance, such as "Target value ± 0.4 mg/dL or ± 20% (greater)", for plasma free hemoglobin?

Much of the answer to this question depends on a few things and how the quality goals are set, i.e., what is acceptable clinically. In other words, what is the effect of the analytical performance on clinical outcomes and what can be tolerated analytically when knowing what is acceptable clinically. What is the biologic variability? What is state of the art? Often, no simple answer can be given for these questions, and many variables and additional questions can come into play when attempting to answer them. Ultimately, laboratories are responsible for setting their own acceptable analytical performance criteria. Frequently, acceptable proficiency testing (PT) limits (via CAP or other deemed agencies) are used for total allowable error (TEa) if they are available and/or if there is not enough existing information, time, or knowledge to inform other ways of figuring it out.

Here is an AACC article that speaks to the topic a bit: https://www.aacc.org/cln/articles/2021/december/total-allowable-error-tea-how-much-error-can-your-laboratory-allow. The accepted practice for understanding and determining acceptable analytical performance in clinical laboratories is referred to Allowable Total Error (or Total Allowable Error). There are a multitude of publications and sources on this topic as well as lists of defined TEa for various analytes with the accompanying info sources (an example: http://rmbiolab.com/UpFiles/Documents/808edaad-0fb5-4412-9235-2921bf9e8b62.pdf). These sources provide information on how to do the calculations, considerations for different analytes and methods, and how to interpret the results. Regarding free hemoglobin, the information above should provide some ideas on how to approach it but certainly, at a minimum, you would need to understand the capabilities or the particular method used in relation to the needs of the clinical application.

How long is a urine specimen in a cup viable to perform a urine analysis, keeping in mind that a culture is reflexed when necessary? We are inspected by The Joint Commission and need correct information. The lab manager says 4 hours, citing no references; the chemistry supervisor says 24 hours citing no reference. I say it is 2 hours and my reference is the abstract from The National Library of Medicine "Preanalytical requirements of urinalysis" Published online 2014 Feb 15. doi: 10.11613/BM.2014.011.

Do you have a different opinion? If so, can you please cite a reference?

Thank you for this excellent question. Pre-analytical errors account for approximately 70% of all errors in laboratory diagnostics.[1] Urine culture is no exception. Urine specimen collection, storage, and preservation significantly affect culture results and thus can negatively impact the diagnosis of urinary tract infections. Improperly collected or preserved specimens can become easily contaminated with bacteria from the periurethral, perineal, and vaginal flora, which can overgrow and mask the presence of true urinary tract pathogens. Perhaps the best resource on this topic is an excellent review published by LaRocco et al, in *Clinical Microbiology Reviews* in 2016.[2]

Based on an extensive review of the literature, LaRocco, et al determined that the combination of boric acid and refrigeration (4 to 10°C) is likely able to adequately preserve urine specimens prior to their processing for up to 24 hours. Additionally, the authors found that urine held at room temperature for more than 4 hours significantly increases risk of bacterial overgrowth of both clinically significant and contaminating microorganisms. However, it is worth noting that the overall strength of evidence was not high indicating a need for future systematic studies evaluating the utility of these measures. Urine specimens should include sufficient information indicating both the methodology of collection (i.e., clean catch, catheterization, and so forth) as well as the timing to allow for an informed determination of adequacy and the possibility of contamination.

REFERENCES

1. Lippi G, Chance JJ, Church S, et al. Preanalytical quality improvement: from dream to reality. *Clin Chem Lab Med.* 2011;49(7). doi:10.1515/cclm.2011.600.

2. LaRocco MT, Franek J, Leibach EK, et al. Effectiveness of preanalytic practices on contamination and diagnostic accuracy of urine cultures: A Laboratory Medicine Best Practices systematic review and meta-analysis. *Clin Microbiol Rev.* 2016;29(1):105-147. doi:10.1128/CMR.00030-15.

Leave fecal WBC smears behind

The LEUKO EZ VUE is an immunochromatographic test for the qualitative detection of elevated levels of fecal lactoferrin, a marker for fecal leukocytes and an indicator of intestinal inflammation. The LEUKO EZ VUE test detects lactoferrin in liquid, semi-liquid, and solid fecal specimens, providing results in 10 minutes.

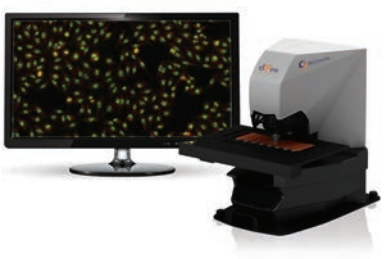
TECHLAB

Focus on the positives

dIFine* is the next generation in indirect fluorescent antibody (IFA) imaging and pattern recognition with an automated digital microscope and intelligent software designed to acquire, analyze, display and store digital images of ZEUS IFA slides. Now, you can increase your lab's productivity by easily screening out negative IFA samples.

Zeus Scientific

*FDA 510(k) cleared. All suggested results obtained with ZEUS dIFine must be confirmed by a trained operator.



Immunoassay

Elecsys Anti-HCV II immunoassay is used for the qualitative in vitro determination of antibodies against HCV. Results, in conjunction with other clinical information, may be used to aid in presumptive diagnosis of HCV infection in persons with signs and symptoms of hepatitis and persons at risk for hepatitis C Infection.

Roche Diagnostics

INDEX OF ADVERTISERS

Advertiser	Web	Page
Abbott Rapid Diagnostics Informatics	rals.com	3
Choyce Products	choyce-products.com	27
CLSI/Clinical Laboratory Standards Institute	clsi.org/gap-analysis	23
Health Care Logistics	GoHCL.com	37
Hologic Total Health	hologic.com/CMVInfections	5
Hologic Total Health	Hologic.com	C2-1
Indigo BioAutomation	indigobio.com/arq	26
Kamiya Biomedical Company	k-assay.com	31
Nova Biomedical	novabiomedical.com	19
Quidel	quidel.com	11
Sysmex America	sysmex.com/us	C4
Werfen (Instrumentation Laboratory) - Acute Care	werfen.com	15
Werfen (Instrumentation Laboratory) - Hemostasis	werfen.com	C3

LABORATORY INNOVATOR

A leader in clinical laboratory consulting

By Christina Wichmann

Philip D. Cotter, PhD, FACMG, FFSC (RCPA) is a Principal and Co-Founder of **ResearchDx**, and the Laboratory Director of **PacificDx Clinical Laboratory**, Irvine, California, a subsidiary of ResearchDx. Dr. Cotter has nearly thirty years' experience in the clinical laboratory industry, as a clinical laboratory director and consultant. He is an A2LA assessor with extensive experience in clinical laboratory regulatory issues; application of new technologies; and clinical laboratory management. He has published extensively in the field of medical genetics and related disciplines. His previous experience includes Vice President and Laboratory Director at Biocept Inc. in San Diego, Laboratory Director at the Illumina Clinical Services Laboratory in San Diego, Laboratory Director at Combimatrix Molecular Diagnostics in Irvine, Director of Molecular Cytogenetics at the Mount Sinai School of Medicine in New York, Director of Cytogenetics and Molecular Genetics at the Children's Hospital and Research Center in Oakland CA, Director of Advanced Molecular Diagnostics at US Labs in Irvine, Laboratory Director at Genuity Sciences in Dublin, Ireland and Laboratory Director of the WuXi AppTec Central Laboratories and Sequanta Technologies in Shanghai, China.

Dr. Cotter received his doctorate in Biomedical Sciences from the Department of Human Genetics at the Mount Sinai School of Medicine in New York. He is Board Certified by the American Board of Medical Genetics and Genomics in Clinical Cytogenetics and Clinical Molecular Genetics, former Associate Clinical Professor of Pediatrics at the University of California San Francisco, a Fellow of the American College of Medical Genetics and Genomics, and a Fellow of the Faculty of Science Royal College of Pathologists of Australasia.

Your company, ResearchDx, provides clinical laboratory consulting services. What are common issues that the consulting services help labs with?

We assist laboratories in preparing for regulatory audits and in maintaining quality systems compliance. Services might include providing a quality management system, managing the regulatory applications and audits, validation design or ongoing compliance.

The common theme in all our services is in assisting clients to meet compliance in what can be a confusing regulatory environment. Navigating the requirements of multiple jurisdictions, federal (CLIA), state licensure, out-of-state licensure, FDA, accreditation agencies, and international standards are our specialty. This is particularly the case for our international clients looking to meet U.S. regulatory standards.

Are there particular lessons learned that you can share through your experiences as a lab director and an A2LA assessor?

Good preparation, an understanding of the requirements, and good documentation are all essential. I have been on both sides of the audit agenda; as an audited laboratory and as the assessor. What has impressed me about A2LA accreditation is that the process is consistent and transparent, there is a dedicated accreditation manager, and the ISO15189 standard takes a more holistic approach to the organization at large, not just the clinical laboratory.

What do you think the future holds for personalized medicine in the next 5–10 years?

With any new paradigm, reality takes some time to catch up with the rhetoric. There are clearly successes to date, but I anticipate a more widespread application and adoption of the concept in the years to come. While oncology has seen the biggest adoption of companion diagnostics in the personalized medicine space, ResearchDx in its assay development services is seeing a wider range of applications across multiple additional specialties. The next decade will see a much more widespread adoption and implementation of personalized medicine and companion diagnostics.

If the VALID Act (S. 2209 and H.R. 4128) for laboratory-developed tests passes, what are some of the changes a lab-developed test process will experience?

In the event that the VALID Act passes, there will be an increase in the regulatory burden on new clinical laboratory assays, particularly for validation and approval. There are varied opinions as to the merits of the VALID Act and the alternative, more CMS-centric VITAL Act. Any resolution to the turf war between CMS and FDA would be desirable. Regardless of the outcome, if there is clarity on the requirements then that removes the current uncertainty in the industry and provides a clear path forward.

You have had a long career in the clinical laboratory field. What advice can you share on career longevity?

Always keep learning! As regulations change and new technologies are introduced, it's important to keep up to date and be adaptable. As the pace of change increases, it's even more important to keep learning.

Hemostasis Innovation is Here.

HemosIL® ASSAYS

- Liquid, ready-to-use
- Superior stability
- Fast, reliable results

Always one step ahead.

Enhance efficiency with our robust liquid, ready-to-use reagents. Central to Werfen's total Hemostasis testing solution, our comprehensive line of HemosIL reagents deliver superior onboard stability and fewer manual steps—from routine to specialty testing. Other key components include ACL TOP® Family 50 Series systems with automated pre-analytical sample integrity checks, and HemoCell Specialized Lab Automation, designed specifically for the automation of Hemostasis testing. Rely on HemosIL reagents for improved laboratory efficiency—for better patient care.

Simply efficient.

For more information, contact your local Werfen representative.

werfen.com

werfen

sysmex | Lighting the way with diagnostics

Simplicity and reliability behind every sample

XN-L Series™ Automated Hematology Analyzers

At Sysmex, we're committed to improving patients' lives — and making yours easier. Every sample run on our analyzers is backed by our dedicated team of experts. Sysmex has simplified the complex processes of QC and calibration, making our analyzers easy to use and simplifying documentation and compliance for labs. For over 50 years, we have been innovating diagnostics, reducing downtime and helping lab professionals focus on the results that contribute to healthier lives.

imv Part of Science and Medicine Group
HEMATOLOGY
ServiceTrak™
2020 2021
2021 BEST SYSTEM PERFORMANCE WINNER:
Sysmex America, Inc.

SYSMEX HAS BEEN RATED HIGHEST IN RELIABILITY, SERVICE AND CUSTOMER SATISFACTION FOR THE PAST 22 YEARS.*

www.sysmex.com/us