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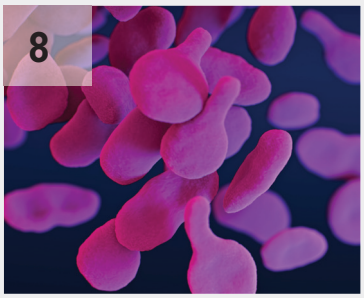

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COVID-19 – Testing, treating and transmission

By Brenda Silva
Senior Editor

Every day more facts and figures about COVID-19 are being published, along with updated forecasts and best guesses of when the world might return to a sense of normal life.

Recent COVID-19-related statistics show – courtesy of Johns Hopkins' Dashboard tracker – the countries that were affected the worst by the virus initially are now starting to show improvement by way of lower numbers of confirmed cases and deaths. As this happens, the rest of the world is carefully watching these countries and hoping for a similar timeframe until their own statistics improve. One factor that is cause for concern, however, is the possibility of reinfection, which has the potential to further impact countries that lack the medical and clinical ability to sustain a second wave of infection.

With the arrival of COVID-19 in the United States, government agencies such as the CDC, FDA and WHO asserted rapid tests and fast results were needed in order to confirm and quarantine suspected cases of the virus as it became a pandemic. The clinical lab industry took this request to heart, with many diagnostics companies diverting key scientific staff members from current projects to COVID-19 test development.

The result of this "call to action" for COVID-19 tests, as per the FDA's website, is more than 270 test developers who plan to submit Emergency Use Authorization (EUA) requests to the FDA, and a notification that more than 150 labs have already begun testing per policies set forth by the FDA. As of April 8, there were 32 EUAs issued for diagnostic tests. In this issue of *MLO*, you can find a table on page 34 that lists all tests approved for EUA by the FDA.

As with many diseases, screening and regular testing can lead to earlier treatments and a better prognosis. As COVID-19 testing ramped up in the U.S, only patients with a host of symptoms present were being tested. That process was complicated by long test results times and asymptomatic patients who continued to circulate in public, shedding the disease.

However, with the advent of drive-thru testing sites, as well as RT-PCR and serology tests that are identifying cases that were not confirmed prior, COVID-19 is being detected earlier in many suspected cases. The earlier confirmation helps limit exposure by quarantining confirmed cases to prevent additional spreading of the disease.

As diagnostics companies work to develop more tests that offer almost-immediate results that can confirm or refute COVID-19 infection, we remain focused on the number of confirmed cases in our cities and wait for the day that this coronavirus is a thing of the past. Until then, I encourage everyone to continue to take appropriate safety precautions – both at home and at work – to protect yourself and your families.

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

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

Senior Editor
Brenda Silva
bsilva@mlo-online.com

Managing Editor
Linda Wilson
lwilson@mlo-online.com

Graphic Artist
Patti Connors
pconnors@endeavorb2b.com

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

Ad Traffic Manager
Norma Machado
nmachado@endeavorb2b.com

eProduct Coordinator
Mary Haberstroh
mhaberstroh@endeavorb2b.com

ADVERTISING

East Coast/Midwest Sales (except IL)
Classified/Recruitment Advertising
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2477 Stickney Point Rd., Suite 221B Sarasota, FL 34231
Phone: (941) 388-7050 Fax: (941) 388-7490
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† Number of actual test results per day may vary based on individual lab practices and workflows.

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Fast Facts COVID-19

The novel coronavirus (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), continues to cause severe illness and death, straining health systems and supply chains, upending daily life and pummeling the global economy.

18%

Share of COVID-19 tests in the U.S. with positive test results.

32*

The number of test kits from diagnostics manufacturers and commercial labs to detect COVID-19 with FDA Emergency Use Authorization

6*

The number of high-complexity molecular lab-developed tests for COVID-19 with FDA Emergency Use Authorization

5*

The number of serological tests to detect immune response to COVID-19

5-10

The number of people with undetected cases of COVID-19 for every confirmed case.

41%

Share of U.S. adult population at higher risk for illness if infected with COVID-19.

86%

The percentage of people with confirmed cases of COVID-19 in China who were infected by people with an undetected case of the disease.

150-plus*

Number of labs that are testing for SARS-CoV-2, the virus that causes COVID-19

Sources:

- https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations
- https://www.kff.org/health-costs/issue-brief/state-data-and-policy-actions-to-address-coronavirus/#policyactions
- https://www.kff.org/health-costs/issue-brief/state-data-and-policy-actions-to-address-coronavirus/#socialdistancing
- https://directorsblog.nih.gov/2020/03/19/to-beat-covid-19-social-distancing-is-a-must/
- https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-april-9-2020

***As of April 10, 2020**

FDA provides guidance to address the need for blood donations

The Food and Drug Administration (FDA) issued new policies to address the need for blood and blood components.

"The COVID-19 pandemic has caused unprecedented challenges to the U.S. blood supply. Donor centers have experienced a dramatic reduction in donations due to the implementation of social distancing and the cancellation of blood drives," the FDA said in a news release.

Based on recently completed studies and epidemiologic data, the FDA said it has concluded that "current policies regarding certain donor eligibility criteria can be modified without compromising the safety of the blood supply."

As a result, the FDA is revising recommendations in three guidance documents about blood donor eligibility. The FDA said it expects the changes, which are effective immediately, to remain in place after the COVID-19 pandemic ends.

Among others, the FDA said it is making the following changes, for immediate implementation, to the December 2015 guidance, "Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products":

- For male donors who would have been deferred for having sex with another man, the agency is changing the recommended deferral period from 12 months to three months.
- For female donors who would have been deferred for having sex with a man who had sex with another man, the agency is changing the recommended deferral period from 12 months to three months.
- For those with recent tattoos and piercings, the agency is changing the recommended deferral period from 12 months to three months.

The FDA also is making changes to the 2013 guidance, "Recommendations to Reduce the Risk of Transfusion-Transmitted Malaria." For those who have traveled to malaria-endemic areas (and are residents of malaria non-endemic countries), the agency is changing the recommended deferral period for blood donations from 12 months to three months. In addition, the guidance provides a notice of an alternate procedure that permits the collection of blood and blood components from such donors without a deferral period provided that the blood components are pathogen-reduced using an FDA-approved pathogen reduction device.

The FDA also said it is finalizing the January 2020 draft guidance, "Recommendations to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease by Blood and Blood Components." The final guidance includes a policy change for travelers and military personnel returning from Europe. Specifically, the FDA said that for people who spent time in certain European countries or on military bases in Europe who were previously considered to have been exposed to a potential risk of transmission of Creutzfeldt-Jakob Disease or Variant Creutzfeldt-Jakob Disease, the agency is eliminating the recommended deferrals and is recommending allowing reentry of these donors.

FDA updates recommendations for human cell or tissue-based products

The Food and Drug Administration (FDA) does not recommend testing asymptomatic donors of human, cells, tissues or other cellular or tissue-based product (HCT/P) for COVID-19, the agency said in a press release.

Noting that routine screening measures are already in place for evaluating clinical evidence of infection in HCT/P donors, the agency said that SARS-CoV-2 has only been detected in blood samples of a small percentage of severely ill patients.

The agency also said it is aware that some HCT/P establishments in the United States are considering additional donor screening and testing measures in response to the COVID-19 outbreak.

The FDA said an HCT/P establishment should evaluate whether a donor in the 28 days prior to the HCT/P procedure:

- Cared for, lived with, or otherwise had close contact with individuals diagnosed with or suspected of having COVID-19 infection; or
- Been diagnosed with or suspected of having a COVID-19 infection.

"While respiratory viruses, in general, are not known to be transmitted by implantation, transplantation, infusion, or transfer of human cells, tissues, or cellular or tissue-based products (HCT/Ps), the potential for transmission of COVID-19 by HCT/Ps is unknown at this time. There have been no reported cases of transmission of COVID-19 via these products," the FDA said.

Hospitals to report COVID-19 test data daily to the federal government

The Centers for Medicare & Medicaid Services (CMS) sent a letter to the nation's hospitals, detailing how they should report data on tests they are performing to detect COVID-19, the agency said in a press release. The letter was sent on behalf of Vice President Mike Pence.

Specifically, the federal government wants hospitals to report daily data on COVID-19 test results conducted at in-house labs to both the Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network. CMS said the data should not include personal identifying information to protect patients' privacy.

"The nation's nearly 4,700 hospitals have access to testing data that's updated daily. This data will help us better support hospitals to address their supply and capacity needs, as well as strengthen our surveillance efforts across the country," said CMS Administrator Seema Verma.

CMS said the White House Coronavirus Task Force is collecting data from public health labs and private laboratory companies.

NIH clinical trial of vaccine for COVID-19 begins

A Phase 1 clinical trial evaluating an investigational vaccine designed to protect against coronavirus disease 2019 (COVID-19) has begun at Kaiser Permanente Washington Health Research Institute (KPWHRI) in Seattle.

The National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, is funding the trial. KPWHRI is part of NIAID's Infectious Diseases Clinical Research Consortium.

The open-label trial will enroll 45 healthy adult volunteers ages 18 to 55 years over approximately six weeks. The first participant received the investigational vaccine on March 16.

The study is evaluating different doses of the experimental vaccine for safety and its ability to induce an immune response in participants. This is the first of multiple steps in the clinical trial process for evaluating the potential benefit of the vaccine.

The vaccine is called mRNA-1273 and was developed by NIAID scientists and their collaborators at the biotechnology company Moderna, based in Cambridge, MA. The Coalition for Epidemic Preparedness Innovations (CEPI) supported the manufacturing of the vaccine candidate for the Phase 1 clinical trial.

The investigational vaccine was developed using a genetic platform called mRNA (messenger RNA). The investigational vaccine directs the body's cells to express a virus protein that researchers hope will elicit a robust immune response. The mRNA-1273 vaccine has shown promise in animal models, and this is the first trial to examine it in humans.

Study participants will receive two doses of the vaccine via intramuscular injection in the upper arm approximately 28 days apart. Each participant will be assigned to receive a 25-microgram (mcg), 100-mcg or 250-mcg dose at both vaccinations, with 15 people in each dose cohort. The first four participants will receive one injection with the low dose, and the next four participants will receive the 100-mcg dose. Investigators will review safety data before vaccinating the remaining participants in the 25- and 100-mcg dose groups and before participants receive their second vaccinations. Another safety review will be done before participants are enrolled in the 250-mcg cohort.

Modeling study suggests 18 months of COVID-19 social distancing

A new modeling study on likely United States and United Kingdom outcomes during the COVID-19 pandemic, published by a team of epidemiologists at the Imperial College of London, which used pandemic data gathered in China, Italy and South Korea, has been lauded by epidemiologists around the world as the most comprehensive prediction of what the U.S. could be facing in the coming months. But it also paints some bleak pictures, including millions of deaths if little is done.

The model analyzes the two approaches to managing the virus. One is mitigation, or "flattening the curve," which sees the novel coronavirus continue to spread, but at a slow rate so as not to overwhelm hospital systems.

The other approach is suppression, which tries to reverse the pandemic through extreme social distancing measures and home quarantines of cases and their families, achieving an R0—or reproduction number—of less than 1.

But suppression requires social distancing measures far longer than the 14 to 30 days Americans have been told to prepare for. Instead, they would need to be in place for 18 months, or until a vaccine is made available.

To understand how mitigation or suppression would play out, the Imperial College team, led by Neil Ferguson, OBE, ran a model based on three scenarios. In the first, U.S. officials do nothing to mitigate the spread of COVID-19, schools and businesses are kept open, and the virus is allowed to move through the population.

This would result in 81 percent of the U.S. population, about 264 million people, contracting the disease. Of those, 2.2 million would die, including 4-8 percent of Americans over age 70. More important, by the second week in April, the demand for critical care beds would be 30 times greater than supply.

If mitigation practices are put in place, including a combination of case isolation, home quarantine and social distancing of those most at risk (over age 70), the peak critical care demand would reduce by 60 percent, and there would be half the number of deaths. But this scenario still produces an eightfold demand on critical care beds above surge capacity.

In order to suppress the pandemic to an R0 of below 1, a country would need to combine case isolation, social distancing of the entire population, and either household quarantine or school and university closure, the authors found. These measures "are assumed to be in place for a five-month duration," they wrote.

In addition, the authors said, these measures may have to be put back into place if restrictions are lifted and cases surge again.

Assay addresses *M genitalium* diagnostic abilities

By Charlotte Gaydos, MS, MPH, DrPH, F(AAM)

Sexually transmitted infections (STI) with the bacteria *Mycoplasma genitalium* are a generally under-recognized health concern due to inherent difficulties in detecting the organism.[1] Historical estimates of *M genitalium* prevalence in men and women in population-based surveillance studies from Australia, Scandinavia, the United Kingdom and United States range from 1 percent to 3 percent.[2-5] Development of a highly sensitive nucleic acid amplification test (NAAT) enabled a large U.S. multicenter study to demonstrate overall *M genitalium* prevalence rates of 16.1 percent in women and 17.2 percent in men, suggesting that infection rates were much higher in populations attending STI and other medical clinics.[6]

In that study, *M genitalium* prevalence was reported to be higher in symptomatic vs asymptomatic subjects (women, 21.1 percent vs 7.5 percent; men, 19.3 percent vs 15.4 percent). Infection rates are also elevated in high-risk populations such as patients presenting to sexual health clinics or men with nongonococcal urethritis.[7] *M genitalium* is now understood to be one of the most common causes of STIs such that in 2015, the Centers for Disease Control and Prevention (CDC) declared *M genitalium* STIs to be an emerging health concern.[8-11]

The role of *Mycoplasma genitalium*

Although *M genitalium* infections can also be found in the respiratory tract, the most clinically important infections are sexually transmitted and occur in the urogenital tract, causing urethritis in men and cervicitis in women.[12,13] Untreated or persistent *M genitalium* infections have been reported to cause complications in men such as reactive arthritis and epididymoorchitis.[14] Studies have reported complications of *M genitalium* infections in women including nongonococcal urethritis, bacterial vaginosis and vaginitis, endometritis, salpingitis and pelvic inflammatory disease (PID). *M genitalium*, as detected by NAAT technology, has been frequently reported among women with PID, with infection rates ranging from 13 percent to 16 percent.[15,16]

Among 125 women diagnosed with acute PID in the ACE Trial, a randomized double-blind study evaluating therapy for acute PID, 22 percent (n = 27) tested positive for *M genitalium*, whereas *C trachomatis* (CT), *N gonorrhoeae* (NG) and bacterial vaginosis were present in 14 percent, 7 percent, and 54 percent of women with acute PID, respectively.[17] These results illustrate the important role that *M genitalium* tentatively plays in the pathogenesis of PID, and suggest that *M genitalium* may possibly be an underlying cause of infertility, preterm delivery and spontaneous abortion observed in women with PID.[6,18,19]

In a study where *C trachomatis* and *N gonorrhoeae* infections in women were accompanied by *M genitalium* infection, the authors concluded that *C trachomatis* and *N gonorrhoeae* infection increased the risk for *M genitalium* infection.[7] Infection with *M genitalium* has been demonstrated to increase the risk for HIV infection and transmission, as well as infections with high-risk human papilloma virus (HPV).[20]

Distinguishing *Mycoplasma genitalium* infections from other STIs

As with STIs in general, *M genitalium* infections are predominantly asymptomatic, contributing to a lack of clinical recognition.[18] Among patients with symptomatic STI, symptoms of *C trachomatis, N gonorrhoeae*, gonococcal and *M genitalium* infections are difficult to differentiate, often leading to misdiagnosis of the specific underlying bacterial infection. A lack of testing and poor testing sensitivity has also impeded adequate diagnosis of *M genitalium*.[1]

First-line treatment for *M genitalium* infection is azithromycin; however, resistance of *M genitalium* to this antibiotic is growing. A dose of azithromycin to treat *C trachomatis* may be insufficient to clear *M genitalium* and may engender *M genitalium* resistance to this macrolide antibiotic.[14] Worldwide *M genitalium* macrolide resistance rates are estimated at 30-100 percent, depending on the country.[7]

Accurate diagnosis of *M genitalium* and antibiotic susceptibility are imperative for appropriate and adequate treatment.[1,21] The absence of Food and Drug Administration (FDA)-cleared diagnostic tests for *M genitalium* prior to 2019 prevented performance of routine testing, leading to missed diagnoses and inappropriately treated or untreated infections, which raised the risk for persistent infections with adverse outcomes.

FDA-cleared *Mycoplasma genitalium* assays – a recent step forward

Numerous factors intrinsic to the *M genitalium* organism contribute to the difficulty in diagnosing this infection. *M*

Earning CEUs

See test on page 14 or online at www.mlo-online.com under the CE Tests tab.

LEARNING OBJECTIVES

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

1. Recognize the historical facts and symptoms of *M. genitalium.*
2. Recall underlying conditions and complications that develop as a result of *M. genitalium* in men and women.
3. Recall difficulties in the detection and diagnosis of *M. genitalium.*
4. Discuss the AMES study in terms of prevalence, detection and findings.

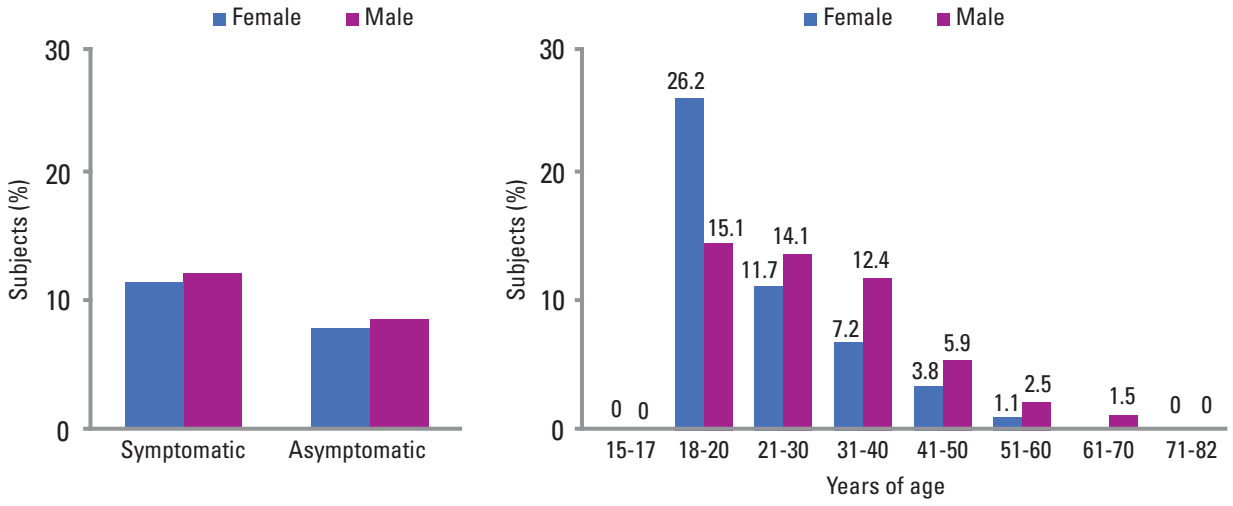

Figure 1. *Mycoplasma genitalium* prevalence by subject symptomology and age.

genitalium is the smallest known self-replicating prokaryote, with a genome size of 580 kb that encodes less than 500 genes.[1,13] The bacterium grows slowly in culture, exhibiting fastidious nutrient and culturing requirements that are prohibitive for routine detection by microscopy.[13] In addition, the *M genitalium* bacterium lacks a cell wall and cannot be visualized in a Gram stain of genital secretions.[7]

Nonfeasibility of routine in vitro culturing for *M genitalium* detection has necessitated the use of more-sensitive NAATs to identify the bacteria. Use of an NAAT is now the CDC-recommended detection method for *M genitalium*.[8] Despite the higher sensitivity of NAATs, *M genitalium* infections have low organism loads and each bacterium has only a single copy of the small *M genitalium* genome, which together limits DNA-based NAAT detection methods.[13,21] Alternatively, each *M genitalium* bacterium contains 100–1,000 copies of 16S ribosomal RNA (rRNA), making this nucleic acid molecule an attractive amplification target for organism detection.

An FDA-cleared, transcription-mediated amplification (TMA) NAAT targets a specific region of the *M genitalium* 16S rRNA for amplification and subsequent detection.[1] The assay has been validated against a composite reference standard for *M genitalium* using other TMA NAATs that amplify different regions of *M genitalium* rRNA.[22] This FDA-cleared assay has been used in research settings to study the epidemiology of *M genitalium*[1] and was recently clinically validated in the AMES Prospective Multicenter Clinical Study.[23] The assay was the first FDA-cleared diagnostic test for *M genitalium.* Recently, another NAAT assay for the detection of *M genitalium* was approved for the cobas 6800 and 8800 systems from Roche Diagnostics.[24]

AMES prospective multicenter clinical study

The AMES Study was conducted to validate the performance of an investigational in vitro diagnostic TMA NAAT for detection of *M genitalium.*[23] In all, 3,393 subjects (1,789 female and 1,604 male) were enrolled from 21 U.S. sites, including clinical research centers, emergency

Specimen Type	No.	Prevalence, %	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	PLR (95% CI)	NLR (95% CI)
Clinician-collected vaginal swab	1709	10.2	92.0 (86.9-95.1)	98.0 (97.2-98.6)	84.2 (79.1-88.6)	99.1 (98.5-99.5)	47.0 (33.4-68.8)	0.08 (0.05-0.13)
Patient-collected vaginal swab	1724	10.2	98.9 (95.9-99.7)	98.5 (97.7-99.0)	87.8 (83.1-91.7)	99.9 (99.5-100)	63.8 (43.4-97.9)	0.01 (0.00-0.04)
Endocervical swab	1715	10.1	81.5 (75.1-86.6)	98.3 (97.5-98.8)	84.4 (78.9-89.1)	97.9 (97.2-98.5)	48.3 (33.3-72.7)	0.19 (0.13-0.25)
Female urine	1773	10.2	77.8 (71.1-83.3)	99.0 (98.3-99.4)	89.5 (84.3-93.6)	97.5 (96.8-98.2)	75.8 (47.5-128.6)	0.22 (0.017-0.29
Male urethral swab	1563	10.6	98.2 (94.8-99.4)	99.6 (99.1-99.8)	96.4 (92.7-98.6)	99.8 (99.4-100)	228.8 (106.8-605.2)	0.02 (0.00-0.05)
Penile meatal swab	1554	10.6	88.4 (82.6-92.5)	97.8 (96.9-98.5)	82.9 (77.4-87.6)	98.6 (97.9-99.1)	40.9 (29.0-59.8)	0.12 (0.07-0.18)
Male urine	1559	10.5	90.9 (85.5-94.4)	99.4 (98.8-99.7)	94.3 (90.0-97.2)	98.9 (98.3-99.4)	140.8 (76.2-294.7)	0.09 (0.05-0.15)

CI, confidence interval; NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

Table 1. Clinical performance characteristics of investigational *Mycoplasma genitalium* assay.

M. genitalium Prevalence					
		Female		Male	
Category	No. of specimens	No. positive/ total no.	% positive (95% CI)	No. positive/ total no.	% positive (95%CI)
Subject age (yr)					
15-17	4	0/3	0 (0.0-56.1)	0/1	0 (0.0-79.3)
18-20	242	39/149	26.2 (19.8-33.8)	14/93	15.1 (9.2-23.7)
21-30	1379	94/805	11.7 (9.6-14.1)	81/574	14.1 (11.5-17.2)
31-40	929	36/500	7.2 (5.2-9.8)	53/429	12.4 (9.6-15.8)
41-50	345	6/157	3.8 (1.8-8.1)	11/188	5.9 (3.3-10.2)
51-60	298	1/94	1.1 (0.2-5.8)	5/204	2.5 (1.1-5.6)
61-70	90	0/25	0 (0.0-13.3)	1/65	1.5 (0.3-8.2)
71-82	13	0/4	0 (0.0-49.0)	0/9	0 (0.0-29.9)
All Females (15-74)	1737	176/1737	10.1 (8.8-11.6)	-	-
All Males (16-82)	1563	-	-	165/1563	10.6 (9.1-12.2)
Symptom statusa					
Symptomatic	1919	122/1053	11.6 (9.8-13.7)	104/866	12.0 (10.0-14.3)
Asymptomatic	1381	54/684	7.9 (6.1-10.2)	61/697	8.8 (6.9-11.1)
Subject race/ethnicityb					
Asian	47	5/29	17.2 (7.6-34.5)	0/18	0 (0.0-17.6)
Black	2025	127/1059	12.0 (10.2-14.1)	125/966	12.9 (11.0-15.2)
White	1131	40/591	6.8 (5.0-9.1)	37/540	6.9 (5.0-9.3)
Unknown/other race	146	6/79	7.6 (3.5-15.6)	6/67	9.0 (4.2-18.2)
Hispanic	720	23/381	6.0 (4.1-8.9)	23/339	6.8 (4.6-10.0)
Non-Hispanic	2556	151/1347	11.2 (9.6-13.0)	140/1209	11.6 (9.9-13.5)
Unknown ethnicity	24	2/9	22.2 (6.3-54.7)	2/15	13.3 (3.7-37.9)
U.S. Geographic Areac					
Mid-Atlantic	260	16/142	11.3 (7.1-17.5)	13/118	11.0 (6.6-17.9)
Midwest	288	23/190	12.1 (8.2-17.5)	14/98	14.3 (8.7-22.6)
Northeast	225	13/106	12.3 (7.3-19.9)	11/119	9.2 (5.2-15.8)
Northwest	65	0/12	0 (0.0-24.2)	3/53	5.7 (1.9-15.4)
Southeast	1424	72/703	10.2 (8.2-12.7)	84/721	11.7 (9.5-14.2)
Southwest	1038	52/584	8.9 (6.9-11.5)	40/454	8.8 (6.5-11.8)

aSymptom status was determined based on subject-reported symptoms
bSubjects could report multiple responses.
cMid-Atlantic: Maryland, North Carolina, Washington DC.; Midwest: Indiana, Michigan, Nebraska, Ohio (2 sites); Northeast: Connecticut and New Jersey; Northwest: Washington; Southeast: Alabama, Georgia, Florida (3 sites), Louisiana; Southwest: California (2 sites), Texas (2 sites).

Table 2. Prevalence of *M. genitalium* urogenital infection by subject demographic status and geographic region.

medicine, family planning, public health, STI and family medicine/obstetrics-gynecologic facilities. The study population included sexually active male or female subjects 14-years-old or older, with or without STI symptoms. Subjects with antibiotic treatment within 21 days of enrollment were excluded.

There were 3,300 subjects evaluable for infected status, and 11,556 specimens were collected and analyzed. Among 1,737 female subjects, four different specimens were collected (clinician-collected vaginal: n=1,709; patient-collected vaginal: n=1,724; endocervical: n=1,714; female urine: n=1,733). Among 1,563 male subjects, three different specimens were collected (urethral: n=1,563; penile meatal: n=1,554; male urine: n=1,559).

Although the subject age in the AMES Study spanned 15–82 in age, most subjects were between 18-40 (females: 84 percent, males: 70 percent).[23] For either sex, approximately 61 percent of subjects were African American, approximately 77 percent were non-Hispanic, and approximately 74 percent were from southeast or southwest clinics.

For investigational assay sensitivity and specificity determinations, results from the investigational assay were compared with those from three different TMA NAATs that target *M genitalium* rRNA. One test amplified a 16S rRNA (alternate [Alt] TMA-1), using a different 16S rRNA locus than the investigational assay, and the other two amplified *M genitalium* 23S rRNA, each at a different locus (Alt TMA-2 and -3).[23] For each assay, amplification and detection of the targeted nucleic acid region was a positive indicator. Each specimen was tested with the investigational assay, and then samples were further tested with Alt TMA-1 and -2.

If results were discordant, missing or invalid between the comparator tests, the specimen was further tested with Alt TMA-3 as a tiebreaker assay. Operators performing the Alt TMA assays were blinded to the investigational assay results and all patient-identifying information. Composite results for each specimen were then compared with the investigational assay result.

Prevalence of *Mycoplasma genitalium* STI

Overall *M genitalium* prevalence in the AMES study was 10.2 percent and 10.6 percent in female and male subjects, respectively.[23] These results were consistent with recent reports of *M genitalium* prevalence estimates based on this TMA

Specimen type and subject symptom status[a]	No of specimens	Prevalence (%)	Sensitivity (% [95% CI])	Specificity (% [95% CI])	PPV (95% CI)b	NPV (95% CI)c	PLR (95% CI)d	NLR (95% CI)e
Clinician-collected vaginal swab								
Sym	1040	11.5	93.3 (87.4-96.6)	97.6 (96.4-98.4)	83.6 (77.3-88.8)	99.1 (98.3-99.6)	39.0 (26.2-60.8)	0.07 (0.03-0.13)
Asym	669	8.1	88.9 (77.8-94.8)	98.7 (97.5-99.3)	85.7 (75.8-92.9)	99.0 (98.0-99.6)	68.3 (35.6-148.8)	0.11 (0.04-0.23)
Overall	1709	10.2	92.0 (86.9-95.1)	98.0 (97.2-98.6)	84.2 (79.1-88.6)	99.1 (98.5-99.5)	47.0 (33.4-68.8)	0.08 (0.05-0.13)
Patient-collected vaginal swab								
Sym	1047	11.6	100 (96.9-100)	98.1 (96.9-98.8)	87.1 (81.1-91.9)	100 (99.6-100)	51.4 (32.7-86.5)	0.00 (0.00-0.03)
Asym	677	8.0	96.3 (87.5-99.0)	99.0 (97.9-99.6)	89.7 (80.4-95.7)	99.7 (98.9-100)	100 (47.4-258.2)	0.04 (0.00-0.13)
Overall	1724	10.2	98.9 (95.9-99.7)	98.5 (97.7-99.0)	87.8 (83.1-91.7)	99.9 (99.5-100)	63.8 (43.4-97.9)	0.01 (0.00-0.04)
Endocervical swab								
Sym	1046	11.5	84.2 (76.6-89.6)	98.2 (97.1-98.9)	85.6 (79.1-90.8)	98.0 (97.0-98.7)	45.9 (29.1-76.4)	0.16 (0.1-0.24)
Asym	669	7.9	75.5 (62.4-85.1)	98.5 (97.2-99.2)	81.6 (70.3-90.2)	97.9 (96.8-98.8)	51.7 (27.5-107.2)	0.25 (0.14-0.39)
Overall	1715	10.1	81.5 (75.1-86.6)	98.3 (97.5-98.8)	84.4 (78.9-89.1)	97.9 (97.2-98.5)	48.3 (33.3-72.7)	0.19 (0.13-0.25)
Female urine								
Sym	1051	11.6	79.5 (71.5-85.7)	98.4 (97.4-99.0)	86.6 (80.0-91.8)	97.3 (96.3-98.2)	49.2 (30.4-85.7)	0.21 (0.14-0.29)
Asym	682	7.9	74.1 (61.1-83.9)	99.8 (99.1-100)	97.6 (88.7-99.9)	97.8 (96.7-98.7)	465.2 (91.6-15,195.2)	0.26 (0.15-0.4)
Overall	1733	10.2	77.8 (71.1-83.3)	99.0 (98.3-99.4)	89.5 (84.3-93.6)	97.5 (96.8-98.2)	75.8 (47.5-128.6)	0.22 (0.17-0.29)
Male urethral swab								
Sym	866	12.0	98.1 (93.3-99.5)	99.9 (99.3-100)	99.0 (94.9-100)	99.7 (99.1-100)	747.4 (136.8-27,947.9)	0.02 (0.00-0.07)
Asym	697	8.8	98.4 (91.3-99.7)	99.2 (98.2-99.7)	92.3 (84.0-97.3)	99.8 (99.2-100)	125.1 (54.7-369.0)	0.02 (0.00-0.09)
Overall	1563	10.6	98.2 (94.8-99.4)	99.6 (99.1-99.8)	96.4 (92.7-98.6)	99.8 (99.4-100)	228.8 (106.8-605.2)	0.02 (0.00-0.05)
Penile meatal swab								
Sym	865	11.9	89.3 (81.9-93.9)	97.8 (96.5-98.6)	84.4 (77.5-90.0)	98.5 (97.6-99.2)	40.0 (25.4-66.7)	0.11 (0.06-0.19)
Asym	689	8.9	86.9 (76.2-93.2)	97.9 (96.5-98.8)	80.3 (70.8-88.1)	98.7 (97.7-99.4)	42.0 (25.0-75.9)	0.13 (0.06-0.24)
Overall	1554	10.6	88.4 (82.6-92.5)	97.8 (96.9-98.5)	82.9 (77.4-87.6)	98.6 (97.9-99.1)	40.9 (29.0-59.8)	0.12 (0.07-0.18)
Male urine								
Sym	866	12.0	89.4 (82.0-94.0)	99.1 (98.1-99.6)	93.0 (86.9-96.9)	98.6 (97.6-99.3)	97.3 (48.5-228.4)	0.11 (0.06-0.18)
Asym	693	8.7	93.3 (84.1-97.4)	99.7 (98.9-99.9)	96.6 (89.0-99.5)	99.4 (98.5-99.8)	295.4 (85.6-2229.8)	0.07 (0.02-0.16)
Overall	1559	10.5	90.9 (85.5-94.4)	99.4 (98.8-99.7)	94.3 (90.0-97.2)	98.9 (98.3-99.4)	140.8 (76.2-294.7)	0.09 (0.05-0.15)

NPV = negative predictive value; PLR = positive likelihood ratio; NLR = negative likelihood ratio.
aSymptom status was determined based on subject-reported symptoms. Asym, asymptomatic; Sym, symptomatic.
bPPV, positive predictive value.
cNPV, negative predictive value.
dPLR, positive likelihood ratio.
eNLR, negative likelihood ratio.

Table 3. Clinical performance characteristics of the Aptima *Mycoplasma genitalium* assay in urogenital specimens from female and male subjects status and geographic region.

NAAT[6,21,25] and were higher than some historical estimates.

Most subjects in the study (female, 61 percent; male, 55 percent) were symptomatic for STIs.[23] *M genitalium* prevalence rates were comparable between symptomatic and asymptomatic subjects for both sexes (Figure).

The highest prevalence of *M genitalium* was observed in the 18-20-year-old category, in which more than a quarter of these younger female subjects were found to test positive for *M genitalium* infection compared with 15 percent for younger male subjects (Figure).[23] In all other age categories, *M genitalium* infection prevalence rates were lower than in the 18–20-year cohort, were higher in male vs female subjects and declined with the age of subjects.

Overall *M genitalium* prevalence rates across all seven specimen types were highly consistent, ranging from 10.1 percent to 10.6 percent (Table).[23] *M genitalium* prevalence was also higher in symptomatic vs asymptomatic subjects across all specimen types. In female subjects, prevalence was lowest (7.9 percent) in endocervical and urine samples from asymptomatic subjects, and highest (11.6 percent) in urine samples and patient-collected vaginal specimens from symptomatic subjects.

In male subjects, the lowest prevalence was found in urine specimens (8.7 percent) from asymptomatic subjects, and highest (12 percent) in urethral swab, self-collected, penile-meatal swabs and urine specimens from symptomatic subjects. Most subjects had positive investigational assay results for approximately two specimen types, and 56 percent of female and 68 percent of male subjects reported positive investigational assay results in all specimen types assessed, indicating the consistency of the assay across specimen types within individuals.

Assay performance

The investigational test exhibited a sensitivity for detection of *M genitalium*-infected subjects that ranged from 77.8 percent (female urine) to 98.9 percent (patient-collected vaginal swab) across the 7 specimen types (Table).[23] These results suggest *M genitalium* infections are more likely to be missed in female subject urine samples compared with other specimen types. Overall specificity was greater than or equal to 97.8 percent for all specimen types. Sensitivity and specificity estimates were comparable in asymptomatic and symptomatic subjects for each specimen type.

Overall positive predictive values ranged from 82.9 percent to 96.4 percent and negative predictive values from 97.5 percent to 99.9 percent across all specimens, indicating high predictive value for the investigational *M genitalium* diagnostic assay (Table). Assay performance was similar among races and ethnicities of subjects for all specimen types.

Summary and conclusions

The AMES Study TMA NAAT investigational assay has been cleared by the FDA as a test for detection of *M genitalium*, which is an important advance in STI diagnostic technology. Lack of an FDA-cleared assay has hindered accurate *M genitalium* diagnosis and appropriate treatment, which has impaired patient outcomes and possibly fostered antibiotic resistance. Inadequate identification of *M genitalium* has delayed our understanding of the natural history of *M genitalium* infections and the long-term consequences of persistent infections.

The results of the AMES Study demonstrated that the assay can reliably assist physicians in identifying the *M genitalium* organism to be able to study its significance in further research studies. More studies are required to assess its significance in asymptomatic patients. The requirement for antibiotic resistance assays will help minimize the risk for development of antibiotic resistance.[21]

The FDA-cleared *M genitalium* test is a highly sensitive RNA based assay that can be performed in clinical settings with a short turnaround time for reporting results. This FDA-cleared testing method allows easy detection of *M genitalium* in a variety of clinical specimens from patients. The AMES Study demonstrated that assay sensitivity is robust for all specimens and that vaginal specimens had the highest detection sensitivity.

The study results confirm *M genitalium* prevalence rates are significant in sexually active young people, particularly in females, even in asymptomatic subjects. Both symptomatic and asymptomatic patients can be diagnosed with this FDA-cleared test. Questions remain about the significance of asymptomatic infections. Future research studies of asymptomatic subjects may be able to help determine the significance of *M genitalium* in such people, possibly guide treatment decisions and clarify the potential negative outcomes associated with asymptomatic *M genitalium* infections.

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Charlotte Gaydos, MS, MPH, DrPH, is a Professor in the Department of Medicine, Infectious Disease Division, Johns Hopkins University School of Medicine, as well as President of the International Union Against Sexually Transmitted Infections (IUSTI), and member of the Center for Global Health. She received her M.S. in medical microbiology from West Virginia University, and her MPH and DrPH in immunology and infectious diseases were from Johns Hopkins University School of Public Health. She is the Director of the University International STI, and Respiratory Diseases, Research Laboratory.

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Assay addresses M genitalium diagnostic abilities

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TEST QUESTIONS

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

1. **Historically, prevalence rates of *M. genitalium* are**
   - A. one to three percent
   - B. five to eight percent
   - C. ten to fifteen percent
   - D. twenty to thirty percent

2. ***M. genitalium* can be found in the urogenital tract and**
   - A. digestive system
   - B. oral cavity
   - C. respiratory tract
   - D. none of the above

3. ***M. genitalium* of the urogenital tract causes urethritis in men and cervicitis in women.**
   - A. True
   - B. False

4. ***M. genitalium* infections in men can lead to**
   - A. COPD
   - B. reactive arthritis
   - C. epididymoorchitis
   - D. both b and c

5. **It is suggested that *M. genitalium* can be an underlying cause of _____ in women with pelvic inflammatory disease.**
   - A. spontaneous abortion
   - B. infertility
   - C. preterm delivery
   - D. all of the above

6. ***M. genitalium* has protective measures against risk of HIV and HPV infection and transmission.**
   - A. True
   - B. False

7. **Symptoms of *M. genitalium* are**
   - A. cough
   - B. dysuria
   - C. fever
   - D. none of the above

8. **Adequate diagnosis of *M. genitalium* has lacked because of**
   - A. predominant lack of symptoms
   - B. lack of testing
   - C. poor testing sensitivity
   - D. all of the above

9. **Macrolide resistance rates to *M. genitalium* are estimated to be between _____ and _____ percent.**
   - A. 5;10
   - B. 10;50
   - C. 20;80
   - D. 30;100

10. **Prior to 2015, there wasn't an available FDA-cleared diagnostic test for *M. genitalium.***
    - A.True
    - B.False

11. **Which factor(s) make *M. genitalium* difficult to diagnosis?**
    - A. fastidious
    - B. absence of a cell wall
    - C. grows slowly
    - D. all of the above

12. **Which testing method does the CDC recommend for detection of *M. genitalium?***
    - A. culture
    - B. NAAT
    - C. latex agglutination test
    - D. immunoassay

13. **The AMES prospective multicenter clinical study was conducted to validate performance of**
    - A. TMA NAAT for detection of *M. genitalium*
    - B. IgG antibody immunoassay for detection of *M. genitalium*
    - C. traditional culture for detection of *M. genitalium*
    - D. none of the above.

14. **The overall prevalence of *M. genitalium* in the AMES study ranged from**
    - A. 2.1 to 2.6 percent
    - B. 5.5 to 5.8 percent
    - C. 7.1 to 7.9 percent
    - D. 10.1 to 10.6 percent

15. **Prevalence was lowest in females who were _____ and from _____ specimens.**
    - A. asymptomatic; vaginal specimens
    - B. asymptomatic; endocervical and urine
    - C. symptomatic; urine
    - D. symptomatic; endocervical and urine

16. **Which gender and specimen type can *M. genitalium* detection be missed?**
    - A. male; urine
    - B. female; endocervical
    - C. female; urine
    - D. male; urethral

17. **The AMES study showed an overall specificity of greater than or equal to _____ percent in the TMA NAAT test.**
    - A. 97.8
    - B. 79.8
    - C. 99.8
    - D. 89.8

18. **Results of the AMES study show that more research needs to be done to assess the test's significance in asymptomatic patients.**
    - 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.

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Overcoming the analytical challenges of forensic laboratories

By Debadeep Bhattacharyya, PhD

The process of identification, monitoring and quantitation of drugs is a crucial component of forensic investigations and clinical research. The increase in number of prescribed analgesics, misuse of opioids and recent attempts to bypass substance laws have overwhelmed the forensic community as laboratories experience ever-increasing caseloads and the need for certain critical technical upgrades.

To meet these demands, forensic scientists and clinical researchers will need robust, reproducible, reliable and sensitive methods to accurately identify and quantify new, unknown compounds, along with known compounds, as well as high-throughput technologies to keep up with the hundreds of samples arriving each day.

Keeping up with increasing demands

The forensic market is expected to grow at the rate of 7 percent annually.[1] In a recent survey conducted with 400 forensic laboratories in the U.S., around 30 percent reported that caseloads were increasing year-on-year.[1] This steep rise stems from an increase in the unlawful manufacturing and trafficking of new designer drugs, distributed either under a mislabeled name or made accessible online. To enable forensic laboratories to stay ahead in the fight against drug abuse, scientists will not only need reliable, sensitive, and robust technology to address the critical analytical challenges, but also technologies with higher-throughput capabilities that can process multiple samples in less time.

The rise in new drugs (also known as designer drugs) requires forensic laboratories to act quickly. Novel psychoactive substances (NPS) such as the opioid fentanyl, which is 50 times more potent than heroin, are being used by drug traffickers to lace diluted heroin. In March 2017, routine testing for NPS at the LGC laboratories in the UK detected the presence of carfentanil, an analog of fentanyl with 100X its potency, in a postmortem blood case.[2] The minimal scientific information available on most of these new drugs has led to them being classified as "known unknowns" and can pose additional challenges to laboratories focused on identifying, monitoring and quantifying them. In fact, almost 60 percent of the surveyed forensic laboratories admitted that the influx of newly identified drugs was a major contributor to their backlog.[1]

With legal and regulatory changes regarding consumption of substances such as cannabis, once more universally considered illegal, forensic laboratories need to constantly optimize processes, develop and validate new methods and consider technology upgrades to meet these changing requirements. The rise in medicinal and recreational use of previously illegal drugs requires forensic scientists to continually comply with the newly established standards for "under the influence."

Pressed for funding and staff training time, many laboratories continue to use time-consuming legacy methods that often fail to address the growing analytical challenges. Often, multiple orthogonal tests are performed to close a single case, increasing the time spent per case and adding to the backlog. To continue offering reliable results at a faster pace, laboratories need to stay updated with information on modern technologies that can advance forensic science quickly and cost effectively while meeting the increasing demands of scientific analysis.

Next-generation analytical technologies

Most forensic laboratories perform immunoassays, a well-established technique often employed to detect drug usage after consumption via drug screening methods.[3] Although easy to use, immunoassays limit the scope of forensic toxicologists. For starters, the sensitivity of an immunoassay in determining traces of a drug depends on the quality of the antibody. Also, the number of available antibodies validated for forensic use limits the number of compounds that can be detected.

The hands-on nature of immunoassay workflows makes it challenging to increase sample throughput. Although immunoassay manufacturers offer multiplexing options, these are, again, dependent on the availability of specific antibodies. If a new drug emerges, current immunoassay options are no longer relevant, and method development for the new analyte can take up to a year. When a cold case reopens, scientists will need to reanalyze or repeat older experiments, adding more time to each case.

Limitations in conventional methods, such as immunoassays, have prompted illegal drug manufacturers to modify the chemical structure of synthetic designer drugs so that they remain undetected even when tested, thereby bypassing the substance laws to continue illegal drug trafficking. Forensic laboratories need better technologies that can first, sustain the ever-changing nature of drug abuse and second, offer robust, adaptable methods that yield accurate results.

With the advent of next-generation technologies in forensics, liquid chromatography (LC) coupled with mass spectrometry (MS) has gained widespread popularity due to its higher analytical sensitivity and selectivity. Advanced MS technologies, namely, high-resolution, accurate mass (HRAM) mass spectrometry, help close the uncertainty gap in forensic analysis with reliable, accurate detection capabilities, confident unknown identification and detection of multiple analytes in a single experiment.

High resolution and mass accuracy are both important factors necessary to resolve the compound of interest from other analytes and complex biological matrices, even at low concentrations. Moreover, MS-based technologies enable retrospective analyses, i.e., if the data needs to be reassessed in the future, scientists can do so without repeating or reanalyzing the experiment.

Even though LC-MS approaches can enable laboratories to expand testing options and enhance revenue streams, thus facilitating cost-savings in the long run, two common barriers to adopting LC-MS techniques are the required capital investment in

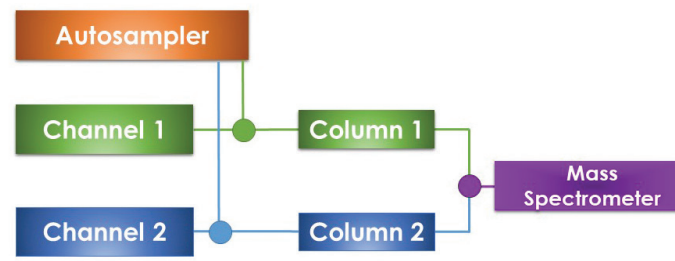

Figure 1. With multichanneling, up to four automated HPLC channels deliver up to four different separations to a single mass spectrometer, streamlining LC-MS workflows and reducing idle time.

equipment, along with the time needed to develop the necessary expertise to maximize the potential of new technology compared to immunoassays. To help overcome these barriers, new-generation LC-MS instruments are usually controlled by software that is easy to use and they also offer method development and optimization guidelines that ensure increased uptime for every laboratory.

Moreover, for laboratories aspiring to higher-throughput capabilities, LC-MS can be particularly beneficial, with its fast turnaround time (for every sample) and improved sensitivity. A university-based forensics laboratory, with a goal of staying self-supported and revenue neutral, made the switch from immunoassays to HRAM-based LC-MS after a thorough cost-recovery analysis. The lab, running almost 70,000 samples a year, got a return on investment within 18 months alongside the other added benefits of higher performance.[1]

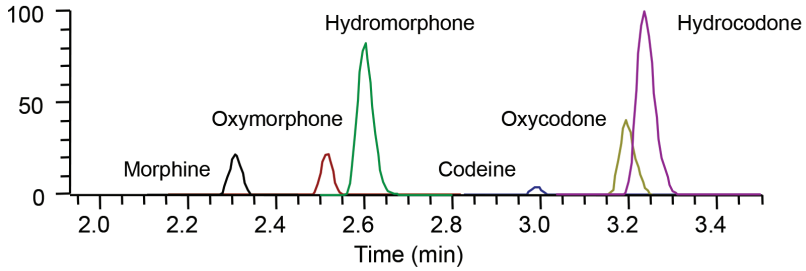

Figure 2. Chromatograms extracted from MS2 spectra obtained from a confirmation PRM experiment for six opiates at their respective LOQs (2.5 ng/mL for codeine, oxycodone and oxymorphone, and 5 ng/mL for hydrocodone, hydromorphone, and morphine) in hydrolyzed and diluted urine.

Benefits of using high-resolution MS technologies in forensic laboratories:

- Higher resolution, selectivity, and specificity for routine identification
- Ability to screen and quantify at the same time
- Confirmation of targeted and untargeted compounds by matching with a database
- Multichanneling capabilities: Able to carry out multiple analytical runs in parallel
- Retrospective analyses: Data can be reassessed in the future without the need to reanalyze

Advanced technologies for current challenges

In order to address the ever expanding number of cases while monitoring, identifying and quantifying a growing list of new drugs that are constantly entering the market, forensic toxicologists need technologies that can screen compounds, detect unknowns and perform sensitive quantification in a fast-paced environment, ultimately helping to achieve the desired scientific and business goals. HRAM spectrometry can leverage a library or many libraries comprising thousands of reference compounds, and so enables researchers to quickly screen, identify and quantify substances with utmost confidence.

For example, using HRAM, toxicologists can screen and detect six common opiates in human urine—morphine, codeine, hydromorphone, hydrocodone, oxymorphone and oxycodone—even at low ng/mL levels, while meeting industry standards.[4] With quintuplicate replicates of quality control over three different days and an assessment with 58 donor samples, this method demonstrates that forensic toxicologists can perform quantitation of specific panels of analytes to industry-established standards using MS-based methods.

HRAM-based methods also allow screening of known/unknown compounds with reliability and reproducibility. In one application, direct injection of urine into an ultra-high-performance liquid chromatography (UHPLC) system coupled with an Orbitrap high-resolution mass spectrometer was used to reliably screen for and identify 14 different fentanyl and fentanyl analogs.[5] With an analysis time of only five minutes, all fentanyl compounds present in the spiked matrix were detected and confirmed at 0.5-5 ng/mL, validating the method for screening in clinical research or forensic toxicology.

After LGC laboratories first detected carfentanil, a fentanyl analog, they performed investigative MS-based analysis and established that carfentanil and its metabolites give highly diagnostic MS^2 data.[2] These findings resulted in a routine methodology to detect the new drug in both post-mortem blood and urine samples, even with limited knowledge about the drug's metabolism. The LGC case study further validates the adaptability of next-generation analytical techniques, empowering forensic scientists to keep up with the ever-evolving landscape of drugs and future-proof their laboratories against changing regulations.

Conclusion

As illegal drug trafficking continues to rise, the use of prescribed drugs continues to grow, and the development and production of novel designer drugs continues to flourish, forensic laboratories shoulder the responsibility to stay updated with current regulations, offer technical capabilities to deal with the unknowns and, ultimately, play a key role in driving investigative decisions. Advances in MS technologies enable scientists to obtain unmatched resolution to accurately identify targeted and untargeted drugs with desired sensitivity and speed.

With the option to add multichanneling and the ability to perform retrospective analyses, LC-HRAM (MS) has expanded the scope of forensic analysis, enabling laboratories to develop new detection methods faster than ever before. By adopting these modern analytical technologies, forensic laboratories can significantly improve their efficiencies, ensure lower running costs and relieve the burden of increased caseloads. Most importantly, scientists can now confidently maintain assured certainty of results, especially when justice is on the line.

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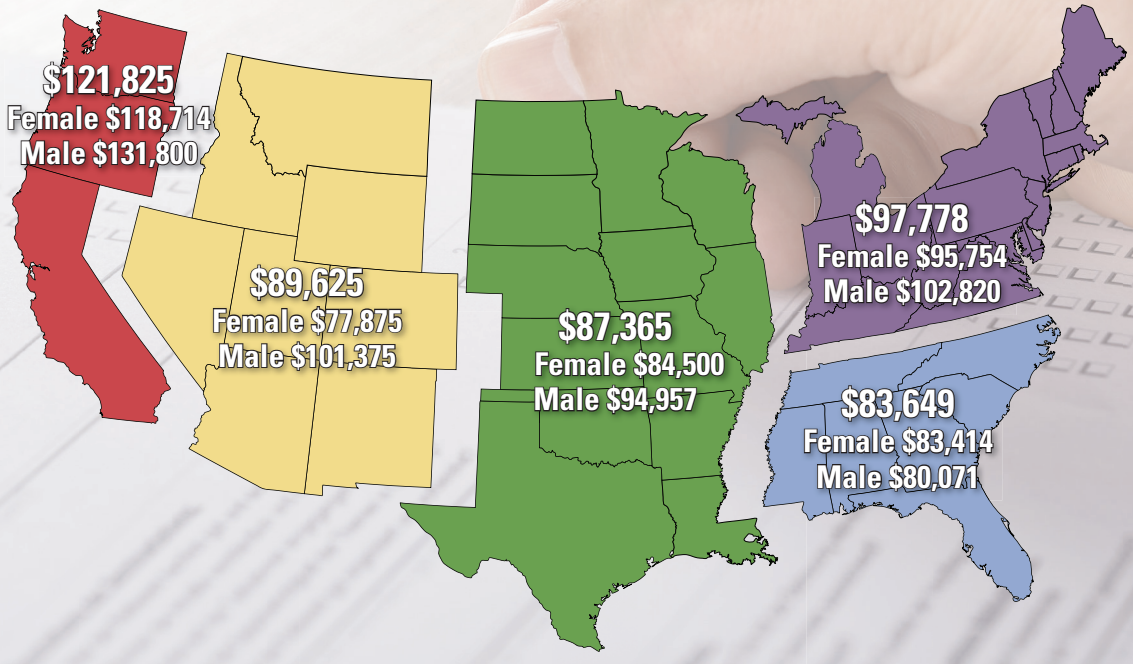
Debadeep Bhattacharyya, PhD, serves as Senior Marketing Manager for Clinical and Forensic Applications at Thermo Fisher Scientific. He has more than 12 years of experience working with mass spectrometers and other high-end analytical instruments, supporting customers across multiple industries and academic institutions. He holds a PhD in chemistry and biochemistry from Emory University.

MLO's 2020 Annual Salary Survey of laboratory professionals

By Linda Wilson



Medical Laboratory Observer's 2020 annual salary survey of laboratory professionals revealed a sizable jump in the average salary, based on the responses of all participants, although quite a few job categories recorded drops in pay.

In *MLO*'s 2020 salary survey, the average compensation across all positions was $93,844, up from $83,538 in 2019. For females, the average was $90,761, up from $79,413 in the 2019 survey, and $99,779 for men, up from $97,328 in the 2019 survey.

To some degree, employment and compensation trends at clinical laboratories reflect robust demand for these professionals. As the U.S. population ages, fueling demand for lab tests, the number of positions available in clinical labs is predicted to grow quickly. The Bureau of Labor Statistics expects employment for clinical lab technologists and technicians to grow 11 percent, adding 35,100 positions, from 2018 to 2028. The bureau expects the number of positions for phlebotomists to grow even faster, by 23 percent, during the same time period, adding 29,500 positions.

Demographics

In addition to demand for employees, the substantial increase in compensation overall and among females could be explained, in part, by the demographics of participants in the 2020 and 2019 surveys.

For example, more survey respondents in 2020 were in management positions than was the case in 2019. In the 2020 survey, 77 percent of respondents were lab directors, managers, administrators, section managers or department heads, compared with 58 percent in 2019.

The proportion of managers involved in the 2020 survey versus the 2019 survey also was reflected in the breakdown of salaried and hourly employees. Nearly three-quarters were salaried employees, or 72 percent, in the 2020 survey, compared to 57 percent in 2019.

And in both 2020 and 2019, the majority of survey respondents—68 percent in 2020 and 76 percent in 2019—were females.

In the 2020 survey, nearly all survey respondents (93 percent) work at hospital labs, compared with three-quarters (76 percent) in 2019. The largest percentage of them (42 percent) were between 56 and 65 years of age, while another 26 percent were between 46 and 55 years of age.

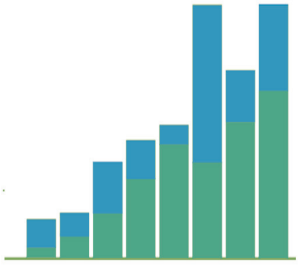
SALARY SURVEY HISTORY	
2020	$93,844
2019	$83,538
2018	$79,006
2017	$84,654
2016	$71,491
2015	80,985
2014	$71,086

Compensation trends

Overall, salaries increased for some positions in the lab in the 2020 survey. Salaries rose $3,522 to $90,329 for lab managers and administrators, $2,750 to $149,100 for pathologists, and $8,083 to $77,500 for microbiologists.

MEDICAL LABORATORY OBSERVER

2020 SALARY SURVEY RESULTS



SALARY BY AGE

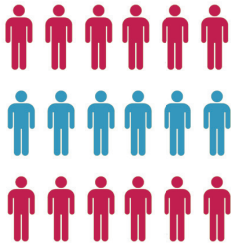
26-35	$81,750
36-45	$91,909
46-55	$96,261
56-65	$92,000
66-70	$95,214
71-plus	$122,500

AVERAGE SALARY BY EDUCATION

High School degree	$50,000
Associate degree(s)	$73,417
Bachelor's degree(s)	$87,785
Post-graduate degree(s)	$109,959

AVERAGE SALARY BY EMPLOYEES SUPERVISED

1-5	$83,561
6-10	$96,227
11-15	$92,337
16-20	$94,842
21-30	$98,708
More than 30	$109,302
None	$82,988



AVERAGE SALARY BY NUMBER OF EMPLOYEES

1-10	$79,629	51-100	$94,733
11-20	$86,175	More than 100	$106,627
21-50	$90,712	N/A	$130,500

AVERAGE SALARY BY GENDER

Female: $90,761 | Male: $99,779

AVERAGE SALARY BY TYPE OF LAB FACILITY

Hospital	$94,228
Independent Lab	$92,700
Group Practice	$72,500
Government/Public Health Lab	$72,500
Physician's Office Lab	$80,000
Medical School/Med Tech/ CLS Ed Programs	$160,000
Blood Bank	$80,000

AVERAGE SALARY BY NUMBER OF YEARS IN THE INDUSTRY

Less than 3	$52,500	15-19	$82,324
3-5	$98,333	20-24	$97,938
6-9	$107,611	25-30	$91,538
10-14	$93,741	More than 30	$94,656

MEDIAN ANNUAL BASE SALARY $72,500

SALARY VS HOURLY

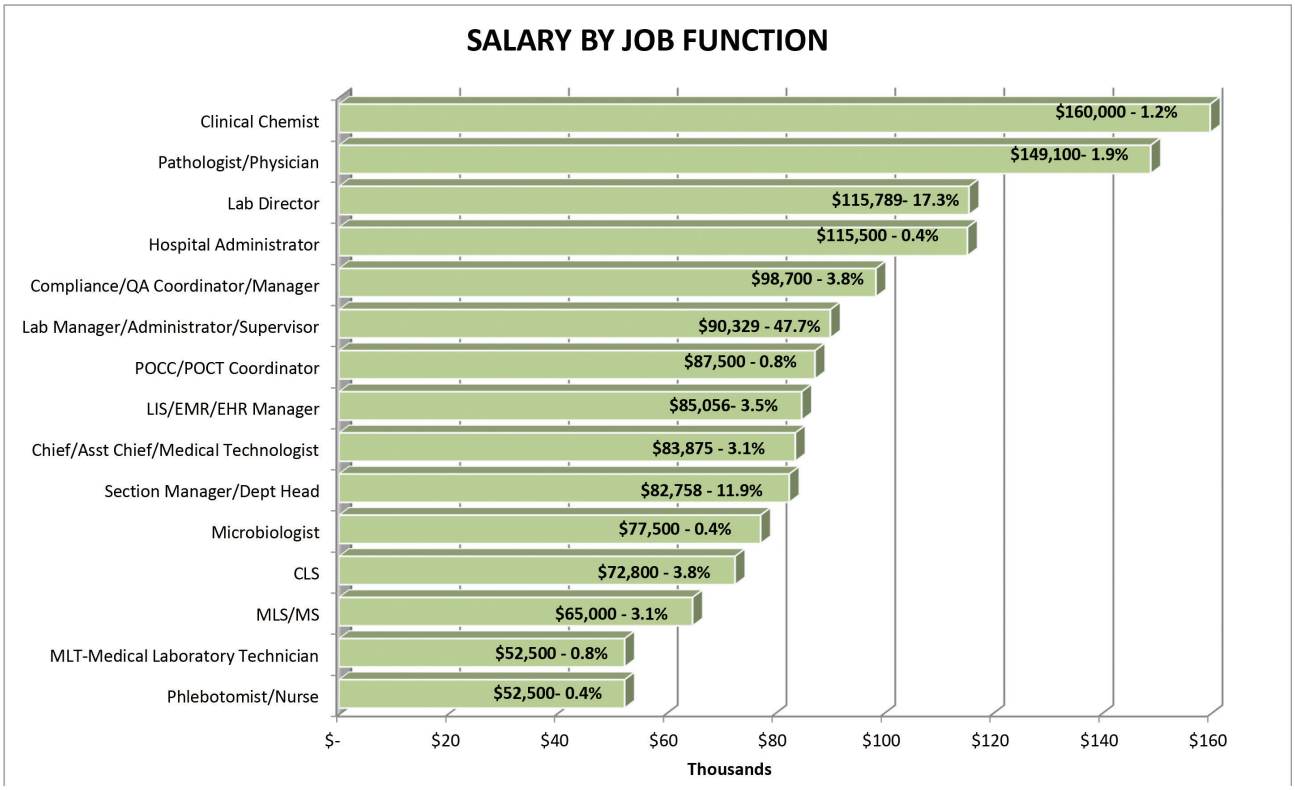
Salaried	72%
Hourly	28%

BASE SALARY CHANGE SINCE LAST YEAR

Increase	71%
Stayed the same	27%
Decreased	2%

BONUS IN 2019

Yes	28%
No	72%



The average salary for compliance and quality assurance coordinators and managers soared by $16,109 to $98,700. However, only 10 people responded to that question on the survey in 2020, compared with 22 people in 2019.

Other salaries dropped. For example, salaries decreased by:

- $2,622 to $115,789 for lab directors
- $1,037 to $82,758 for section managers and department heads
- $2,060 to $52,500 for medical technologists
- $3,610 to $65,000 for medical laboratory scientists
- $2,111 to $85,056 for LIS/EHR/EMR managers

When asked what their annual base salary was expected to be in 2020, the median among survey respondents was $72,500. Fifty percent said they expect a pay increase of between 2 and 4 percent, and 22 percent said they expect a pay bump of less than 2 percent.

When asked about their salary in 2019, 71 percent reported an increase and 27 percent reported a decrease.

Bonuses and benefits

In terms of bonuses and benefits, the results of the 2020 survey were similar to the 2019 survey.

The percentage of survey respondents (72 percent) who said they did not receive a bonus in 2019 was nearly identical to the percentage of respondents (71 percent) who said they did not receive a bonus in 2018.

Nearly all respondents in the 2020 survey said their employers offer health insurance, dental insurance and a 401K plan or pension.

Other benefits showed modest growth in prevalence between the 2019 and 2020 surveys including:

- 91 percent with vision insurance in 2020, up from 87 percent in 2019
- 88 percent with life insurance in 2020, up from 86 percent in 2019
- 85 percent with paid time off in 2020, up from 81 percent in 2019
- 78 percent with disability insurance in 2020, up from 77 percent in 2019
- 13 percent with flex time in 2020, up from 12 percent in 2019.

Some benefits saw declines between 2019 and 2020 such as paid holidays (67 percent versus 58 percent), overtime pay (43 percent versus 33 percent) and childcare (6 percent versus 5 percent).

Regional salary breakdown

As has been the case for numerous years, the Pacific region reported the highest average salary in the 2020 survey: $121,825 ($118, 714 for females and $131,800 for males).

For the other regions, salaries were as follows:

- $97,778 in the Northeast ($95,754 for females and $102,820 for males)
- $89,625 in the Mountain States ($77,875 for females and $101,375 for males)
- $87,365 in the Central region ($84,500 for females and 94,957 for males)
- $83,649 in the Southeast ($83,414 for females and $80,071 for males)

Compensation and organization size

Employees at larger organizations—measured by either number of employees or volume of tests—often earned

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- This test 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 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.

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more than their counterparts at smaller organizations.

Among the largest labs, or those with more than 100 employees, the average salary was $106,627, compared with $94,733 for facilities with 51 to 100 employees, $90,712 for facilities with 21-50 employees, $86, 175 for facilities with 11-20 employees and $79,629 for facilities with 1-10 employees.

Labs with largest test volume—more than 2 million tests—had the largest average salary at $113,308. The average salary declined as the volume of tests declined, except for the smallest category (fewer than 25,000 tests), where the average salary was $96,478. In other categories, the average salary ranged from $98,250 for labs with 1-2 million tests to $75,250 for labs with between 25,001 and 50,000 tests.

Satisfaction and security with current position

Overall, laboratorians are secure and satisfied with their work.

When asked how secure they are in their current position, 50 percent of respondents said they were "very secure" and 43 percent said they were "somewhat secure," while 5 percent said they were "somewhat insecure" and less than 1 percent said they were "very insecure."

In a similar vein, 47 percent said they were "very satisfied" with their job and 39 percent said they were "somewhat satisfied," while 11 percent said they were "somewhat dissatisfied" and 2 percent said they were "very dissatisfied."

Education and training

Laboratorians take education and training seriously.

When asked about their highest level of education, 35 percent said they have post-graduate degrees, 55 percent have bachelor's degrees and 9 percent have associate degrees. Less than 1 percent said a high school diploma was their top education credential.

In two of three higher-education categories, females earn less than their male counterparts. The average salary was $109,959 ($105,087 for females and $117,016 for males) for those with post-graduate degrees, $87,785 ($87,757 for females and $85,357 for males) for those with undergraduate degrees, and $73,417 for associate degrees ($70,950 for females and $85,000 for males).

The most common professional certification was from the American Society for Clinical Pathology, which was held by 76 percent of survey participants. The other common certifications were from state governments (13 percent of respondents) and the National Credentialing Agency for Laboratory Personnel (9 percent of respondents).

Laboratorians also reported many hours of continuing education in the 2020 survey. Fifteen percent earned more than 20 hours and nearly 29 percent earned between 11-20 hours.

Tenure

Clinical labs include employees with long tenure as well as relative newcomers. In 2020, the number of years survey respondents have been working at their current employer was as follows:

- 11 percent for less than 3 years
- 12 percent for 3-5 years
- 11 percent for 6-9 years
- 12 percent for 10-14 years
- 9 percent for 15-19 years
- 14 percent for 20-24 years
- 10 percent for 25-30 years
- 21 percent for more than 30 years

Lab operations and management

As has been the case in previous years, the *MLO* salary survey also included questions about laboratory operations.

The ongoing shortages of qualified personnel continues to impact laboratory operations, with 26 percent of respondents describing it as a "large" impact and 47 percent describing it as a "moderate" impact. A minority (22 percent) said the shortages had a "low" impact.

Despite the challenges involved in hiring enough people, 82 percent said they have not outsourced more lab tests, compared with 85 percent in the 2019 survey.

To build test volumes, many labs are focused on outreach efforts to other organizations. Among *MLO*'s survey participants, the focus of outreach efforts included:

- Physician's practices (55 percent)
- Nursing homes (37 percent)
- Community members (30 percent)
- Other laboratories (18 percent)
- Home care (15 percent)

In addition, 29 percent of survey participants said they had minimal or no outreach efforts at their organization.

In other management trends, labs continue to embrace molecular diagnostics in microbiology and adopt automated solutions.

Adoption of molecular diagnostics in microbiology was on an upward trend—from 67 percent in 2019 to 73 percent in 2020.

However, the percentage of survey participants who have adopted molecular diagnostics in other sections of the lab showed very little change from 2019 to 2020:

- from 12 percent to 11 percent in chemistry
- from 8 percent 7 percent in hematology
- from 4 percent for both years in blood bank operations.

The percentage of labs that automated new procedures was 42 percent, down from 49 percent in the 2019 survey.

Conclusion

The *MLO* Salary Survey depicts a laboratory workforce that is highly educated, embraces ongoing training to further hone their skills, and feels secure and satisfied in their jobs. But as is the case in many fields, laboratorians are confronted with a persistent gender pay gap.

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Lab Innovators Worth Watching

Putting patients first

By Linda Wilson

What makes lab innovators worth watching? They develop procedures or processes to improve testing, allowing for faster and more accurate diagnoses, treatments and, ultimately, better patient outcomes.

In *Medical Laboratory Observer's* (*MLO*) inaugural Lab Innovators Worth Watching, we profile organizations that are making a lasting impact on patients' health and well-being.

Kaiser Permanente in California begins COVID-19 testing

In the crosshairs of the COVID-19 pandemic, Kaiser Permanente's California employees are hustling to meet patients' needs for diagnosis and treatment.

Its reference laboratories associated with the Permanente Medical Groups are no exception. Divided into southern and northern regions, the California labs have responded to COVID-19 by bringing testing in house, allowing the healthcare giant to expand testing capacity for anxious patients.

In fact, just one week after Roche Diagnostics received an emergency use authorization (EUA) from the Food and Drug Administration (FDA) for its cobas SARS-CoV-2 Test, the labs began analyzing specimens using the assay. The test is performed on Roche's cobas 6800 instrument in Southern California and the cobas 8800 instrument in Northern California.

Jonathan Gullett, MD

Patients and their providers generally receive results in between 18 and 24 hours, which includes the time it takes to transport the specimens from medical clinics to the labs.

The Southern California regional reference labs, which include facilities in Chino Hills and North Hollywood, began processing about 750 tests daily, which has quickly increased to approximately 1,600 tests daily. The Northern California reference lab is in Berkeley.

The workflow for the test is integrated into the electronic health records (EHR) and laboratory information system (LIS), allowing orders and results to flow back and forth electronically. Positive test results also are called into the medical center that ordered the test or a Kaiser Permanente COVID-19 command center.

Rolling out the test so quickly required that the reference labs work with the region's infectious disease physicians, information technology department and EMR support and regional COVID-19 command centers.

In addition to the challenges of coordinating among numerous groups to develop processes and workflows, the regional labs in Southern California also had to validate the test against several swab types and transport media, including sterile saline. Even so, Kaiser Permanente is still struggling to purchase enough swabs for the tests.

In Southern California, the tests are currently offered to healthcare workers, first responders and symptomatic patients in hospitals, emergency departments, long-term care and skilled nursing facilities and medical clinics.

Kenneth Van Horn, PhD

In addition, "having the test with a more rapid turnaround time (TAT) and capacity to perform testing allowed the group to open up testing to patients in outside affiliated hospitals as well as to hospitals outside of the Kaiser Permanente system, who were in desperate need of more rapid testing results," said Timothy M. McSkane, Executive Leader for the Laboratory Care Delivery System for the Southern California Permanente Medical Group, in a nomination letter to *MLO*.

McSkane and Steven R. McLaren, DO, Assistant Regional Medical Director at the Laboratory Care Delivery System, nominated eight individuals for their work in rolling out COVID-19 testing in California.

At the Southern California Permanente Medical Group Regional Reference Laboratory, those people are: Jonathan Gullett, MD, Physician Director in Microbiology; Kenneth Van Horn, PhD, Technical Director in Microbiology; Vahe Khanlian, CLS, Director of Operations for Microbiology Services in North Hollywood; Onie Bueno, CLS, Director of Operations for Microbiology Services in Chino Hills; Nimfa Burgos, CLS, Assistant Operations Director in Immunology in North Hollywood; and Robert Elazegui, MHA, CLS, MLS, Operations Manager in Molecular Infectious Disease in Chino Hills.

At The Permanente Medical Group in Northern California, McSkane and McLaren nominated Jeffrey Schapiro, MD, Associate Medical Director of the Regional Reference Laboratory and Brian Missett, MD, Associate Executive Director of the medical group.

The northern and southern regions are not standing still. Both regions are considering adding two additional tests: Abbott's Real time SARS-CoV-2 rRT-PCR and Cepheid, Xpert Xpress SARS-CoV-2.

"The group in Southern California really mobilized and at the onset took on investigating what testing could occur and where, and then quickly shifted to prepare for performing the test once approved by the FDA. Partnerships and strong working relationships with the vendors

helped to speed the process of internalization," McLaren wrote. "For as large of an organization as KP Southern California is, we have adapted to the crisis with remarkable agility."

Kaiser Permanente molecular genetic pathology lab adopts non-invasive test

Kaiser Permanente's Southern California Molecular Genetic Pathology Regional Reference Laboratory improved the lives of pregnant women substantially when it brought a non-invasive prenatal test in house that is based on analyzing Cell Free DNA (cfDNA) in blood samples.

Ruan Ramjit, MD

Anatole Ghazalpour, PhD

Mike Moradian, PhD

Bringing testing capability in-house reduced the turnaround time from seven to 10 days to two to three days and saves Kaiser Permanente's Southern California region $1 million annually in external lab costs.

The test is used to screen fetuses for Down syndrome, Edwards syndrome (Trisomy 18) and Patau syndrome (Trisomy 13). It also can determine fetal sex. The test, which can be performed as early as 10 weeks gestation, is generally safer than chorionic villus sampling (CVS) or amniocentesis, which both carry a slight risk for miscarriage.

The molecular genetic pathology lab conducts the tests using next-generation sequencing (NGS) on the Illumina platform. Normal test results are routed to patients through the KP.org patient portal while abnormal results are sent to genetic counselors.

The program has been so successful that Kaiser Permanente is evaluating whether to expand it to other regions in the organization.

McSkane and McLaren also sent a nomination letter to *MLO*'s Lab Innovators Worth Watching for this project, naming Ruan Ramjit MD, Physician Director; Mike Moradian, PhD, Director of Operations; and Anatole Ghazalpour, PhD, Technical Director.

The Center for Telehealth at the University of Mississippi Medical Center reduces HbA1c

Sometimes a lab innovator isn't a medical scientist, technician or pathologist. That's the case with Tearsanee Davis, DNP, FNP-BC, who is the Director of Clinical and Advanced Practice Operations for the Center for Telehealth at the University of Mississippi Medical Center in Jackson, MS.

As director, she leads the Center for Telehealth in its work to address chronic diseases—particularly among rural low-income populations. When patients enroll in the telehealth program, the staff then teaches patients about self-testing and self-care at home, using Bluetooth-enabled digital monitoring devices, such as glucose monitors and tablets.

Many of these patients find it challenging to make it to in-person appointments both with specialists and with labs for routine testing because of living in underserved areas. But without proper testing, patients could have medical regimens that aren't optimized for their needs, potentially leading to a deterioration in their chronic illnesses.

To address these problems and improve the health of chronically ill Mississippi residents, the Center for Telehealth began a study in 2014 to evaluate a telehealth-based approach to managing patients with diabetes in Sunflower County—a geographic area with a population of 25,000 and a median income of $30,029.[1]

The Mississippi Diabetes Telehealth Network was formed to conduct the study, and included the University of Mississippi Medical Center (UMMC) and General Electric (GE), which provided the equipment for education and biometric data collection; North Sunflower Medical Center (NSMC), which provided the rural clinic; and Telepex, based in Jackson, MS, which provided free wireless connections through its C Spire service.[2]

Tearsanee Davis, DNP, FNP-BC

In addition to at-home monitoring, each patient in the study also attended quarterly appointments at the rural clinic, which included blood tests.

A total of 115 patients completed the 12-month study program. The study logged impressive results, including a significant difference in in HbA1c, total cholesterol, low density lipoproteins (LDL), high density lipoproteins (HDL), triglycerides, creatinine clearance, glomerular filtration rate and potassium.

Jamie Phillips, PhD, Senior Scientific Affairs Manager at Roche Diagnostics, who nominated Davis for Lab Innovators Worth Watching, explains, "Dr. Davis' work has impacted clinical laboratory operations by promoting better patient care through patient self-testing and the use of telehealth."

Phillips also notes that nurses involved in the telehealth program can remind patients about their quarterly in-person blood tests, helping ensure that patients keep their appointments. "Dr. Davis is 100 percent a lab innovator by ensuring the lab testing can be completed by the patient to ensure the cadence of testing can occur in rural and low-income areas… pretty innovative!"

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Temperature monitoring – from the clinical lab to the cloud

By Brenda Silva

Among the many daily duties within the clinical lab, temperature monitoring was historically one of the most tedious and error-prone activities performed by staff, regardless of their experience. It often required lab personnel to record equipment temperatures at multiple times throughout the day and/or night. One common method involved placing a thermometer inside an equipment chamber and then opening the chamber door to observe and record the temperature at specific intervals of time. This practice not only exposed samples and reagents to outside air, causing temperatures to fluctuate and rise, it was the exact opposite of what temperature monitoring is intended to do.

Over time, lab management and automated programs established better ways to maintain sample integrity and adhere to lab protocols so that the importance of temperature monitoring is never overlooked or at risk because of human errors.

Methods of temperature monitoring

Aside from the aforementioned thermometer, other options for temperature monitoring may have been considered more reliable, with some still in practice today.

Marigale Walsh, Director of Merchandising at MarketLab, said, "Traditional methods relied on thermometers, chart recorders and digital meter/data loggers. Thermometers were read at established intervals with manual documentation. Chart recorders have also been used in the past and are still very popular. Digital recorders with varying degrees of sophistication have also been in place and offer additional benefits and convenience, but also have some downfalls."

The importance of temperature monitoring methods isn't lost on Michael Hanssens, Director of Business Development at Rees Scientific, who pointed out some of the key features of successful automated temperature monitoring systems.

"It continuously logs temperature, humidity and other environmental factors in critical lab equipment. It protects valuable assets, efforts and products. Along with real-time monitoring, it provides automated daily printouts, alarm notification, audit trails and complete data encryption to help meet compliance."

Monitoring lab temperatures today

In the same way that the temperature of the clinical lab industry changes over time, so have the options for temperature monitoring within the same labs. While tried-and-true, hands-on methods remain, other methods offer the confidence and accuracy provided by automated solutions.

Joe Arteaga, Director of Product Management – Controlled Temperature Technologies at Thermo Fisher Scientific, asserted that one of the most common and preferable methods of temperature monitoring today is "wireless monitoring solutions that offer 24/7/365 continuous monitoring and alarm notification, even during a power outage. These types of systems are scalable, so they can be designed to monitor one lab, or an entire enterprise with multiple locations and multiple brands of equipment. In clinical environments, a system that is also compatible with the FDA's 21CFR Part 11 initiative is extremely important."

Also referencing industry requirements is Mark Fauber, Product Manager – Continuous Monitoring at MesaLabs, who pointed out that, "Today, the most explicit requirements for temperature monitoring in a healthcare environment are published by the Centers for Disease Control (CDC) publication titled *Vaccine Storage and Handling Kit* dated January 2020. Monitoring systems meeting the requirements of the CDC's publication are easily adapted for use in a wide variety of applications including the clinical laboratory."

Fauber added, "The use of third-party automated monitoring systems is all but a requirement for laboratories, hospitals, blood banks and other testing and production industries today. These systems allow for real-time notification of out of specification (OOS) conditions and allow for the rescue of stored materials before they are lost. Automated monitoring systems also allow for thorough data gathering and investigation of non-conformances through access to historical data and reports that are saved in their databases."

In addition to adhering to established protocols for temperature monitoring, close attention also needs to be paid to the condition and age of lab equipment and its capacity to carry out temperature-related procedures.

Colleen Holtkamp, Market Manager at Helmer Scientific, reminds lab professionals, "Temperature monitoring is critical for ensuring compliance and quality. The use of medical-grade cold storage designed for clinical applications is also essential. Equipment that is not medical-grade, such as dormitory and commercial-grade units, may not provide the temperature uniformity or performance required to safeguard stored products."

She continued, "While automated central monitoring is common, many clinical labs still rely on chart recorders as part of their overall monitoring program. In addition, some labs require medical-grade units that offer local monitoring capabilities with features such as automatic alarm testing and the ability to download event logs and PDF temperature graphs. These features help ensure the integrity of stored products and improve efficiency by saving time that can be spent on more productive activities."

Established standards and protocols

When looking to the generally accepted best practices for temperature monitoring, lab professionals have many existing standards and protocols in place that allow for industry compliance requirements to be met.

Thermo Fisher's Arteaga asserts that, "In clinical environments, there are a few critical elements that need to be considered." Among these is the use of independent sensors – a second confirmation that the temperature on the equipment's display is accurate, and FDA 21CFR Part 11 compatibility, which addresses electronic signatures and records." (Source: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/part-11-electronic-records-electronic-signatures-scope-and-application)

Helmer's Holtkamp adds, "Capabilities such as automatic high and low temperature alarm testing help support regulatory compliance. For example, the College of American Pathologists

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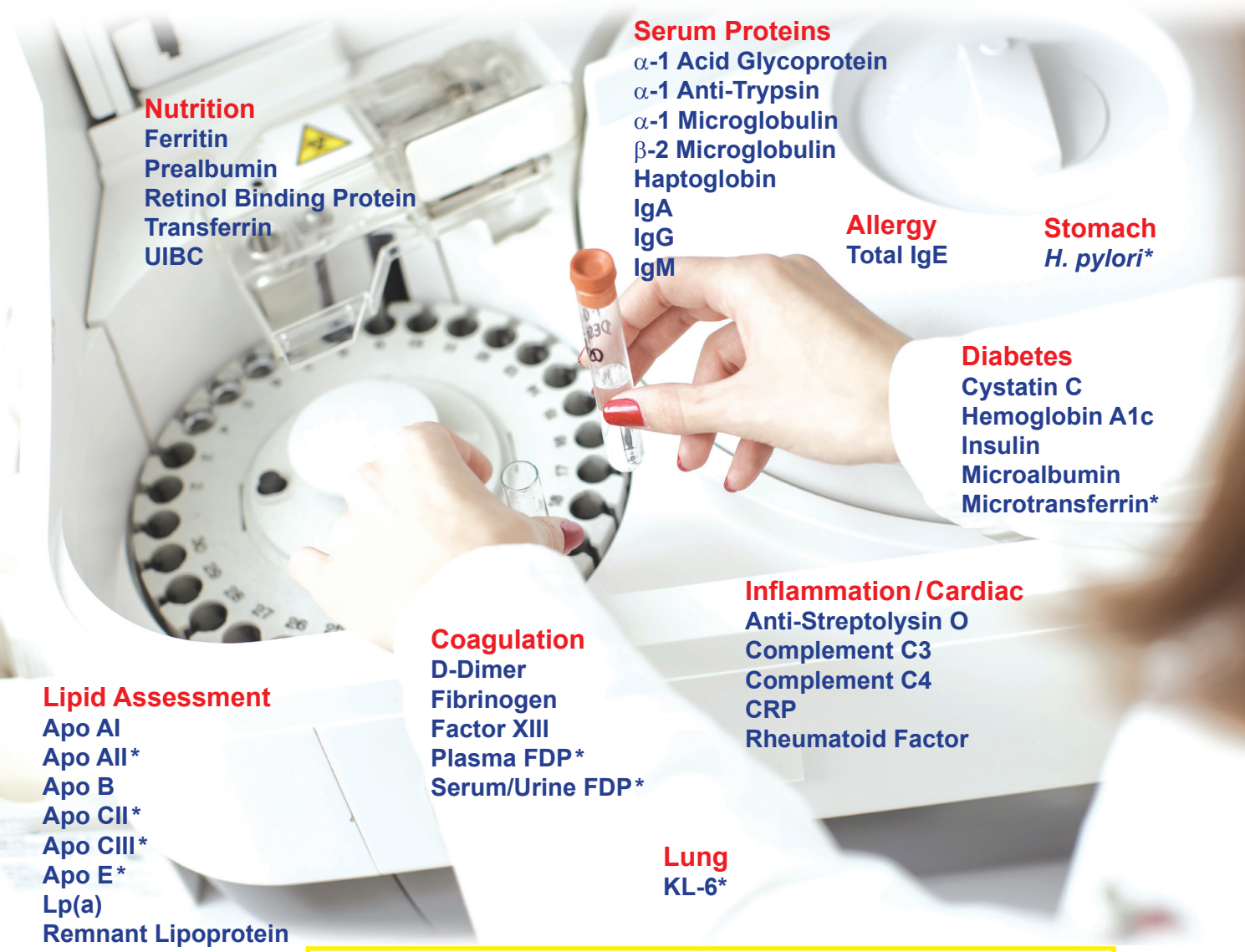

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(CAP) now requires a record of the temperature at which the alarm activated during an alarm test. Electronic records, such as a downloadable event log, provide an effective and efficient means of maintaining compliance."

According to Rees Scientific's Hanssens, there is a wide range of standards for compliance from the CDC, WHO and FDA. Some of the best practices include: "keep valuable assets at an ideal temperature 24 hours a day/7 days a week, accurately record temperatures daily, report out-of-range temperatures immediately, keep a diary of all events, ensure instant notification of alarms and keep results for at least three years or according to individual state requirements."

Fauber of MesaLabs pointed out, "SOPs and compliance issues vary widely and thus it becomes difficult to truly assess 'best practices' for temperature monitoring between labs, hospitals and other industries. There are specific guidelines for the different areas, and even those may be interpreted differently by the management, state or other regulatory agencies."

MarketLab's Walsh said, "Everyone needs to be held accountable to ensure compliance with established protocols. While this sounds obvious, strict adherence to best practices is critical, but this needs to be consistently checked and monitored with a schedule developed by that particular lab. There must be a quality management program written into standard operating procedures."

She continued, "Nothing can be taken for granted. Everything needs to be documented and addressed before there is a temperature monitoring breakdown or a procedure not followed. If not, there could be potential loss of irretrievable specimens and very expensive reagents."

Looking to the future

As the clinical lab industry watches the horizon for new temperature monitoring products and technologies to come, some forecasts would have all eyes looking to the clouds.

Arteaga said,"Clinical labs are starting to adopt remote temperature monitoring that is cloud-based so that they can stay more connected to their equipment. If a unit alarms, personnel can now receive notifications through email/text so that they have time to take action to protect their samples."

Concurring, Fauber added, "Cloud-based services, such as Software as a Service (SaaS) and Platform as a Service (PaaS), continue to grow at 20 percent plus annually and are now well accepted in the healthcare industry. Cloud-based monitoring systems provide a cost-efficient and highly reliant system easily adapted from a single site clinical lab to a large, geographically dispersed lab provider."

He added, "Another trend in monitoring systems is the emergence of multi-purpose sensors, or universal transmitters, capable of monitoring multiple different parameters, in addition to temperature, with a simple change of probe type and programming. This flexibility helps to decrease the complexity, maintenance and cost of automated temperature monitoring systems by allowing for an existing sensor to be repurposed without the need to purchase a new one."

Walsh summed up, "In many cases, temperature monitoring has moved to electronic-based systems. When standard maintenance and compliance are strictly enforced, the best offense is a good defense. And when maintained properly, the clinical lab can quickly address an issue before it becomes a problem."

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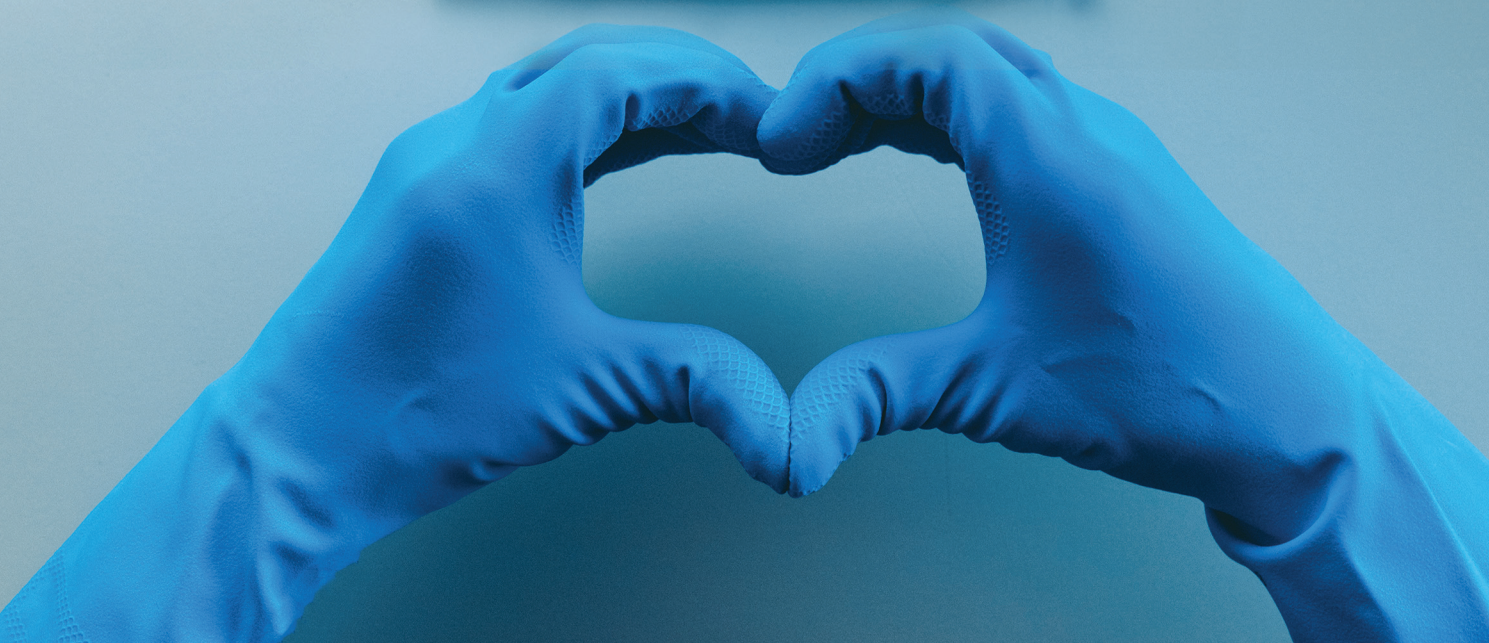

Companion diagnostics in leukemia – the importance of subtypes

By Myla M. Patterson, MBA, PhD, and Yelina Noskina, PhD

Blood cancers such as leukemia, lymphoma, and myeloma are the third leading cause of cancer deaths in the United States. Acute myeloid leukemia (AML) is the most lethal of these cancers, and responsible for more than 10,000 deaths annually.[1,2,3] Despite treatment advances in other blood cancers, the standard of care for AML consists of a combination of chemotherapies, and has remained consistent for more than 40 years. The overall prognosis for AML patients continues to be poor, with a five-year survival rate below 20 percent for patients over age 60.[2]

AML is a form of blood cancer characterized by clonal expansion of poorly differentiated precursor blast cells of myeloid lineage. AML originates in the bone marrow and over time migrates to the blood. Proliferation of immature myeloid cells leads to accumulation of immature progenitor blasts and causes impairment of normal hemopoiesis.[3] As a result, patients can develop severe infections, anemia and hemorrhages. Malignant cells can metastasize to other parts of the body including the lymph nodes, liver, spleen, central nervous system and testicles.[2] These rapidly occurring aspects of the disease make it imperative to be able to diagnose and treat as early as possible.

Diagnosing AML

AML is not staged like most other cancers because the malignant cells do not usually form tumors. Generally, the disease is widespread throughout the bone marrow and, in some cases, has spread to other organs, such as the liver and spleen. Therefore, the prognosis for a patient with AML greatly depends on the subtype of AML, which is determined by a series of diagnostic tests, the patient's age and clinical history.[2,3,8] The diagnostic tests include an assessment of cells in the blood and bone marrow and specialty tests, such as cytogenetic analysis and other molecular assays.

AML Subtypes

Identifying the subtype of AML can be very important, as it can affect patient outcomes and help to identify the best treatment plan. For example, the acute promyelocytic leukemia (APL) subtype is often treated using drugs that are different from those used for other subtypes of AML.[2,3,8] There have been two systems followed to subtype AML. The French-American-British (FAB) classification for AML system, which relies on the microscopic analysis of the cells. While the World Health Organization (WHO) classification of AML includes genetic abnormalities common to AML subtypes, such as chromosomal translocations, specific gene fusions and gene mutations.[2,3]

Prognostic factors for AML

The subtype of AML can be important in helping to determine a person's prognosis; however, other factors can also affect why some patients with AML have a better outlook than others. Prognostic factors help clinicians to determine a person's risk of relapse/recurrence after treatment, and if they should get intensive treatment.[2] The patient's age, clinical presentation, cellular markers and chromosomal abnormalities observed via cytogenetics and molecular mutations all contribute to the prognosis of the patient.[2,3]

AML cells can have many kinds of chromosome changes, and the National Comprehensive Cancer Network (NCCN) guidelines group chromosome abnormalities into three categories of risk stratification: favorable, intermediate and poor/adverse.[1,8]

Favorable abnormalities[8]

- t(8;21)(q22;q22.1); RUNX1-RUNX1T1
- inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11
- Biallelic mutated CEBA
- Mutated NPM1 without FLT3-ITD or with FLT3-ITD (low allelic ratio)

Intermediate abnormalities[8]

- Mutated NPM1 and FLT3-ITD (high allelic ratio)
- Wild-type NPM1 without FLT3-ITD or with FLT-ITD (low allelic ratio) (without adverse-risk genetic lesions)
- t(9;11)(p21.3;q23.3); MLLT3-KMT2A
- Cytogenetic abnormalities not classified as favorable or adverse

Poor/adverse abnormalities[8]

- t(6;9)(p23;q34.1); DEK-NUP214
- t(v;11q23.3);KMT2A rearranged

- t(9;22)(q34.1;q11.2);BCR-ABL1
- inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2);GATA2,MECOC M(EV11)
- -5 OR DEL(5q);-7; -17/abn(17p)
- Complex karyotype, monosomal karyotype
- Wild-type NPM1 and FLT-ITD (high allelic ratio)
- Mutated RUNX1
- Mutated ASXL1
- Mutated TP53

Treating AML patients

For many years, the standard of care of for AML patients has been chemotherapy with the possibility of post-remission therapy that may include haemopoietic stem cell transplantation. A patient achieves remission when the signs and symptoms of cancer have lessened or are undetectable, having no evidence of disease. For AML, complete remission means, bone marrow specimens contain fewer than 5 percent blast cells, the complete blood counts are within normal limits and the patient usually demonstrates no signs or symptoms of the leukemia.

A complete *molecular* remission means there is no evidence of leukemia cells in the bone marrow, even when using very sensitive tests, such as those based on PCR (polymerase chain reaction).[2,3] Complete remission is at times difficult to achieve (as in refractory disease) or temporary, as approximately two-thirds of patients relapse after frontline therapy and most relapses occur within the first 18 months.[9]

As more information is learned about the molecular complexity of cancer, including AML, the involvement of specific genes and the proteins they express are being identified. This information is feeding the field of personalized medicine, which continues to evolve, as pharmaceutical companies work to develop and launch targeted therapies for oncology patients. For example, AML patients whose leukemia cells have specific gene mutations may benefit from advancements in personalized medicine.

In fact, 7 percent to 14 percent of AML patients have isocitrate dehydrogenase 1 (IDH1) mutations, which are associated with unfavorable prognosis in older adults, especially with a cytogenetically normal karyotype.[5] The product of mutated IDH1, is the molecule 2-hydroxyglutarate (2-HG), an oncometabolite, that has been shown to inhibit normal cell differentiation(development). Tibsovo (Ivosidenib) is an isocitrate dehydrogenase-1 (IDH1) inhibitor that decreases abnormal production of 2-HG, thus allowing normal myeloblasts to continue with normal development. With the highly targeted mechanism of action of Tibsovo, it is necessary to identify the specified patients who could benefit from this therapy. In this case, patients who are either 75 years or older, or have comorbidities precluding them from receiving intensive induction chemotherapy, or those with refractory or relapsed AML, harboring a mutation in the IDH1 gene as detected by the FDA-approved companion diagnostic, are eligible for Tibsovo.[5,10]

Additionally, between 10 percent and 20 percent of people with AML have a mutation in the Isocitrate dehydrogenase-2 (IDH2) gene, which, similarly to the IDH1 mutation, prevents myeloblasts from maturing, due to an accumulation of 2-HG.[3] Unlike standard AML therapies, that aggressively target all white blood cells, IDHIFA (Enasidenib) inhibits the mutated IDH2 gene, reducing the amount of 2HG being produced, allowing immature white blood cells to naturally mature.[3,7] As with inhibition of mutated IDH1, IDHIFA specifically targets the mutated IDH2 enzyme. Therefore, it is indicated for the treatment of adult patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) with an isocitrate IDH2 mutation as detected by an FDA-approved companion diagnostic.[7]

The field of hematology has shown significant progress in recent years, with several new drugs gaining approval for the treatment of adults with acute myeloid leukemia.[2,9] Therefore, having the right diagnostic tools to identify these treatment specific mutations (companion diagnostic), as well as distinguishing the molecular characteristics of the various subtypes of AML, is critical both for patient treatment and research. Research efforts to understand the genomic background of AML, including the mechanisms by which each subtype drives the disease phenotype, will be crucial – not only in risk stratification of AML, but also in developing novel targeted therapies.

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Myla M. Patterson, MBA, PhD, is a Senior Brand and Product Manager at Abbott Molecular. Prior to joining Abbott, she worked in Product Management and Commercialization for the past 11 years. Her industry career has included time spent at Roche Tissue Diagnostics and Leica Biosystems. She received her PhD from Meharry Medical College and her MBA from the University of Notre Dame.

Yelina Noskina, PhD, is the Global Scientific Affairs and Innovation Manager focusing on Oncology and CDx at Abbott Molecular. She has been with Abbott for over 15 years, with 10 of those years spent focused on Oncology. Her previous positions at Abbott Molecular have covered Assay Support and Laboratory Operations Management and Training. She received her PhD from Rush University in Chicago, IL.

Effectiveness of NIV fecal immunochemical test for colorectal cancer screening

By Shi Bai, MD, PhD, and Shu-Ling Fan, PhD

Colorectal cancer (CRC) is a leading cause of death among digestive diseases and the second leading cause of cancer-related death in the United States.[1] According to the American Cancer Society (ACS), the lifetime risk of developing CRC is about one in 21 (4.7 percent) for men and one in 23 (4.4 percent) for women.[2]

Several health organizations have colorectal cancer screening recommendations, including the U.S. Multi-Society Task Force (MSTF), the U.S. Preventive Services Task Force and ACS. Colonoscopy is the most frequently used screening test in the United States, and it is often performed in average-risk, asymptomatic adults 50 years and older. However, only 60-65 percent of the eligible population is currently screened, a rate that is much lower than the goal of 80 percent by 2018.[2] This alarming gap shows concerns over the test and strategy for screening.

Test methods for CRC detection

Many people experience anxiety and fear for a colonoscopy due to the need of full bowel preparation, sedation during the procedure and risk of bleeding, infection or bowel tears, which can often discourage people from having the screening done promptly—if at all. On the contrary, several other countries use annual or biennial stool blood tests or a combination of stool testing and lower endoscopy as the major screening strategy.[3]

The stool blood tests detect "occult blood," meaning blood that cannot be seen with the naked eye. Although stool occult blood may come from several possible causes, one important cause is the presence of polyps or cancers in the digestive tract. Two tests are designed to detect occult blood in stool. Each is designed to detect hemoglobin in red blood cells, but different components of the molecule.

The fecal immunochemical test (FIT)

FIT detects the globin protein of hemoglobin, specifically in humans. It does not detect globin from non-human blood, such as beef and other meats. Moreover, it can specifically identify bleeding from the lower digestive tract. (Hemoglobin from the upper digestive tract bleed would be broken down before it reaches the lower digestive tract.) FIT is considered more specific and sensitive than the guaiac-based test.

The guaiac-based test

It measures the heme (non-protein) part of hemoglobin from blood, which is common in blood from all sources. The method cannot distinguish the source of blood (food vs body) or site of bleeding (upper vs lower digestive tract). It may also be interfered with by some foods and medications. It is, therefore, less specific than the FIT for the detection of bleeding from the colon. Due to the low, single-application sensitivity, more than one specimen is usually required.

Method	Detecting	Specific for	Interferences
FIT Testing	Human hemoglobin Protein	Lower digestive track	Not found
Quaiac-based Testing	Heme	Can't distinguish bleeding location	Other sources of heme (i.e. beef)

Table 1. Comparisons between the FIT and Quaiac-based testing.

Figure 1. Adding the run buffer to develop the result lines.

Study: FIT versus colonoscopy

A recent study conducted by Indiana University School of Medicine and the Regenstrief Institute provides the strongest evidence to date to support recommendations that average-risk patients can safely opt for a non-invasive, easy-to-use FIT test instead of colonoscopy.[4]

The study reviewed and analyzed the findings from 31 colon cancer-screening studies with a total of 120,255 asymptomatic, average-risk adult participants who received FIT and a follow-up colonoscopy. "Average risk for developing colon cancer" is defined as having no family history of colon cancer, no personal history of inflammatory bowel disease, and no previous colon cancer or precancerous polyps (for example, advanced adenomas).

FIT has demonstrated that for the average-risk adults, it had a moderate to high detection rate for colorectal cancer when compared to colonoscopy, the reference method. Sensitivity (true positive rate) in detecting colorectal cancer ranged from 71 percent to 91 percent, based on various thresholds of blood amount present in stool. It has an even higher specificity or true negative rate. FIT was able to rule out colorectal cancer 90-95 percent of the time when colonoscopies were negative. FIT sensitivity and specificity of detecting advanced adenomas

in the colon or rectum were lower, but many of these benign polyps almost never advance into cancer.

The lead author, Dr. Imperiale, said, "Our analysis finds that FIT is a good 'pre-screening' test for average risk, asymptomatic adults, saving them hassle and the U.S. healthcare system costs." Furthermore, "If annual FIT results remain negative, it buys you time until a colonoscopy may be required, and it could be the case that a colonoscopy for screening may never be necessary or required."

This study warrants for more information to be shared with patients and healthcare practitioners about the use of annual FIT for colorectal cancer screening. It also demonstrates that FIT is not a "second-best" or less than "gold standard" strategy for average-risk individuals than colonoscopy. FIT might also be a better option for colorectal cancer screening in people under 50 years old, not only because colonoscopy is unlikely to be covered by insurance for this younger population, but also with the alarming 51 percent increase in colorectal cancer in this population since 1994.[2]

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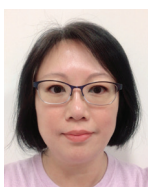
(SB) Shi Bai, MD, PhD, is the chief resident of the Department of Pathology at University of Massachusetts (UMass) Memorial Medical Center. Her research focus is diagnosis of cancer and non-cancer diseases based on microscopic and biomedical examinations.



(SF) Shu-Ling Fan, PhD, , is the director of clinical laboratories and point-of-care testing at UMass Memorial Medical Center, Worcester, MA. Her research focus is biomarker development for disease diagnosis. She is fully committed to providing quality results to support clinical diagnosis.

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INDICATION OF USE
Abbott RealTime IDH1 is indicated as an aid in identifying acute myeloid leukemia (AML) patients with an isocitrate dehydrogenase-1 (IDH1) mutation for treatment with TIBSOVO® (ivosidenib).

LIMITATIONS OF THE PROCEDURE FOR IDH1 ASSAY
Abbott RealTime IDH1 is for use with human blood (EDTA) and bone marrow aspirate (EDTA) specimens only. A "Not Detected" result does not preclude the presence of IDH1 mutations in the specimen. Assay results may be affected by inadequate specimen integrity, mutation content in the sample, and amount of amplifiable DNA. Abbott RealTime IDH1 is designed to detect IDH1 R132C, R132H, R132G, R132S, and R132L mutations. Specimens with results reported as "Not Detected" may contain mutations that are not targeted by the assay.

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Abbott RealTime IDH2 is indicated as an aid in identifying acute myeloid leukemia (AML) patients with an isocitrate dehydrogenase-2 (IDH2) mutation for treatment with IDHIFA® (enasidenib).

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COVID-19 TEST UPDATES

Current test options offer first wave of virus detection.

As the first wave of the novel coronavirus (2019-nCoV) arrived on the shores of Washington state, the need for rapid infection detection arrived as well. Since that time, governmental agencies such as the CDC, FDA and WHO stressed the importance of having accurate and fast diagnostic test options that could meet growing concerns and growing cases of what has become known as COVID-19.

With this in mind, many diagnostics companies shifted some in-house priorities and dedicated personnel to creating RT-PCR and/or antibody tests that could offer some relief to increased patients and demands for test results that could confirm or negate suspected infections.

While many diagnostics companies worked hard to be the first to cross the industry finish line with an FDA-approved test for nationwide distribution, additional companies worked just as hard to create the consumables and disposables required of some new tests.

The table below lists the tests that have garnered FDA approval as of April 8, with antibody tests listed separately from PCR tests. With a number of dedicated companies still working on creating first or additional tests, or who are waiting on FDA approval of a previously submitted test, we can be sure there will be more waves of test options to follow.

Company Name	Website	Name of Test	Type of Test	Platform/Application	Time to Results
A. Menarini/ Credo Diagnostics Biomedical	https://www.menarini.com/Home/Menarini-News/News/News-details/ArticleId/2664/COVID-19-Menarini-Diagnostics-kit-for-diagnosis-in-20-minutes	SARS-CoV-2 Assay Kit	POC molecular test	VitaPCR molecular testing platform	20 minutes
Abbott Diagnostics	https://www.alere.com/en/home/product-details/id-now-covid-19.html	ID NOW COVID-19	POC molecular test	Abbott ID NOW instrument	5 minutes
Abbott Molecular	https://www.molecular.abbott/us/en/products/infectious-disease/RealTime-SARS-CoV-2-Assay	Abbott RealTime SARS-CoV-2 Assay	Real-time RT-PCR test	Abbott m2000 RealTime System	470 tests/24 hours
Avellino Lab USA	https://www.avellinocoronatest.com/	AvellinoCoV2 test	Real-Time RT-PCR test	Applied Biosystems 7500 Fast Real-Time PCR System with software version 2.3.	6-24 hours
BD/BioGX	https://www.bd.com/en-us/company/news-and-media/press-releases/bd-biogx-announce-fda-emergency-use-authorization-submissions-for-new-covid-19-diagnostics-for-use-in-us	SARS-CoV-2 test	Rapid diagnostic test	BD MAX system	3 hours
BGI Americas (A subdivision of BGI Genomics)	https://www.bgi.com/us/2019-ncov-real-time-fluorescent-rt-pcr-kit-ivd/	Real-Time Fluorescent RT-PCR for Detecting SARS-2019-nCoV	Real-Time RT-PCR test	QIAamp Virus RNA Mini Kit and the Applied Biosystems Real time PCR system 7500 with software v2.0.5	3 hours
BioFire Defense (A subdivision of BioMerieux)	https://www.biofiredx.com/covid-19/	BioFire COVID-19 test	Real-time RT-PCR test	FILMARRAY 2.0 and FILMARRAY TORCH	45 minutes
Cepheid	https://www.cepheid.com/coronavirus	Xpert Xpress SARS-CoV-2 test	Real-time RT-PCR test	GeneXpert Systems	45 minutes
Co-Diagnostics	http://codiagnostics.com/products/diagnostic-solutions/logix-smart-covid19/	Logix Smart Coronavirus Disease 2019 (COVID-19) Kit	Real-Time RT-PCR test	Designed for the CoDx Box and compatible with other open systems, using the FAM and HEX channels	1 hour
DiaCarta	https://diacarta.com/products/coronavirus-test	QuantiVirus SARS-CoV-2 Test kit	Real-time RT-PCR test	Thermo Fisher (ABI) QuantStudio 5, Thermo Fisher (ABI) 7500 Fast Dx, and Bio-Rad CFX 384	2 hours
DiaSorin Molecular	https://molecular.diasorin.com/us/kit/simplexa-covid-19-direct-kit/	Simplexa COVID-19 Direct Assay	Real-time RT-PCR test	Liaison MDX real-time PCR instrument	1 hour
Emperical Bioscience	https://empiricalbioscience.com/quantiscript-one-step-rt-qpcr-kit/	QuanTASE and QuanTASE Plus One Step RT-qPCR kit	RT-qPCR kit	N/A	4 hours
GenMark Diagnostics	https://www.genmarkdx.com/solutions/panels/eplex-panels/eplex-sars-cov-2-test/	ePlex SARS-CoV-2 Test	Nucleic Acid Multiplex assay	GenMark ePlex System	Less than 2 hours
Gnomegen	N/A	Gnomegen COVID-19 RT-Digital PCR Detection Kit	RT-Digital PCR Detection Kit	Applied Biosystems QuantStudio 3D Digital PCR system	N/A
Hologic	https://www.hologic.com/coronavirus-test	Panther Fusion SARS-CoV-2	Real-time RT-PCR test	Panther Fusion	3 hours
InBios International	https://inbios.com/smart-detecttm-sars-cov-2-rrt-pcr-kit/	Smart Detect SARS-CoV-2 rRT-PCR Kit	Real-time RT-PCR kit	"7500 Fast Dx Real-Time PCR Instrument by Applied Biosystems CFX96 Touch Real-Time PCR Detection System (Bio-Rad) and CFX Maestro Software (Bio-Rad)"	4 hours

Join Us for an Important COVID-19 Webinar

COVID-19 Bedside Glucose Management

Risk of Ascorbic Acid and Hematocrit Interference

Interest in the antioxidant properties of ascorbic acid use in critically ill patients is growing, especially during the COVID-19 pandemic.[1,2] For these critically ill patients, severe anemia is also a common underlying condition. This webinar examines the risk of inaccurate glucose meter results due to interference from ascorbic acid and anemia. The only glucose meter that measures and corrects for these interferences will also be described.

Learning Objectives

- The use of adjunctive therapies such as ascorbic acid with COVID-19 patients
- The risk of glucose meter error due to ascorbic acid and anemia interferences
- How hospitals can protect their COVID-19 patients from glucose meter interferences

Intended Audience

- Point of Care Coordinators
- Lab Managers
- Critical Care Clinicians

Presenter

Charbel Abou-Diwan, PhD
Director, Medical
and Scientific Affairs
Nova Biomedical

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Two Webinar Times are Available

Thursday, May 28th, 1 PM Eastern Daylight Time

Thursday, June 18th, 4 PM Eastern Daylight Time

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1. Fowler AA, 3rd, et al., Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI Randomized clinical trial. *JAMA*. 2019;322:1261-1270.
2. Arabi YM et al., Critical care management of adults with community-acquired severe respiratory viral infection. *Intensive Care Medicine*. 2020;46:315-328.

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Ipsum Diagnostics	https://www.ipsumdiagnostics.com/for-physicians/supply-order-form-covid-19/	COV-19 IDx assay	Real-Time RT-PCR test	Applied Biosystems QuantStudio12 Flex (QS12) instrument with software version 1.2.2	24 hours
LabCorp	https://www.labcorp.com/coronavirus-disease-covid-19	COVID-19 RT-PCR Test	Real-time RT-PCR test	N/A	Up to 4 days
Luminex	https://www.luminexcorp.com/aries/	ARIES SARS-CoV-2 Assay	Qualitative Assay	ARIES Systems	2 hours
Luminex Molecular Diagnostics	https://investor.luminexcorp.com/news-releases/news-release-details/luminex-receives-fda-emergency-use-authorization-nxtagr-cov	NxTAG CoV Extended Panel Assay	Multiplex PCR test	MAGPIX system	96 samples/4 hours
Mesa Biotech	https://www.mesabiotech.com/coronavirus	Accula SARS-CoV-2 test	Real-time PCR test	Accula Dock and Silaris Dock	30 minutes
MicroGenDx Laboratories	https://microgendx.com/covid19/	SARS-CoV-2 Molecular Diagnostic Assay	Real-Time RT-PCR test	N/A	24 hours
NeuMoDx Molecular	https://www.neumodx.com	NeuMoDx SARS-CoV-2 Assay	Real-Time RT-PCR test	NeuMoDx 288 Molecular and NeuMoDx 96 Molecular Systems	1 hour
Novacyt/Primerdesign	http://www.primerdesign.co.uk/home	Primerdesign COVID-19 genesig Real-Time PCR assay	Real-time PCR test	"Applied Biosystem 7500 Real-Time PCR System Bio-Rad CFX96 Roche LightCycler 480 II"	1 hour
PerkinElmer	https://perkinelmer-appliedgenomics.com/home/products/new-coronavirus-2019-ncov-nucleic-acid-detection-kit/	PerkinElmer New Coronavirus Nucleic Acid Detection Kit	Real-Time RT-PCR test	Applied Biosystems 7500 Real-Time PCR System	96 samples/4 hours
QIAGEN	https://www.qiagen.com/us/products/diagnostics-and-clinical-research/infectious-disease/qiastat-dx-syndromic-testing/qiastat-dx-eua-us/#orderinginformation	QIAstat-Dx Respiratory SARS-CoV-2 Panel	Multiplexed nucleic acid test	QIAstat-Dx instrument	1 hour
Quest Diagnostics	https://testdirectory.questdiagnostics.com/test/test-detail/39433/sars-cov-2-rna-qualitative-real-time-rt-pcr?q=39433&cc=MASTER	Quest SARS-CoV-2 rRT-PCR	Real-time RT-PCR test	N/A	4-5 days
Quidel	https://www.quidel.com/molecular-diagnostics/lyra-sars-cov-2-assay	Lyra SARS-CoV-2 Assay	Real-time RT-PCR test	Applied Biosystems 7500 Fast Dx, Applied Biosystems 7500 Standard, Roche LightCycler 480, Qiagen Rotor-Gene Q.	Less than 75 minutes
Roche Molecular Systems	https://diagnostics.roche.com/us/en/products/params/cobas-sars-cov-2-test.html	cobas SARS-CoV-2	Real-Time RT-PCR test	cobas 6800/8800 Systems	96 results/3 hours
ScienCell Research Laboratories	https://www.sciencellonline.com/sars-cov-2-coronavirus-real-time-rt-pcr-rt-qpcr-detection-kit.html	ScienCell SARS-CoV-2 Coronavirus Real-time RT-PCR (RT-qPCR) Detection Kit	Real-Time RT-PCR test	Roche LightCycler 96 RT-PCR system	2-4 hours
Thermo Fisher Scientific	https://www.thermofisher.com/us/en/home/clinical/clinical-genomics/pathogen-detection-solutions/coronavirus-2019-ncov/genetic-analysis/taqpath-rt-pcr-covid-19-kit.html	TaqPath COVID-19 Combo Kit	Real-time RT-PCR test	Applied Biosystems 7500 Fast Dx Real-Time PCR instrument	4 hours

Company Name	Website	Name of Antibody Test	Type of Test	Platform/Application	Time to Results
BD (Becton, Dickinson and Company)	https://www.bd.com/en-us/company/news-and-media/press-releases/bd-biomedomics-announce-launch-of-rapid-serology-test-to-detect-exposure-to-covid-19	BD BioMedomics COVID-19 Test	Serological point-of-care test	N/A	15 minutes
Carolina Liquid Chemistries	https://www.carolinachemistries.com/2020/03/27/clc-now-offers-covid-19-rapid-screen-antibody-test/	AllTest 2019-nCoV IgG/IgM Rapid Test Cassette	Immunoassay	N/A	10 minutes
Cellex	https://cellexcovid.com/	qSARS-CoV-2 IgG/IgM Rapid Test	POC immunoassay	N/A	15 minutes
Chembio Diagnostics	https://chembiodiagnosticsinc.gcs-web.com/news-releases/news-release-details/chembio-announces-launch-dpp-covid-19-serological-point-care	DPP COVID-19	Serological point-of-care test	MicroReader 1 and MicroReader 2 analyzers	15 minutes
Diazyme Laboratories	http://www.diazyme.com/diazyme-laboratories-inc-announces-availability-of-covid-19-antibody-tests	DZ-Lite SARS-CoV-2 IgM Kit and DZ-Lite SARS-CoV-2 IgG Kit	Serological tests	DZ-Lite 3000 Plus chemiluminescence analyzer	35 minutes
Henry Schein	http://investor.henryschein.com/news-releases/news-release-details/henry-schein-announces-availability-coronavirus-2019-covid-19	Standard Q COVID-19 IgM/IgG test	POC Antibody test	N/A	15 minutes
Ortho Clinical Diagnostics	https://www.orthoclinicaldiagnostics.com/en-us/home/covid-19-antibody-test-released-by-ortho-clinical-diagnostics	VITROS Immunodiagnostic Products ANTI-SARS-CoV-2 Total Reagent Pack	SARS-CoV-2 antibody test	VITROS XT 7600 Integrated System VITROS 3600 Immunodiag. System VITROS 5600 Integrated System VITROS Eci/ECiQ Immunodiagnostic Systems	150 tests/1 hour

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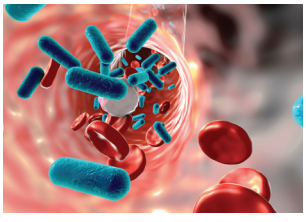
BioFire Diagnostics

Beckman Coulter Early Sepsis Indicator



With the potential to revolutionize emergency department sepsis identification, Beckman Coulter's Early Sepsis Indicator is the only hematology-based biomarker that is FDA cleared specifically for augmenting the diagnosis of sepsis. Know sooner, act faster.

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Designed for facilities, academic programs and healthcare systems, the Phlebotomy Channel streams 17 training videos wherever there's a high-speed internet connection. The platform includes CE quizzes to assess comprehension and real-time tracking reports that reflect who watched assigned videos and when. All content reflects the CLSI standards. Center for Phlebotomy Education **(CPE)**

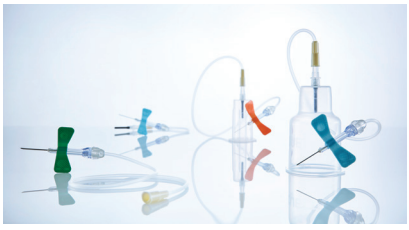
A1C Test System

The OneDraw system consists of the OneDraw Blood Collection Device, intended for the collection and stabilization of capillary blood by a healthcare professional, and the OneDraw A1C Test, intended for monitoring the long-term control of blood sugar (glucose) in people with diabetes. The system is patient-friendly and FDA-approved and provides accurate HbA1c results when compared with venipuncture.
Drawbridge Health

Serology Centrifuge

The SERO 12 is designed for blood typing, cross matching and cell washing using the same rotor as the BD Sero-Fuge. The system easily fits into a blood bank's existing workflow and allows users to set the spin time in five- or 15-second increments or save validated cycles in one of 10 presets.
Drucker Diagnostics

Blood Collection Sets



The VACUETTE safety blood collection sets are designed to increase the safety of routine venipuncture procedures. The winged blood collection needle has a safety mechanism that is activated after blood collection, as the needle is removed from the vein, for maximum protection against needlestick injuries. An audible click ensures the safety mechanism is properly engaged.
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VACUETTE® Safety Blood Collection Set

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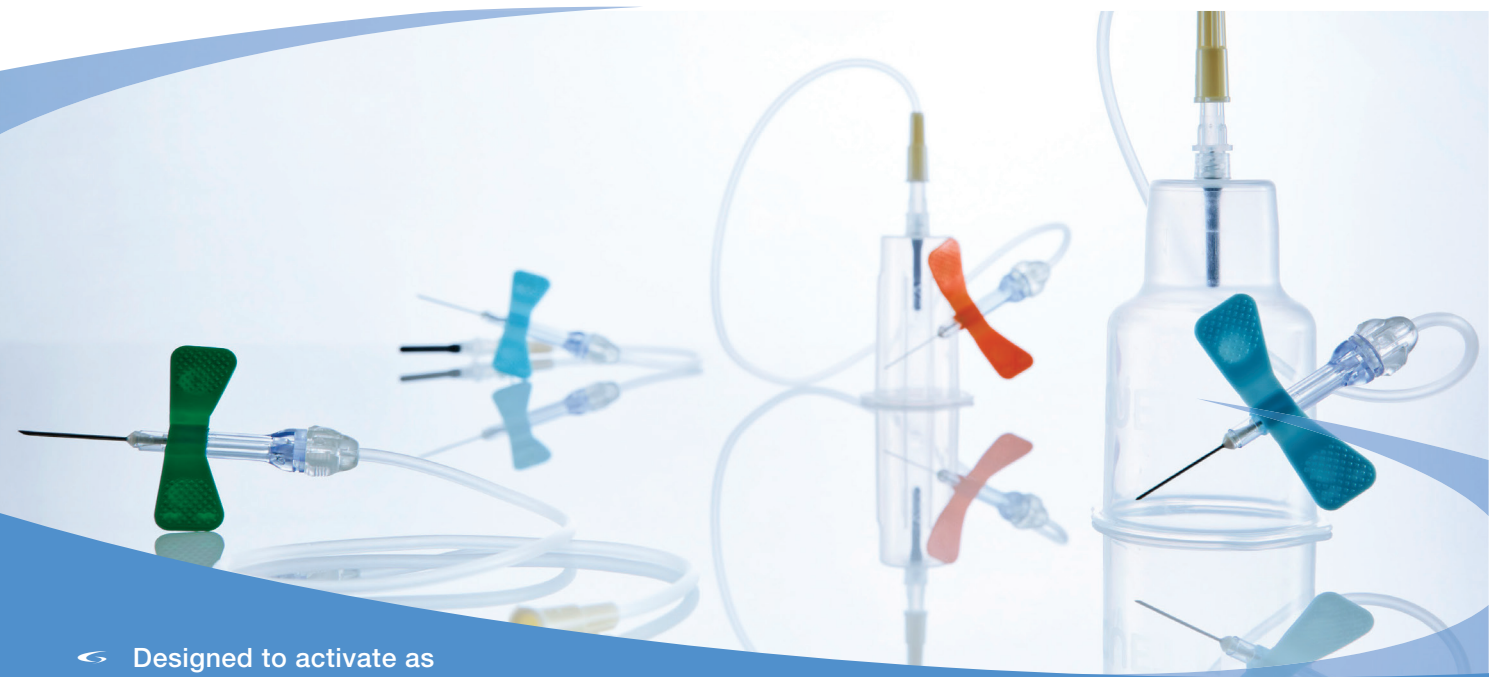

- Designed to activate as the needle is being removed from the vein
- Audible click assures the safety mechanism is properly engaged
- Clear body for 'flash' visibility

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Primera Technology

Sample Transport System

The UniTranz-RT 3ml filled vial and 6" sterile ultrafine flock swab is designed for the collection and preservation of viruses, Chlamydia, Mycoplasma and Ureaplasma. The ready-to-use system can accommodate different sample sites and is stable at room temperature, and features a leakproof, self-centering cap and a shelf life of 18 months.
Puritan Medical Products

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LABORATORY INNOVATOR

Enhancing future lab workflows with advanced analytics and AI

Dr. Christoph Moellers is vice president and general manager of **Beckman Coulter's** Workflow and Informational Technology Solutions business. In this role, he focuses on Laboratory Automation Systems and Clinical Information Management Tools. Prior to joining Beckman Coulter in 2009, Dr. Moellers worked with Olympus and Roche Diagnostics.

Early in your career, what prompted your transition from laboratory manager to a manager of systems integration?

From the very beginning of my career, I knew I wanted to work in the healthcare industry. I had a passion for helping patients, and I enjoyed the scientific aspect of work in the clinical laboratory.

However, there was one major challenge I had to face to make that dream a reality. To succeed in the laboratory in Germany, you needed a medical degree, which I did not have. Therefore, it was a natural progression for me to move from the hospital environment into an operational role within the healthcare industry. This career move allowed me to use the skills and education I already had, while still enabling me to make a difference in patients' lives.

After nearly 15 years in R&D in chemistry, how easy was it to move into IT, informatics and automation?

The world of clinical informatics is very different from the analyzer business. With informatics, the focus is on harnessing the data, discovering insights to support patient care and elevating institutional performance. Making the change and immersing myself in this field has been a very rewarding challenge.

The experience I have had designing analyzers, and my deep understanding of the laboratory's needs—especially from an analytical point of view—gave me a good, solid base from which to dive into the world of informatics and automation. This solid base of understanding, combined with the awareness of what data is critical from a patient, physician and laboratory manager perspective, really helped ease the transition for me.

How did your experience in R&D prepare you for your role in design automation systems for clinical laboratories?

Knowing the value of in vitro diagnostics for laboratory personnel has been critical for me as I moved into the world of laboratory automation. Because of my R&D experience, I also began to see the links between what happens outside of the laboratory and what happens inside of the laboratory more clearly. That's because automation can be used to solve so many problems, so it makes sense to think broadly.

For example, the steps that are involved in the pre- and post-analytical preparation of samples are so different from the analytical part of the job. Many factors that occur during the pre-analytical stage, outside the laboratory, can affect the quality of the result within the laboratory. Knowing the details and critical pitfalls of the analytical part helped me to work on the automation that could potentially resolve or mitigate those pre-analytical issues.

Relationships are important, too. In addition to my experience, my personal network within the company—and my connections in the analytical world—have been very helpful when making this move.

What aspects of designing automation and IT systems are you most involved?

As the general manager of the automation and informatics group, I am involved in all areas of the design, ranging from the early ideation stage, all the way through to the launch and post-launch activities. However, my primary focus is always at the beginning of a project to make sure that we understand the needs of our customers and address their main pain points. I also enjoy visiting customers around the world, seeing firsthand how laboratories are evolving and working to find new opportunities to advance patient care, starting in the laboratory. I consider this one of the most important responsibilities of my role.

What role will advanced analytics and AI play in the future to help lab managers improve the timeliness and accuracy of test results?

Advanced analytics will, I believe, be a key driver of laboratory success going forward. Now more than ever, the laboratory can do so much more than just churn out fast test results at scale (although this is important, too.) Laboratories have a tremendous opportunity to deliver value throughout the patient care continuum, with insights that can drive preventative measures, optimal care and improved cost control.

We see this already in several areas, such as sepsis detection and acute myocardial infarction. In both cases, early detection is critical for the success of therapy. I am excited by the promise of novel sepsis biomarkers, such as monocyte distribution width, which can give clinicians early insight into the possibility of sepsis in the emergency department, with a routine complete blood count with differential test. True high-sensitivity troponin assays can now help clinicians rule in or rule out a severe cardiac issue in just 60 minutes.

I also firmly believe that artificial intelligence (AI) will help laboratory managers and clinicians make better decisions for their patients. One key area of artificial intelligence that may play an important role is in the field of oncology. Here, artificial intelligence could be used to optimize the treatment of cancer patients, based on laboratory data combined with visual data from various scans.

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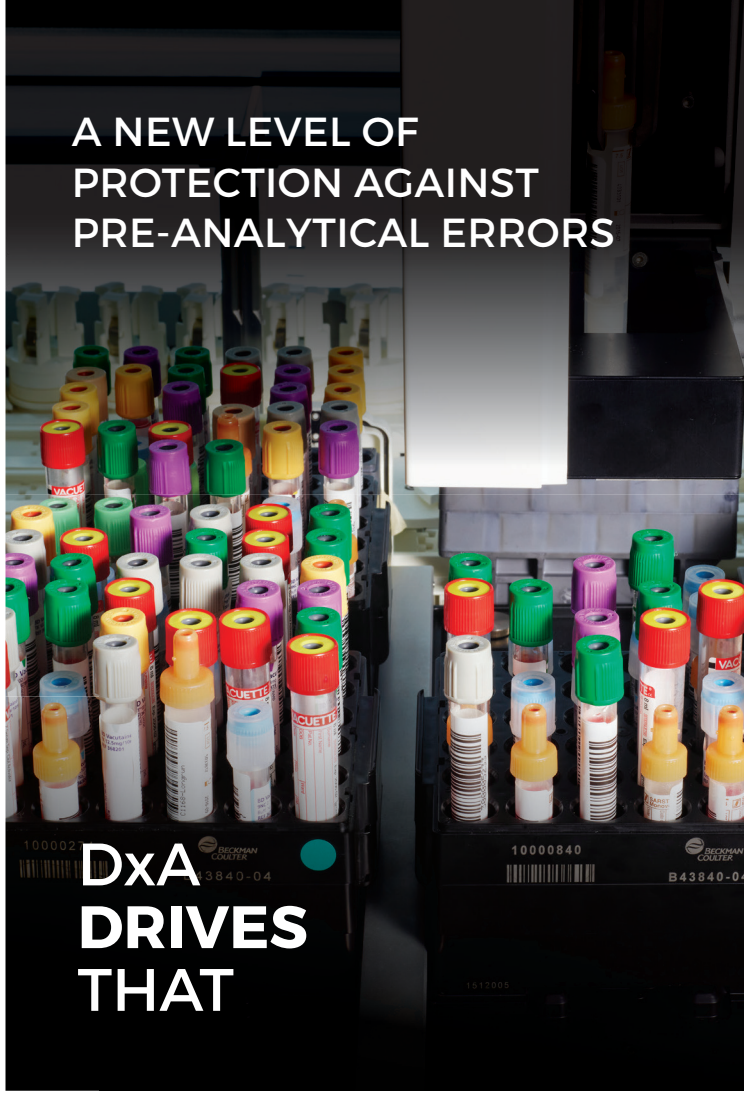

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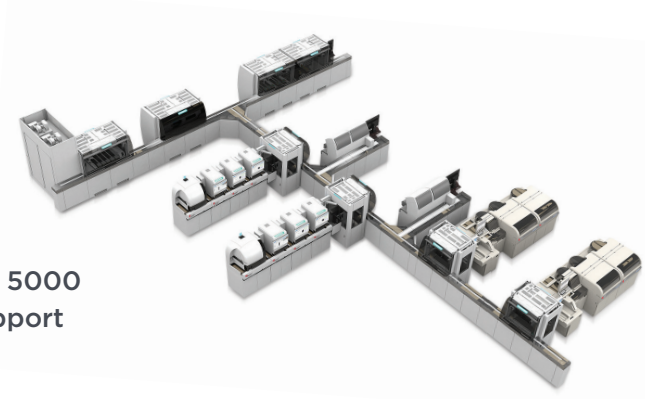

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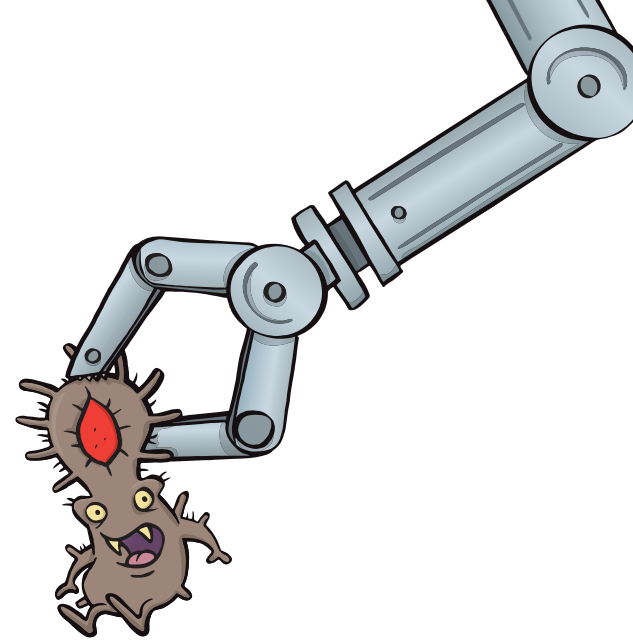

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