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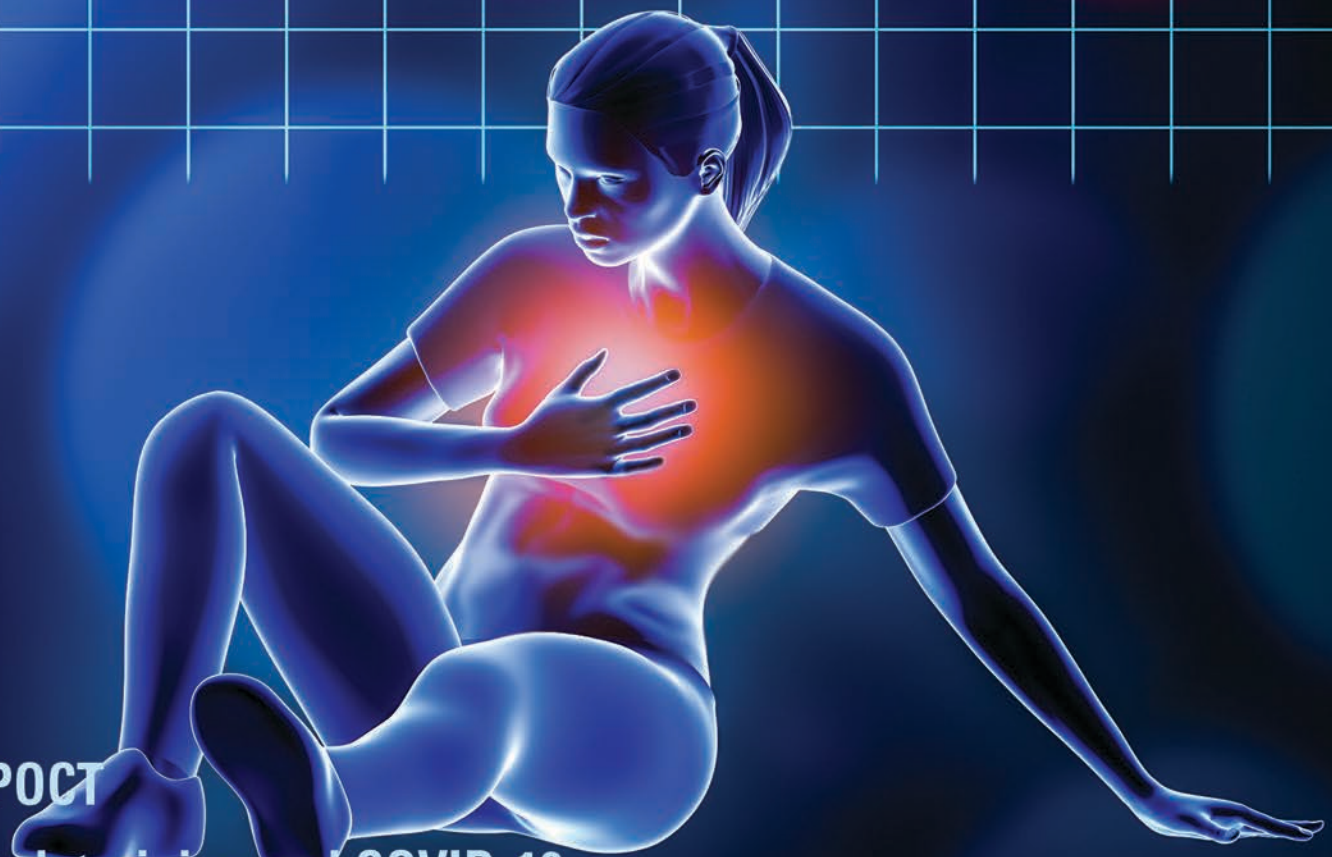

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Reference: 1. Compared with other high-throughput, fully automated systems. U.S. Food and Drug Administration. SARS-CoV-2 Reference Panel Comparative Data. Last reviewed December 07, 2020. Accessed February 23, 2021. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-refere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

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What can labs do to assess vaccine-induced blood clots with low platelets?

By Linda Wilson
Senior Editor

Vaccines from AstraZeneca and Janssen Pharmaceuticals are associated with a risk of a rare and severe blood clot occurring with low platelets.

This is something labs should be prepared for – although the likelihood of being called on to assist in one of these cases is probably minimal.

The issue first arose in the United Kingdom earlier this year when health officials noted cases of the rare blood clots in people who had received the AstraZeneca vaccine (now known as Vaxzevria, which is not authorized for use in the United States). Both the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom and the European Medicines Agency (EMA) reviewed the cases, decided the benefits of the vaccine outweighed the risks, and vaccinations continued.

The issue arose again this spring with the COVID-19 vaccine from Janssen Pharmaceuticals, a division of Johnson & Johnson. In this case, the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) recommended a pause in the use of the vaccine while the agencies weighed the evidence. The EMA followed a similar course. In these cases, the organizations also concluded that the benefits of the vaccine outweighed the risk, and the use of the Johnson & Johnson COVID-19 vaccine has resumed.

The cases in question involve severe blood clots that occur mostly at unusual sites, such as in veins in the brain (cerebral venous sinus thrombosis, CVST), the abdomen (splanchnic vein thrombosis), and in arteries. The cases are usually accompanied with low levels of blood platelets, or thrombocytopenia, according to the EMA.

The EMA also said one explanation for the combination of blood clots and low blood platelets could be an immune response, leading to a condition similar to one that happens sometimes in patients treated with heparin, called heparin induced thrombocytopenia (HIT).

When the FDA and CDC initiated the pause in the use of the Johnson & Johnson vaccine, they said they wanted time to warn providers about the potential for this serious side effect and the unique treatment required for the condition, also known as thrombosis-thrombocytopenia syndrome (TTS). The typical treatment for blood clots, an anticoagulation medicine, can make the situation worse – even deadly.

What should clinicians and laboratorians do if they suspect a case of blood clots combined with low platelets in a patient after the administration of Johnson & Johnson's COVID-19 vaccine?

The CDC recommends that they obtain platelet counts and screen for evidence of immune thrombotic thrombocytopenia. They also should evaluate the patient with a screening PF4 enzyme-linked immunosorbent (ELISA) assay – just as they would for a suspected case of autoimmune HIT. If HIT testing is positive, or if it cannot be performed, the CDC recommends the use of non-heparin anticoagulants and high-dose intravenous immune globulin. The American Society of Hematology adds that tests to measure the levels of fibrinogen and D-dimer in blood also are indicated. And, of course, a hematologist should be involved from the beginning.

Some of the symptoms, which typically occur within 3 weeks of vaccination, include a severe headache, new neurological symptoms, abdominal pain, leg pain, back pain, and shortness of breath, the CDC said.

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

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Fast Facts

Deep vein thrombosis and pulmonary embolism (DVT/PE)

10 to 30%
of people will die within one month of DVT diagnosis

25%
of people who have a PE, their first symptom is sudden death

33 to 50%
will have long-term complications (post-thrombotic syndrome), such as swelling, pain, discoloration, and scaling in the affected limb

33%
of people with DVT/PE will have a recurrence within 10 years

5 to 8%
of the U.S. population has one of several genetic risk factors, also known as inherited thrombophilias, in which a genetic defect can be identified that increases the risk for thrombosis

Most common
cause of death during pregnancy is a blood clot

5x
more likely to develop a blood clot while pregnant

2x
the risk of a blood clot from having a c-section

Source: https://www.cdc.gov/ncbddd/dvt/data.html and https://www.cdc.gov/ncbddd/dvt/infographics/blood-clot-pregnancy-info.html

CDC updates SARS-CoV-2 testing recommendations

The Centers for Disease Control and Prevention (CDC) updated its recommendations for SARS-CoV-2 testing for healthcare personnel.

The CDC says people, regardless of vaccination status, should be tested if they have symptoms of COVID-19. Asymptomatic healthcare personnel with a higher-risk exposure and patients or residents with prolonged close contact with someone with SARS-CoV-2 infection, regardless of vaccination status, should have a series of two viral tests for SARS-CoV-2 infection. In these situations, the CDC recommends testing immediately and 5-7 days after exposure.

In healthcare facilities with an outbreak of SARS-CoV-2, recommendations for viral testing healthcare personnel, residents, and patients (regardless of vaccination status) have not changed. In nursing homes with an outbreak of SARS-CoV-2, healthcare personnel and residents, regardless of vaccination status, should have a viral test every 3-7 days until no new cases are identified for 14 days.

The CDC also said hospitals and dialysis facilities with an outbreak of SARS-CoV-2 should follow current recommendations for viral testing of potentially exposed healthcare personnel and patients, regardless of vaccination status.

In nursing homes, unvaccinated healthcare personnel should continue expanded screening tests as previously recommended. At other healthcare facilities, however, fully vaccinated personnel who do not have a known exposure can be excluded from screening tests.

NGS test for prostate cancer and pre-treating aortic aneurysms

Researchers at the University of Michigan Rogel Cancer Center have developed a new urine-based, multi-biomarker test to detect aggressive prostate cancer that performed better than existing biomarker tests in initial preclinical evaluations.

The Urine Prostate Seq test, or UPSeq for short, uses next-generation genomic sequencing to analyze urine collected from men following a digital rectal exam.

The team used machine learning, a form of artificial intelligence, to zero in on 15 RNA transcripts that together create a "liquid biopsy" that outperformed the standard prostate-specific antigen blood test alone, a previous test developed at U-M called Michigan Prostate Score (MiPS) and several other existing biomarker tests, according to findings published in *European Urology Oncology*.

If a man is found to have an elevated PSA level, doctors first need to determine whether it's a sign of prostate cancer, and if it is cancer, whether that cancer is aggressive. "The problem is that a patient can have multiple areas of cancer in the prostate and these areas may be different than each other," explains senior study author Simpa Salami, MD, MPH, Assistant Professor of Urology at Michigan Medicine. "Because of this, both prostate biopsies and MRI scans can miss evidence of aggressive disease. So, this urine test is designed to tell us what's really happening throughout the whole prostate."

The research team believes the test has several potential clinical applications, including early detection of aggressive cancer in men at the time of an initial biopsy, and ruling out aggressive disease in men considering active surveillance – which involves monitoring their cancer through regular physical exams, blood tests, biopsies and imaging tests, and delaying treatment until the cancer shows signs of worsening.

A different University of Michigan study investigates a genetic culprit behind abdominal aortic aneurysm (AAA), a serious condition that puts people at risk of their aorta rupturing – a potentially deadly event.

For this study, a team of Michigan Medicine researchers investigated the role of an epigenetic enzyme called JMJD3 in the development of AAAs. They found the gene was turned on in people who had an AAA and that the gene promoted inflammation in monocyte/macrophages. When they blocked the enzyme, it prevented an aneurysm from forming.

"Targeting the JMJD3 pathway in a cell specific-manner offers the opportunity to limit AAA progression and rupture," says lead author Frank Davis, MD, Vascular Surgery Resident at the Frankel Cardiovascular Center at Michigan Medicine.

"We are the first to perform an extensive single-cell RNA sequencing and gene expression analysis on human AAAs and non-aneurysmal aortic control samples," Gallagher adds.

Software package enables deeper understanding of cancer immune responses

Researchers at the Bloomberg-Kimmel Institute for Cancer Immunotherapy

at the Johns Hopkins Kimmel Cancer Center have developed DeepTCR, a software package that employs deep-learning algorithms to analyze T-cell receptor (TCR) sequencing data.

T-cell receptors are found on the surface of immune T cells. These receptors bind to certain antigens, or proteins, found on abnormal cells, such as cancer cells and cells infected with a virus or bacteria, to guide the T cells to attack and destroy the affected cells.

DeepTCR is a comprehensive deep-learning framework that includes both unsupervised and supervised deep learning models that can be applied at the sequence and sample level.

DeepTCR will enable investigators to study the function of the T-cell immune response in basic and clinical sciences by identifying the patterns in the receptors that confer the function of the T cell to recognize and kill pathological cells.

The software package, which employs a type of deep-learning architecture called a convolutional neural network, provides users the ability to find T-cell sequencing patterns that are relevant to a specific exposure, like a flu infection, a cancer or an autoimmune disease.

AMP urges caution in applying Ct values in clinical practice

The Association for Molecular Pathology (AMP) and the Infectious Diseases Society of America (IDSA) urge caution in the use of SARS-CoV-2 PCR cycle threshold (Ct) values for clinical decision-making.

"This all may change in the future based on expanded development and standardization of test methods and more robust clinical data, but at the current time, routine use of Ct values to inform clinical decisions is not advised," said Blake W. Buchan, PhD, D(ABMM), who is a member the AMP Clinical Practice Committee (Infectious Diseases Subdivision) and Associate Professor in the Department of Pathology at the Medical College of Wisconsin.

He notes that current real-time PCR tests for SARS-CoV-2 are designed as qualitative assays that generate a binary result of "positive" or "negative."

"Some of the tests also generate and report a cycle threshold (Ct) value, referring to the number of PCR cycles required to amplify the targeted viral nucleic acid to a detectable level, Buchan wrote. However, "there are no commercially available molecular tests for SARS-CoV-2 that have data supporting an indication to report quantitative results, including Ct values."

Many factors could impact the precision of the Ct values, he said, such as the use of different specimen collection devices, specimen types, nucleic acid extraction methods, genomic targets, and RT-PCR chemistries.

"Reporting Ct values for public health or epidemiologic studies may be important to the continued research and understanding of SARS-CoV-2 infection and transmission dynamics. However, caution is urged in reporting these values formally into the medical record," he wrote.

STDs at record high for 6th year in a row

The CDC reported a record high for sexually transmitted diseases (STDs) in 2019 for the sixth year in a row. Three most reported STDs were chlamydia, gonorrhea and syphilis, with nearly a 30% increase from 2015. Cases of syphilis among newborns nearly quadrupled.

In 2019, STD rates:

- For African American or Black people were 5-8 times that of non-Hispanic white people.
- For American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander people were 3-5 times that of non-Hispanic White people.
- For Hispanic or Latino people were 1-2 times that of non-Hispanic white people.

The study also found that gay and bisexual men make up nearly half of all 2019 primary and secondary syphilis cases. It also found that young people 15–24 years old make up 61% of chlamydia cases and 42% of gonorrhea cases.

EMA finds possible links to blood clots with COVID-19 vaccines

The safety committee of the European Medicines Agency (EMA) concluded that unusual blood clots with low blood platelets should be listed as very rare side effects of Vaxzevria (formerly COVID-19 Vaccine AstraZeneca).

Separately, a Global Advisory Committee on Vaccine Safety from the World Health Organization (WHO) reviewed information from the EMA, the United Kingdom and others, concluding that "a causal relationship between the (AstraZeneca) vaccine and the occurrence of blood clots with low platelets is considered plausible but is not confirmed. Specialized studies are needed to fully understand the potential relationship between vaccination and possible risk factors."

The EMA also said a warning about unusual blood clots with low blood platelets should be added to the product information for the COVID-19 vaccine from Janssen Pharmaceuticals. The committee concluded these events should be listed as very rare side effects of the vaccine. However, the EMA stressed that the overall benefits of the COVID-19 vaccine from Janssen outweigh the risks.

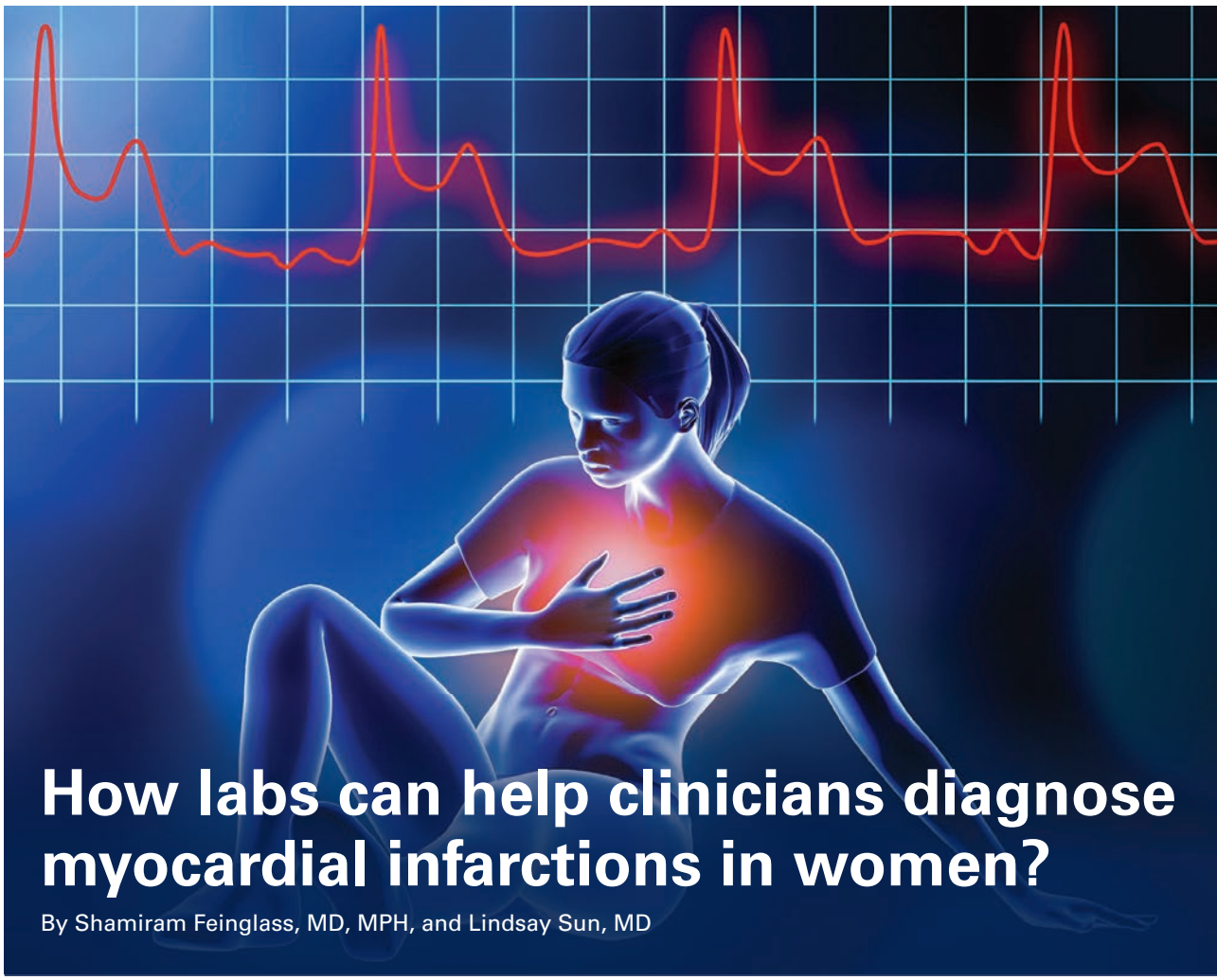
Johnson & Johnson said the company will resume shipments, as the rollout of the vaccine was temporarily paused in the United States.

The EMA committee took into consideration eight reports from the United States of serious cases of unusual blood clots associated with low levels of blood platelets, one of which had a fatal outcome. It reviewed 62 cases of cerebral venous sinus thrombosis and 24 cases of splanchnic vein thrombosis reported in the EU drug safety database (EudraVigilance), 18 of which were fatal.

All cases were people under 60 years of age within three weeks after vaccination, the majority in women. Specific risk factors have not been confirmed.

THE EMA's committee noted that the blood clots occurred mostly at unusual sites, such as in veins in the brain (cerebral venous sinus thrombosis, CVST), the abdomen (splanchnic vein thrombosis) and in arteries, together with low levels of blood platelets and sometimes bleeding. The cases reviewed were very similar to the cases that occurred with the COVID-19 vaccine developed by AstraZeneca, Vaxzevria (previously COVID-19 Vaccine AstraZeneca).

One plausible explanation for the combination of blood clots and low blood platelets is an immune response, leading to a condition similar to one seen sometimes in patients treated with heparin, called heparin induced thrombocytopenia, HIT.



How labs can help clinicians diagnose myocardial infarctions in women?

By Shamiram Feinglass, MD, MPH, and Lindsay Sun, MD

Photo Credit Adobe Stock image By Matthieu

Take a look around your lab. If you're in the United States, one of your five female colleagues is likely to die from undiagnosed heart disease.[1] Even after accounting for age, within a year of a first heart attack, survival rates are lower in women than in men. Within five years, 47% of the women will die, develop heart failure, or suffer from a stroke, compared with 36% of the men.[2]

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LEARNING OBJECTIVES

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

1. Describe the reasons why clinicians misdiagnose myocardial infarctions (MI), including the role of implicit gender bias
2. Describe the differences between men and women with regards to heart attacks
3. Describe how a high-sensitivity troponin assay can improve MI diagnoses in women
4. Recall what laboratories can do to transition to a high-sensitivity troponin assay

Despite these high numbers, doctors may be more likely to dismiss heart attack symptoms as not being heart-related in women younger than age 55.[3] In fact, regardless of age, women die of a heart attack more often than men because clinicians may not recognize heart disease in women.[4] Studies have shown that women are not only less likely to receive blood clot prophylaxis,[5] but may also receive less intensive treatment for a heart attack.[6] Women older than 50 who are critically ill are at risk of not receiving lifesaving interventions.

Several biomarkers are influenced by sex, including high-sensitivity cardiac troponin (hs-cTn), with men reportedly presenting higher concentrations than women. Accordingly, the need for sex-specific reference values has been pointed out by several authors,[7] supporting the idea that sex differences should be taken into account when approaching laboratory tests.

A prospective cohort study in the United Kingdom found that a high-sensitivity troponin assay with sex-specific diagnostic thresholds may double the diagnosis of myocardial infarction in women and identify those at high risk of reinfarction and death,[8] because women have lower cTn values, which a high-sensitivity cardiac troponin assay can detect.

Women in pain are ignored by physicians

The word hysteria originates from the Greek word for "uterus," and still holds a pervasive belief in the medical community when a woman has a health concern. Female hysteria was once

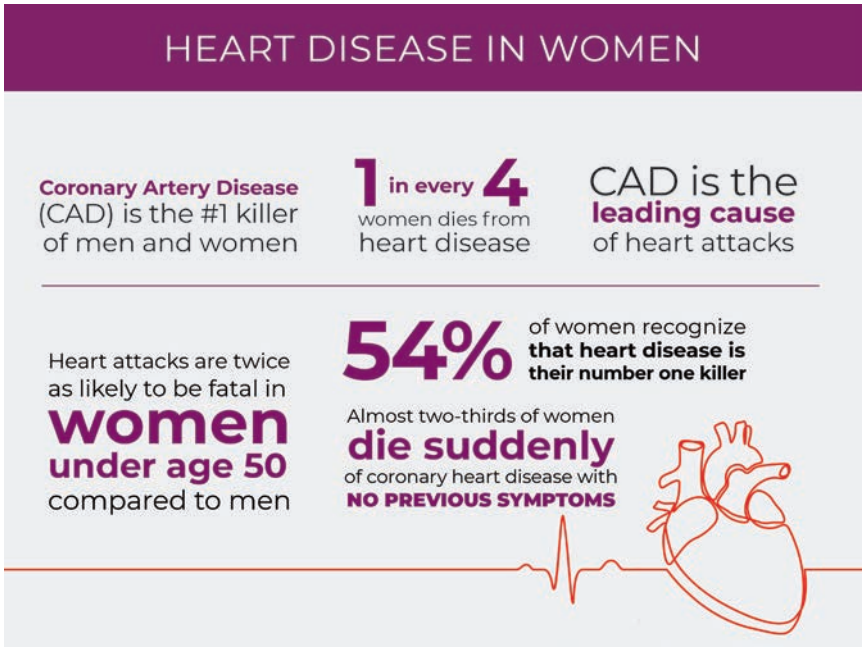

Figure 1: Heart Disease in Women
Source: *joekeenan. American heart month: Heart disease in women [infographic]. Vitaloptions.org. Published March 9, 2020. Accessed March 24, 2021. https://www.vitaloptions.org/american-heart-month-heart-disease-in-women-infographic/*

a common medical diagnosis for women, applied whenever women displayed "inappropriate" emotions, such as anxiety, anger, and even sexual desire. For centuries, it was believed that the uterus itself was the cause of a woman's "hysterical" symptoms.[9] There is more than anecdotal evidence to back up these gender discrepancies – statistics also show that women are more likely to be told their pain is "psychosomatic" than men are.[10] This implicit gender bias in medicine leads to poor outcomes for women.

The data is concerning. Women in pain are more likely than men to receive prescriptions for sedatives rather than pain medication.[11] Women wait an average of 65 minutes before receiving an analgesic for acute abdominal pain in the ER in the United States, while men wait for only 49 minutes.[12] The undertreatment of pain in women may also be due to the widely held, but false notion, that women have higher pain tolerance than men.[13] In addition, one in five women believe that a healthcare provider has ignored their symptoms and feel they are ignored within the healthcare system, blocking them from receiving the care they desperately need. For example, women who receive coronary bypass surgery are only half as likely to be prescribed painkillers, compared to men who receive the same procedure.[14]

One alarming finding is that women are seven times more likely than men to be misdiagnosed and discharged in the middle of having a heart attack, because the symptoms are missed.[15]

In general, women with suspected acute coronary syndrome are less likely to undergo a complete medical workup or receive treatment than men, and women consistently have worse outcomes.[16]

Misunderstanding a woman's heart attack

There is a perception that heart disease is a man's domain, and women are more likely to die of breast cancer. Although women tend to develop heart disease a decade later than men, they fare worse after a heart attack, in large part due to the failure to identify heart attack symptoms. In fact, 35% of heart attacks in women are believed to go unnoticed or unreported.[17]

Women exhibit different symptoms of a heart attack than men and may be told they are suffering from reflux or anxiety.

Women are underrepresented in clinical trials for heart failure, coronary artery disease and acute coronary syndrome, but are proportionately or overrepresented in trials for hypertension, atrial fibrillation and pulmonary arterial hypertension, when compared to incidence or prevalence of women within each disease population.[18] This may well be why women are missed in typical cardiac workups: if they weren't in the trials, then their common symptoms won't be represented in the clinical care pathways.

To summarize, here are the key reasons why women fare more poorly when it comes to heart attack mortality:

- Women have different heart attack symptoms than men, and clinicians and women often miss them.
- Clinicians have implicit gender bias and dismiss female symptoms as non-cardiac.
- Women were underrepresented in traditional clinical trials.

Women and men respond differently to a cardiac incident

When we think heart attack, we imagine a man clutching his chest in agony, five minutes prior having complained about pain in his left arm. Even though chest pain is still the most common sign of a heart attack for most women, studies have shown that women are more likely than men to have symptoms other than chest pain or discomfort when experiencing a heart attack or other form of acute coronary syndrome.[19]

Even though heart disease is the number one killer of women in the United States, women often chalk up their symptoms to less life-threatening conditions, like acid reflux, the flu or normal aging. This dismissal of symptoms means that women wait longer before going to the hospital, which worsens their condition and opens the door for a deadly condition known as cardiogenic shock.[20]

In the context of cardiovascular disease, a significant relationship between increasing age and stroke risk in women, compared to men, is most evident at the age of 65 years or older.[21]

Here are some key differences between men and women when it comes to heart attacks:[22]

- Women are more likely to have cardiac chest pain syndromes not directly associated with obstruction of the large epicardial coronary vessels as men do.
- On average, women are almost a decade older than men at the time of their initial MI.
- Women are less likely to be referred for coronary angiography than men.
- Women are less likely to receive fibrinolytic therapy, a percutaneous coronary intervention, or a coronary artery bypass surgery.
- In-hospital and long-term mortality after MI is higher in women than in men.
- In younger women with MI, short- and long-term mortality may be worse than mortality in younger men, even after adjusting for several prognostic characteristics.

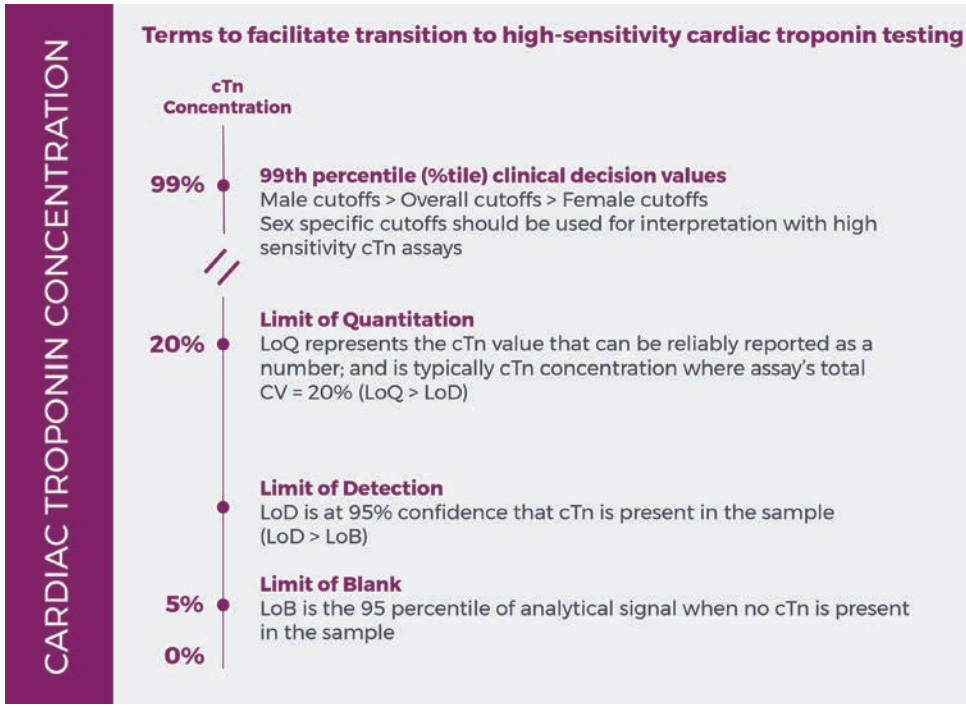

Figure 2: Terms to facilitate the transition to high-sensitivity cardiac troponin testing
Source: de Haan, J. All you need to know about troponin measurements. Acutecaretesting.org. (2020, February). https://acutecaretesting.org/en/articles/all-you-need-to-know-about-troponin-measurements.

Understanding a woman's heart attack

As noted, women often exhibit different symptoms than men. Women tend to have symptoms more often when resting, or even when asleep, than men. Stress can play a role in triggering heart attack symptoms in women.[23]

Because women do not always recognize their symptoms as those of a heart attack, they tend to show up in emergency rooms after heart damage has occurred. Also, because their symptoms often differ from men's, women might be diagnosed less often with heart disease than men.[24]

The American Heart Association[25] suggests that if women have any of the below signs, they should call 9-1-1 and get to a hospital right away:

- Uncomfortable pressure, squeezing, fullness or pain in the center of their chest, especially if it lasts more than a few minutes, or goes away and comes back
- Pain or discomfort in one or both arms, the back, neck, jaw or stomach
- Shortness of breath with or without chest discomfort
- Other signs, such as breaking out in a cold sweat, nausea or light-headedness
- As with men, women's most common heart attack symptom is chest pain or discomfort, but women are somewhat more likely than men to experience some of the other common symptoms, particularly shortness of breath, nausea/vomiting and back or jaw pain.

The sooner the patient gets to an emergency room, the sooner treatment can begin to reduce the amount of damage to the heart muscle. At the hospital, healthcare professionals can run tests to find out if a heart attack is happening and decide the best treatment.[26]

Improving care for female patients

To offer customized patient care, it is clinically important to determine myocardial injury (which is variable among reagents, age, sex, or race), which can be achieved by defining the 99th percentile upper reference limits (URL) of cardiac troponin I (cTnI).[27] An important finding in studies has been that the 99th percentile of hs-cTn assays in healthy individuals is significantly lower in women, as compared to men, in part, related to the smaller size of women's hearts.[28] Sex-specific 99th percentiles are recommended for defining abnormal cTnI concentrations, especially for hs-cTn assays; otherwise, acute myocardial infarction may be underdiagnosed in women.[29] According to the U.S. Food and Drug Administration (FDA), the sex-specific cutoffs in the United States for women is 13.6 ng/L for women, and is 19.8 ng/L for men, or a single cutoff of 18.1 ng/L, with recommended use in conjunction with other signs and symptoms for the diagnosis of MI.[30]

Adoption of high-sensitivity cardiac troponin (hs-cTn) I or T assays has taken off around the world, including the United States. With the transition to more sensitive troponin assays comes the need to develop a consensus regarding aspects that medical systems should consider before the implementation of these assays, which differ considerably from "conventional" cardiac troponin (cTn) methods. Additionally, even within the category of hs-cTnI or T assays, there will be variability in cutoff values, sensitivity, and specificity, as well as in the way in which these tests are interpreted.[31]

Some key questions that laboratorians must answer as they transition to hs-cTn:

- Is the lab ready to provide the necessary analytical education?
- Has an assay been selected?
- Was assay performance acceptable in the local clinical lab?
- Which 99th percentile cutoff(s) will be used?
- Is the lab able to process samples within a reasonable time frame?
- Is the reporting of results integrated well with the electronic health record?

Besides the lab, the ED must also prepare itself by educating clinicians about the basic concepts of how high-sensitivity troponin differs from the previous troponin methods and understand the differential diagnosis of an abnormal hs-cTn concentration

There are many benefits of implementing high-sensitivity troponin to diagnose MI. Among patients with suspected acute coronary syndrome, hsTnI may help rule out patients sooner in acute myocardial infarction (AMI) or early diagnosis of AMI, [32] and also reclassify some unstable angina pectoris diagnoses (UAP) to myocardial infarction (MI).[33]

The hsTnI assay allows more accurate and earlier detection of MI, enabling physicians to improve patient care and outcomes.[34] More accurate diagnosis of AMI can lead to timelier and more efficient triage, more accurate therapeutic and management approaches, reduced time in the emergency department, reduced healthcare costs, reduced disease complications, and improved clinical outcomes.[35]

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More importantly, a high-sensitivity troponin assay can reduce implicit gender bias, as clinicians will have sex-based data to aid their diagnosis, instead of dismissing a woman's heart attack symptoms as anxiety. This does require a change in clinicians' behavior, ensuring they order hsTnI for women who come to their emergency room with symptoms that do not look like a typical heart attack in a man. Time is muscle, and every minute counts. Suspect an MI in women early, and you may well save a life.

REFERENCES

1. Women and Heart Disease. Centers for Disease Control and Prevention. https://www.cdc.gov/heartdisease/women.htm. Published January 31, 2020. Accessed March 21, 2021.
2. Harvard Health Publishing. The heart attack gender gap. Harvard.edu. https://www.health.harvard.edu/heart-health/the-heart-attack-gender-gap Accessed March 21, 2021.
3. Harvard Health Publishing. Clinicians sometimes misread heart attack symptoms in women. Harvard.edu. https://www.health.harvard.edu/heart-health/clinicians-sometimes-misread-heart-attack-symptoms-in-women Accessed March 21, 2021.
4. Time: women die from heart attacks more often than men. Here's why – and what doctors are doing about it. Cedars-Sinai Medical Center. Published April 5, 2019. https://www.cedars-sinai.org/newsroom/time-women-die-from-heart-attacks-more-often-than-men-heres-why--and-what-doctors-are-doing-about-it/ Accessed March 21, 2021.
5. Pietropaoli AP, Glance LG, Oakes D, Fisher SG. Gender differences in mortality in patients with severe sepsis or septic shock. *Gend Med.* 2010;7(5):422-437. doi:10.1016/j.genm.2010.09.005.
6. Vaccarino V, Rathore SS, Wenger NK, et al. Sex and racial differences in the management of acute myocardial infarction, 1994 through 2002. *N Engl J Med.* 2005;353(7):671-682. doi: 10.1056/NEJMsa032214.
7. Romiti GF, Cangemi R, Toriello F, et al. Sex-specific cut-offs for high-sensitivity cardiac troponin: Is less more? *Cardiovasc Ther.* 2019;2019:9546931. doi:10.1155/2019/9546931.
8. Shah ASV, Griffiths M, Lee KK, et al. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study. *BMJ.* 2015;350:g7873. doi: 10.1136/bmj.g7873.
9. Gaslighting in women's health: No it's not just in your head. Northwell Health. https://www.northwell.edu/katz-institute-for-womens-health/articles/gaslighting-in-womens-health Accessed March 21, 2021.
10. Lindy. Doctors don't always take women seriously, and it's an issue. Fair Care Project. Published January 7, 2020. https://medium.com/faircareproject/doctors-dont-always-take-women-seriously-and-it-s-an-issue-8085d40c7c10 Accessed March 21, 2021.
11. Calderone KL. The influence of gender on the frequency of pain and sedative medication administered to postoperative patients. Sex Roles. 1990;23(11-12):713-725. doi: 10.1007/bf00289259.
12. Fassler J. How doctors take women's pain less seriously. The Atlantic. Published October 15, 2015. https://www.theatlantic.com/health/archive/2015/10/emergency-room-wait-times-sexism/410515/ Accessed March 21, 2021.
13. Smith S. Who's Really Hurting? Virtual Mentor. 2002;4(8):virtualmentor.2002.4.8.jdsc1-0208. Published 2002 Aug 1. doi:10.1001/virtualmentor.2002.4.8.jdsc1-0208.
14. Fields I. Gender bias in health care is playing a dangerous role in COVID-19 care. Ms. Published October 15, 2020. https://msmagazine.com/2020/10/15/gender-bias-health-care-covid-19 Accessed March 21, 2021.
15. Nabel EG. Coronary heart disease in women – an ounce of prevention. *N Engl J Med.* 2000;343(8):572-574. doi: 10.1056/NEJM200008243430809.
16. Shah ASV, Ferry AV, Mills NL. Cardiac biomarkers and the diagnosis of myocardial infarction in women. *Curr Cardiol Rep.* 2017;19(5). doi:10.1007/s11886-017-0839-9.
17. Giardina EG. Heart disease in women. *Int J Fertil Womens Med.* 2000;45(6):350-357.
18. Scott PE, Unger EF, Jenkins MR, et al. Participation of women in clinical trials supporting FDA approval of cardiovascular drugs. *J Am Coll Cardiol.* 2018;71(18):1960-1969. doi: 10.1016/j.jacc.2018.02.070.
19. Heart attack symptoms in women — are they different? National Institutes of Health. Published September 30, 2015. https://www.nih.gov/news-events/news-releases/heart-attack-symptoms-women-are-they-different Accessed March 21, 2021.
20. Women get worse care for heart attack. Webmd.com. https://www.webmd.com/heart-disease/news/20200929/women-get-worse-care-for-heart-attack Accessed March 21, 2021.
21. Marzona I, Proietti M, Farcomeni A, et al. Sex differences in stroke and major adverse clinical events in patients with atrial fibrillation: A systematic review and meta-analysis of 993,600 patients. *Int J Cardiol.* 2018;269:182-191. doi: 10.1016/j.ijcard.2018.07.044.
22. Canto JG, Goldberg RJ, Hand MM, et al. Symptom presentation of women with acute coronary syndromes: myth vs reality: Myth vs reality. *Arch Intern Med.* 2007;167(22):2405-2413. doi. 10.1001/archinte.167.22.2405
23. Heart disease in women: Understand symptoms and risk factors. Mayoclinic.org. Published October 4, 2019. https://www.mayoclinic.org/diseases-conditions/heart-disease/in-depth/heart-disease/art-20046167 Accessed March 21, 2021.
24. Szabla M. Women and heart disease. Mayo Clinic. Published February 16, 2021. https://www.cpaawa.org/2021/02/16/women-and-heart-disease-blog-post/. Accessed March 21, 2021.
25. Heart attack symptoms in women. *J Okla State Med Assoc.* 2012;105(2):66-67.
26. Heart attack symptoms, risk, and recovery. Centers for Disease Control and Prevention. Published January 12, 2021. https://www.cdc.gov/heartdisease/heart_attack.htm Accessed March 21, 2021.
27. Kim S, Yoo SJ, Kim J. Evaluation of the new Beckman Coulter Access hsTnI: 99th percentile upper reference limits according to age and sex in the Korean population. *Clin Biochem.* 2020;79:48-53. doi: 10.1016/j.clinbiochem.2020.02.005.
28. Giannitsis E, Kurz K, Hallermayer K, Jarausch J, Jaffe AS, Katus HA. Analytical validation of a high-sensitivity cardiac troponin T assay. *Clin Chem.* 2010;56(2):254-261. doi: 10.1373/clinchem.2009.132654.
29. Clerico A, Zaninotto M, Ripoli A, et al. The 99th percentile of reference population for cTnI and cTnT assay: methodology, pathophysiology and clinical implications. *Clin Chem Lab Med.* 2017;55(11):1634-1651. doi: 10.1515/cclm-2016-0933.
30. 30. Food and Drug Administration. 510(k) Substantial equivalence determination: determination. Assay only template. https://www.accessdata.fda.gov/cdrh_docs/reviews/K172783.pdf Accessed March 21, 2021.
31. Januzzi JL Jr, Mahler SA, Christenson RH, et al. Recommendations for institutions transitioning to high-sensitivity troponin testing: JACC scientific Expert Panel. *J Am Coll Cardiol.* 2019;73(9):1059-1077. doi: 10.1016/j.jacc.2018.12.046.
32. Keller T, Zeller T, Ojeda F, et al. Serial changes in highly sensitive troponin I assay and early diagnosis of myocardial infarction. *JAMA.* 2011;306(24):2684-2693. doi: 10.1001/jama.2011.1896.
33. Januzzi JL, Sharma U, Zakroysky P, et al. Sensitive troponin assays in patients with suspected acute coronary syndrome: Results from the multicenter rule out myocardial infarction using computer assisted tomography II trial. *Am Heart J.* 2015;169(4):572-8.e1. doi: 10.1016/j.ahj.2014.12.023.
34. Giannitsis E, Katus HA. Troponins: established and novel indications in the management of cardiovascular disease. *Heart.* 2018;104(20):1714-1722. doi: 10.1136/heartjnl-2017-311387.
35. Christenson RH, Peacock WF, Apple FS, et al. Trial design for assessing analytical and clinical performance of high-sensitivity cardiac troponin I assays in the United States: The HIGH-US study. *Contemp Clin Trials Commun.* 2019;14(100337):100337. doi: 10.1016/j.conctc.2019.100337.

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1. **One of _____ females is likely to die from undiagnosed heart disease.**
   - A. three
   - B. five
   - C. four
   - D. ten

2. **Within a year of a first heart attack, survival rates are _____ in women than in men.**
   - A. higher
   - B. the same
   - C. lower
   - D. significant

3. **Within five years, _____ of the women will die, develop heart failure, or suffer from a stroke, compared with _____ of the men.**
   - A. 47%, 36%
   - B. 36%, 42%
   - C. 25%, 36%
   - D. 53%, 17%

4. **Doctors may be more likely to dismiss heart attack symptoms as not being heart-related in women younger than age _____.**
   - A. 35
   - B. 65
   - C. 45
   - D. 55

5. **Regardless of age, women die of a heart attack more often than men, because clinicians may _____.**
   - A. not recognize heart disease in women
   - B. misdiagnose women as hysterical
   - C. not take into account the stress women endure
   - D. misdiagnose the symptoms as menopause

6. **Studies have shown that women are less likely to _____.**
   - A. follow up with their doctor regularly
   - B. follow strict diet advice as they should
   - C. worry about themselves, as opposed to others
   - D. receive blood clot prophylaxis

7. **Several biomarkers are influenced by sex, including _____, with men reportedly presenting higher concentrations than women.**
   - A. BRCA1
   - b. PIK3CA
   - C. high-sensitivity cardiac troponin (hs-cTn)
   - D. GDF-15

8. **The high-sensitivity troponin assay with sex-specific diagnostic thresholds may _____ the diagnosis of myocardial infarction in women and identify those at high risk of reinfarction and death.**
   - A. impact
   - B. double
   - C. triple
   - D. depend upon

9. **The word hysteria originates from the Greek word for "_____."**
   - A. laugh
   - B. history
   - C. placenta
   - D. uterus

10. **Women in pain are more likely than men to receive prescriptions for _____ rather than pain medication.**
    - A. allergies
    - B. sedatives
    - C. hysteria
    - D. anxiety

11. **Women who receive coronary bypass surgery are _____ as likely to be prescribed painkillers, compared to men who receive the same procedure.**
    - A. twice
    - B. just
    - C. a quarter
    - D. only half

12. **Women are _____ likely than men to be misdiagnosed and discharged in the middle of having a heart attack, because the symptoms are missed.**
    - A. seven times more
    - B. twice as
    - C. not as
    - D. half as

13. **There is a perception that heart disease is a man's domain, and women are more likely to_____.**
    - A. die of old age
    - B. die of breast cancer
    - C. get diabetes
    - D. hoard cats as they age

14. **In fact, _____ of heart attacks in women are believed to go unnoticed or unreported.**
    - A. half
    - B. a quarter
    - C. 65%
    - D. 35%

15. **In the context of cardiovascular disease, there are several differences between men and women—a significant relationship between increasing age and stroke risk in women compared to men is most evident at age _____.**
    - A. 49
    - B. 57
    - C. 65 years or older
    - D. 37

16. **Women tend to have symptoms _____ when resting, or even when asleep, than men.**
    - A. less often
    - B. more often
    - C. just as often
    - D. that are hard to detect

17. **_____ can play a role in triggering heart attack symptoms in women.**
    - A. An underlying genetic condition
    - B. An undiagnosed arrhythmia
    - C. Hysteria
    - D. Stress

18. **Because women do not always recognize their symptoms as those of a heart attack, they tend to show up in emergency rooms _____.**
    - A. thinking it is something else
    - B. hysterical
    - C. after heart damage has occurred
    - D. DOA

19. **According to the Food and Drug Administration, the sex-specific cutoffs in the United States for women is _____ for women.**
    - A. 13.6 ng/L
    - B. 19.8 ng/L
    - C. 18.1 ng/L
    - D. 16.3 ng/L

20. **The high-sensitivity troponin assay can reduce implicit gender bias, as clinicians will have sex-based data to aid their diagnosis, instead of dismissing a woman's heart attack symptoms as _____.**
    - A. hysteria
    - B. stress
    - C. psychosomatic
    - D. anxiety

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Speed meets sensitivity to limit infectious spread in rapid microfluidic antigen testing

By Richard H. Noel, MS

What's the difference between microfluidic and lateral flow assays? Prior to the pandemic, these were esoteric terms typically confined to conversations within the four walls of the hospital laboratory; however, with the emergence of next generation point of care testing, it's important to highlight the differences between these two technologies and what it means for SARS-CoV-2 antigen testing. In short, not all antigen assays are the same.

Lateral flow tests use passive capillary action to drive an immunochromatographic assay. Simply, in these tests, the liquid sample is absorbed throughout the nitrocellulose material, like a wick, and the reaction provides a result. Results are either read directly often by non-laboratory trained personnel with results determined by subjective observation (e.g., visually read rapid antigen flu tests), or more recently, in an effort to improve sensitivity, are coupled with a digital reader. These simple tests are cheap, portable, and provide results in about 5-15 minutes; however, notable limitations on sensitivity present challenges for SARS-CoV-2 testing. Requirements for higher concentrations of analyte to detect a positive signal constrain the sensitivity. They work well to rapidly identify infectious individuals with high viral loads, but performance is mitigated in individuals with relatively lower viral loads, but yet who may still be contagious. Hence, the proposed need for serial testing where sometimes, there will be negatives, but you'll catch the positives if testing over the course of several days.

Microfluidic tests

Microfluidic tests integrate several technologies, which until now, have only been available in sophisticated, high complexity hospital laboratories. These novel systems actively manipulate microliter volumes with nanoliter levels of precision to deliver exceptional performance at the point of care. Reagent test strips interfaced with an analyzer through printed carbon electrodes and piezoelectric benders provide precise fluidic control to mix specimens. The microfluidic architecture can not only control mixing to accelerate reaction kinetics, but also control the analytical environment by washing away residual specimen. This enables liquid-free analysis to improve the resolution of the optical engine, enhancing the limit of detection (LoD) to

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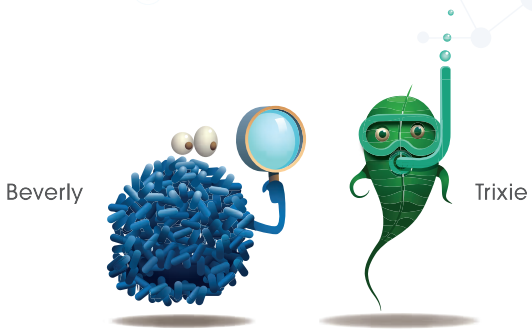

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ranges usually reserved for high-complexity instrumentation and test kits. These tests also precisely control reaction times and temperatures. Reaction times in microfluidic systems are much quicker than conventional devices due to the smaller dimensions of the systems, leading to a shorter diffusion time for any given molecule.[1] Integrating these assets onto a single test strip provides the potential to revolutionize POCT by bringing the technology out of the conventional hospital laboratory and into the clinic, closer to the patient. This empowers uncompromised testing, where patients are seen, rather than sending a sample to be run elsewhere.

Microfluidic test strips are designed on similar principles as lab analyzer systems to deliver laboratory comparable performance across a number of parameters in a portable, easy to use, point of care solution. The SARS-CoV-2 Antigen tests are designed to detect the presence of nucleocapsid protein (N) at lower concentrations than what is typically feasible on POC lateral flow platforms. These high sensitivity, Rapid Microfluidic Immunoassays (RMI) have important implications in terms of how, where, and when a test can be used for pandemic control. We need rapid, accurate testing to fight COVID-19, because organizations, doctors, and individuals need to know if people are infectious, even when they are not symptomatic. But neither PCR nor conventional lateral flow antigen tests are optimized to meet those needs. The exceptional analytical sensitivity from RMI for SARS-CoV-2 nucleocapsid antigen is just right: it is fast and accurate, without being so sensitive it picks up remnant RNA from previously infected — but now recovered — non-infectious individuals.[2] Recovered patients can continue to have SARS-CoV-2 RNA detected in their upper respiratory specimens for up to 12 weeks after symptom onset.[2,3,4] Investigation of 285 "persistently positive" adults, which included 126 adults who had developed recurrent symptoms, found no secondary infections among 790 contacts to these case patients. Efforts to isolate replication-competent virus from 108 of these 285 case patients were unsuccessful.[2]

Winning the war against the pandemic will require extinguishing the wildfire of infectious spread. Tests that rapidly and accurately identify contagious spreaders, while being sufficiently inexpensive and easy to execute to allow frequent testing, can be a powerful tool for breaking the chain of transmission.[5] PCR is the premier finder of nucleic acids, bar none. But molecular detection does not necessarily denote the presence of recoverable infectious virus. Recent data from a lab at Johns Hopkins suggests that antigen tests correlate better with viral culture, perhaps the best proxy for infectivity, than PCR.[6] Recovering patients that are no longer infective can actively shed viral RNA at a level detected by PCR for weeks or possibly months.[7] Detecting all viral shedders is an expensive luxury that does not necessarily serve society's best interests.

Lateral flow antigen tests

Antigen-based testing, by contrast, could help to rapidly identify people who have high levels of virus — those who are most likely to be infectious to others — and isolate them from the community. However, not all antigen tests are the same. Lateral flow antigen (LFA) tests provide rapid results, but may not provide sufficient sensitivity to cover the full range of infectivity, which can be as long as 10 days. LFA tests are authorized for use in patients presenting within five to seven days post-symptom onset, depending upon the vendor. In a study published in the NEJM, viable virus was isolated from specimens collected up to nine days after the first evidence of typical symptoms;[8] while in other studies, there is evidence that some individuals continue to spread the virus up to eight to ten days after showing symptoms.[9] Serial testing algorithms compensate for sub-optimal sensitivity in an asymptomatic population, but negative results may provide a false sense of security to asymptomatic or presymptomatic individuals. In certain settings, this may lead to additional contacts, before the second test is performed 2-3 days later.

Conclusion

What society really needs is a point of care test sensitive enough to adequately cover the broadest range of contagiousness, provide results quickly, and at a reasonable cost, enabling widespread implementation across a variety of use-cases. Unlike lateral flow antigen tests, the emerging, next-generation microfluidic technologies simplify, scale down, and integrate techniques used in laboratory analyzers to provide lab-comparable diagnostic tests that can be easily used in community care settings. One system is authorized by FDA for emergency use during the COVID-19 pandemic for use on patients presenting up to 12-days post symptom onset, has superior sensitivity over most lateral flow assays, allows for the longest testing window currently available in waived settings, and shows a high positive predictive agreement (PPA) when compared to RT-PCR.[10] The right test for *this time* catches the infectious of the COVID-19 pandemic, while minimizing false alarms.

REFERENCES

1. Convery N, Gadegaard N. 30 years of microfluidics. Micro and Nano Engineering. https://www.sciencedirect.com/science/article/pii/S2590007219300036. Published January 26, 2019. Accessed May 1, 2021.
2. Interim gGuidance on dDuration of iIsolation and pPrecautions for aAdults with COVID-19. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html. Published February 13, 2021. Accessed May 1, 2021.
3. Li N, Wang X, Lv T. Prolonged SARS-CoV-2 RNA shedding: Not a rare phenomenon. Wiley Online Library. https://onlinelibrary.wiley.com/doi/10.1002/jmv.25952. Published May 22, 2020. Accessed May 1, 2021.
4. Liu W-D, Chang S-Y, Wang J-T, et al. Prolonged virus shedding even after seroconversion in a patient with COVID-19. *J Infect*. 2020;81(2):318-356. doi:10.1016/j.jinf.2020.03.063
5. Mina MJ, Parker R, Larremore DB. Rethinking Covid-19 tTest sSensitivity — A sStrategy for Ccontainment. *N Engl J Med*. 2020;383(22). doi:10.1056/nejmp2025631
6. Pekosz A, Parvu V, Li M, et al. Antigen-based testing but not real-time polymerase chain reaction correlates with severe acute respiratory syndrome coronavirus 2 viral culture. *Clin Infect Dis*. January 2021. doi:10.1093/cid/ciaa1706
7. Guglielmi G. Fast coronavirus tests: what they can and can't do. *Nature*. 2020;585(7826):496-498. doi: 10.1038/d41586-020-02661-2. https://www.nature.com/articles/d41586-020-02661-2#ref-CR3. Published September 16, 2020. Accessed May 1, 2021.
8. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N Engl J Med*. 2020;382(22):2081-2090. doi:10.1056/nejmoa2008457
9. Walsh KA, Spillane S, Comber L, et al. The duration of infectiousness of individuals infected with SARS-CoV-2. *J Infect*. 2020;81(6):847-856. doi:10.1016/j.jinf.2020.10.009
10. Drain PK, Ampajwala M, Chappel C, et al. A rapid, high-sensitivity SARS-CoV-2 nucleocapsid immunoassay to aid diagnosis of acute COVID-19 at the Ppoint of Ccare: A clinical performance study. *Infect Dis Ther*. February 2021. doi:10.1007/s40121-021-00413-x

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How data analytics improves operational performance at clinical labs

By Linda Wilson

Labs are using increasingly sophisticated approaches to data analytics to improve their operations.

Most labs use what is known as descriptive analytics, which involves interpreting what has already happened. Examples include: the average lab test turnaround time yesterday or total units of red blood cells used last week.


Dennis Winsten

"If you go back 10 years, the descriptive analytics was very crude and not that many people were on board. But now, at virtually any lab, you're going to see some use of descriptive analytics. Some of it is pretty sophisticated," says Dennis Winsten, President of Dennis Winsten Associates, a consulting firm specializing in the use of information technology in laboratories.

According to *Medical Laboratory Observer's* 2021 State of the Industry survey, 77% of labs are now using analytics.[1] The same survey found that many labs are monitoring the following key performance indicators (KPIs): test turnaround time, cost per test, billable versus performed tests, staff productivity goals, medical necessity, and unnecessary tests.

"Labs are data factories, and analytics is the tool to understand what all this data is telling us. Not only does analytics shine a brighter light on the available data, but it integrates disparate data and reveals new information that leads to better insight and decision-making. All of this affects (return on investment) ROI," says Maarten van As, New Markets Development Leader at LabVantage Solutions.

More sophisticated uses of descriptive analytics can involve the use of data sources that are updated more frequently than monthly, although instantaneous data availability is rare at labs, according to Winsten, who adds that timely access to data is a critical for labs that want to improve their operational performance.

Another issue with the approach to data analytics at many labs is the use of manual steps. "Today, many labs use manual or partially manual methods to identify and track key lab metrics.

Table 1: How Labs Are Using Data Analytics to Support Lab Operations and Management

	2020	2021
We are utilizing data analytics in some aspects, and we are planning more	40%	53%
We are using data analytics for all aspects of lab management	23%	11%
We are using data analytics for some aspects, and we are not planning more	14%	13%
We are not using data analytics in any significant way, but we plan to start	14%	17%
We are not using analytics for lab management, and we have no plans to start	9%	6%

Source: MLO State of the Industry surveys, January 2020, February 2021

In addition to evaluating the traditional ROI metrics like improved turnaround time and other operational parameters, it's important for labs to consider the opportunity cost of manual analytics processes," says Ryan Stephens, Group Marketing Manager for Automation and Core Lab IT at Roche Diagnostics.

Leading indicators

At Henry Ford Health System, the Department of Pathology and Laboratory Medicine is tapping into real-time data, allowing it to monitor work in progess and then intervene to improve performance – rather than analyzing past performance to improve future performance.


J. Mark Tuthill

"One way to use analytics to support workflow is the use of leading versus lagging indicators. Lagging indicators are yesterday's data today. The classic example is yesterday's turnaround time," explains J. Mark Tuthill, MD, Division Head, Pathology Informatics at Henry Ford Health System. "Leading indicators are things that we use to tell us what is coming at the lab or what is likely to go wrong based on early information," he said. For example, three analyzers went offline today, which caused turnaround time to increase. In this case, the leading indicator is the fact that the analyzers went down – and lab managers knew this information as it was happening.

"Right now, we are trying to find all the leading indicators of value that we can," Tuthill explains. "We know leading indicators are what create the information that you're going to see in tomorrow's data."

One example is how the lab tracks samples from patients in the emergency room – where the goal is to report test results for 90% of those samples within 45 minutes.

To help achieve this performance metric, the lab monitors the progress of those samples in real time and displays the information on a large electronic screen mounted on the wall in the core lab. "If Mr. Jones' test has not been resulted at fifty minutes, he moves to the top of the screen and has a red coloration in his row. And we know that Mr. Jones' testing was delayed. If we look at the monitor, and there are seventeen rows, and they're all red, we know that we've got a little problem going on. What's the problem? Well, who knows? Maybe the line is jammed, or maybe the instrument went down," Tuthill explains.

There are seven of these boards hanging on walls in the lab, and they each display different information. In addition to the emergency department, some boards track orders for outreach physicians or the surgery department, while another board tracks the movement of couriers picking up specimens.

Tracking COVID-19 testing

Edward-Elmhurst Health, based in Warrenville, IL, sometimes uses what it calls near real-time data in analytics. For example, it refreshes data as often as hourly to monitor COVID-19 testing.

The data comes in through a dashboard, with details about whether the test is pre-procedural or not; type of test, such as high-throughput or rapid test; turnaround times; and average

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Table 2: Types of Data Analytics	
Descriptive Analytics	Analyzes past facts to answer questions about what has happened
Predictive Analytics	Analyzes past or current facts to make predictions about the future
Prescriptive Analytics	Suggests actions based on past performance, current performance or other factors

turnaround time over the last seven days. Most of the data is updated daily. However, the lab also tracks tests as they are ordered in the electronic health record (EHR), and this information is refreshed as frequently as hourly.


Mary Cluver

Mary Cluver, Service Line Director for Lab at Edward-Elmhurst Health, explains, "We know how many specimens we've received in the lab, but we really never had a grasp of how many orders were out there; meaning, how many clinician orders were being placed?"

The ability to monitor COVID-19 test orders as physicians place them has been particularly useful since September, when lab staff began collecting samples at eleven locations. Before then, the health system collected all samples for patients with symptoms (unless they came through the emergency department) at a single, outdoor location.

"It helps us predict what kind of volume we're going to have, and that was extremely helpful when we had our surge from the middle of October until the end of December," Cluver says. "We could adjust our staffing, not only to perform the testing, but to do the collections as well."

Now that testing demand is more predictable, Cluver says lab managers are no longer monitoring the information hourly; they are reviewing it daily.

About one-third of the lab's COVID-19 tests are rapid tests done at the health system's clinics, and two-thirds are PCR tests done in the lab, primarily done on high-throughput analyzers.

Enabling performance improvement

Another area in which labs use descriptive data analytics is in conjunction with quality improvement projects.

For example, Northwell Health measured the volume of blood in vials collected for blood cultures using an automated system across ten hospitals for four months to obtain baseline levels. The system repeated the measurements after it completed a 36-month educational program with providers to improve fill rates.


Joe Castagnaro

This was an important project for the health system because the sensitivity of blood cultures can be reduced by up to 50% if there is not enough blood in the vials, says Joe Castagnaro, Vice President of Lab Integration and Operations at Northwell Health, a 23-hospital system based in New Hyde Park, NY.

Incorrect culture results lead to overuse of antibiotics, exasperating antimicrobial resistance, or to underuse of antibiotics, leading to poor health outcomes.

Reimbursement also can be impacted. An incorrect fill rate, "quite frankly, could cause a patient coming through our ED to have a negative culture result. Then we find out that, in fact, the patient did have something going on, and now we have a hospital acquired infection, which will impact our reimbursement," says Castagnaro, referring to the fact that the Centers for Medicare & Medicaid Services (CMS) will not reimburse providers for the costs associated with treating some hospital-acquired infections.

For adult patients at Northwell, staff fills two vials, with an ideal fill volume of 8-10 mL per bottle, he said.

Before the improvement project, the average fill volume was 2.3 mL. After the project, the health system's average fill rate increased to 8.6 mL. The sample positivity rate for pathogens increased from 7.39% to 8.85%. The contamination rate did not change.[2]

Castagnaro says the health system continues to collect data on blood vial fill rates. "We haven't stopped because it's an important metric," he says.


Tim Bickley

Tim Bickley, MT(ASCP), MBA, CPHIMS, Vice President of Sales at Visiun, said other popular quality improvement projects at clinical laboratories involving stewardship among providers include appropriate test or blood product utilization. However, he adds that many labs struggle with implementing successful stewardship programs because they do not have analytics in place to aggregate and analyze data on over- or under-ordering by clinicians.

Advanced analytics

Despite the utility of descriptive analytics, experts say that predictive analytics and prescriptive analytics allow for even greater operational improvement, although they are not widely used in clinical laboratories. Predictive analytics involves assessing the likelihood of a future event based on a set of facts, while prescriptive analytics takes that a step further by suggesting actions.

"The level of sophistication jumps up significantly from each of these levels," Winsten says.

"Even though there's a lot of great of artificial intelligence out there, it's not widely disseminated yet."

Bickley says examples of predictive analytics in which lab data is critical include models that assess the risk of septicemia and acute kidney injury. "Labs can play a vital role in improving immediate care and patient outcomes with access to data. There are many protocols that can be automated with laboratory analytics," he says.

REFERENCES

1. Nadeau K. Lab administrators prioritize accurate and timely financial and operational performance. *Medical Laboratory Observer*. January 21, 2021. https://www.mlo-online.com/information-technology/analytics/article/21206709/lab-administrators-prioritize-accurate-and-timely-financial-and-operational-performance. Accessed May 1, 2021.

2. Khare R, Kothari T, Castagnaro, et. al. Active monitoring and feedback to improve blood culture fill volumes and positivity across a large integrated health system. *Clin Infect Dis*. 2020; 70(2): 262–268. https://doi.org/10.1093/cid/ciz198.

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The analysis of coagulation

By Marisa L. Williams

Coagulation analysis became important for my family when my then 30-year-old cousin wound up in the emergency room with a double pulmonary embolism after a two-hour car ride. Medical professionals scrambled to figure out why a woman so young would be suffering from such a diagnosis; thus, coagulation analysis answered the question, revealing a genetic clotting mutation known as Factor V Leiden.

Had it not been for this nearly tragic event, my family would have never known to be tested for this condition, and it answered the question as to why so many in the family had various blood clots over the years – as well as why many women in the family did not have any children.

Clotting disorders

Factor V Leiden is a genetic mutation where people may develop blood clots very easily. This mutation can be either heterozygous (inherited from one parent) or homozygous (inherited from both parents), with the homozygous genetic factor putting patients at risk for blood clots when in bed too long without moving, something essential for healthcare providers to know about after surgeries, for example, during the recovery process.

"The Activated Protein-C Resistance assay, or APCR, is a common screening assay for Factor V-Leiden performed in the coagulation laboratory," explained John G. Chromczak, MLS (ASCP)^{cm} SH^{cm}, Instrument Product Manager at Diagnostica Stago Inc. Some analyzers may require third-party APCR assays for

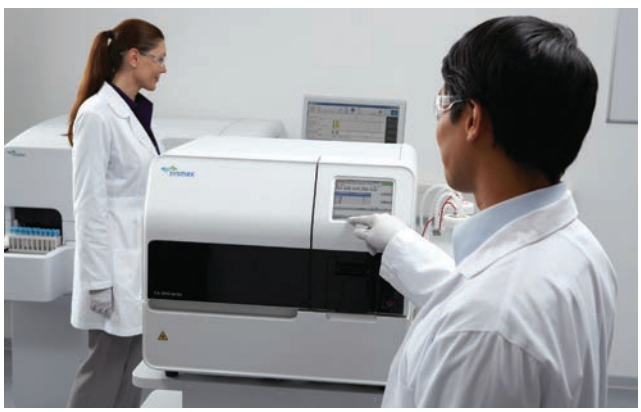

Photo courtesy of Sysmex

screenings to determine if additional genetic testing is required. "Early detection of a Factor V-Leiden mutation by a healthcare provider may reduce the probability of a patient developing a thromboembolism through the prophylactic use of anti-coagulant medications."

Public awareness about screening for clotting disorders, such as Factor V-Leiden and Lupus Anticoagulants/Antiphospholipid Syndrome, is becoming more prevalent as clinicians, laboratorians, and laboratory professionals educate patients and healthcare providers on the benefits of ordering these simple coagulation assays.

"Lupus Anticoagulants (LAs) may also cause a patient to develop blood clots; although, the name is counterintuitive. Testing for LAs involved a series of coagulation assays, such as: Stago's STA DRVV (dilute Russel Viper Venom) Screen and Confirm assays; PTT-LA, a highly lupus anticoagulant aPTT assay; and Staclot LA, a hexagonal phase reagent that neutralizes a circulation LA. Screening for LAs in the coagulation laboratory have become more popular, due to more awareness about their effect on women's health. If undiagnosed, LAs may cause a woman to experience multiple miscarriages and/or thromboembolisms," added Chromczak.

In sharing with Chromczak about my family history, he added, "like you, I've had someone close to me who struggled for years with carrying a fetus to term, and it wasn't until she was properly diagnosed that she was able to have another child. Women's Health has such a long way to go in my opinion." He shared a patient video describing the struggle: https://www.youtube.com/watch?v=B6qPRciOADs.

Blood thinners

Coagulation analysis can also be important for people taking blood thinning medications, as some blood thinners require regular laboraotry monitoring to keep the patient in the proper therapeutic range. Warafin is one such drug. Abbott[2] and Roche[3] have home-use coagulation tests for INR, which is a prothrombin time based test.

"Direct oral anticoagulation (DOAC) may interfere with aPTT test results," shared William M. Trolio, Vice President and Chief Scientific Officer at Bio/Data Corporation. Patients undergoing orthopedic procedures like knee or hip replacement surgery may be treated with heparin, Aspirin or Xarelto (rivaroxaban). Heparin therapy is monitored by aPTT test results. Aspirin therapy is often not monitored but can be followed with ADP and Arachidonic Acid induced platelet aggregation.

DOAC therapy is often used to the thrombotic risk in people that have pro-thrombotic conditions like Factor V Leiden.

"Contrary to the perception that DOAC does not affect haemostasis testing, most tests of haemostasis, including those commonly used to assess the prothrombotic status of a patient who has had a thrombotic event, are significantly affected by DOAC."Trolio added 1 PT and APTT reagents are very in their sensitivity to DOAC agents.

Antiplatelet therapy, which includes drugs like Aspirin, clopidogrel (Plavix), Prasugrel (Effient), ticagrelor (Brilinta)and ticlopidine (Ticlid), is routinely used in patients who have had thrombotic or clot caused event, such a heart attack or stroke.

There is a simple, single test device, which can determine a patient's ability to respond to clopidogrel (and similar drugs), based on the presence or absence of a genetic mutation (CYP2C19*2). About 30 % of people cannot metabolize Plavix.

You need to know what the patient's ability to respond to a drug in order to determine the proper medication choice and dose.

Coagulation analyzers do not discover genetic pathways, and some analyzers specifically analyze platelets."Platelet functions affect more than hemostasis. They are involved in cancer, cancer treatment and metastasis, sepsis, autoimmune disorders, inflammatory responses and COVID 19," explained Trolio.

He pointed out that people with high grade viruses usually have elevated D-dimer levels. "D-dimer is easy to order, but people don't order platelet function studies as much as they should."

Automation

Not all analyzers are created equal, as some smaller capacity models may not have the fully automated features of some of

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the larger bench models for optimum convenience. In **Table 1**, we compare analyzers for small, medium, and large sized labs.

Automation may be a bonus to some and a necessity to others. Lower volume labs might be fine with small, manual bench analyzers that perform basic laboratory testing, such as PT, aPTT, Fib and D-dimer. Intermediate labs may be interested in free-standing semi-automated analyzers that have a larger testing menu to include factor and hypercoagulation assays.

High volume labs may enjoy the convenience of fully automated floor model analyzers, especially when connected to a total laboratory automation system that will spin tubes to separate plasma. Fully automated systems are known for their high-throughput testing and reagent capacity to help the lab increase efficiency and turn-around-times.

"Table and floor models will pick up blood factors, but the little ones do not," explained Trolio.

When comparing coagulation analyzers, some systems are optical based while others are both mechanical and optical based, depending on the assay type (clot based vs. chromogenic vs. immunoturbidometric). Trolio explained, "if it's more sensitive, you can work up more patients. Both do the job, but both have bias."

With so many different brands on the market, Trolio advises that you get what you pay for. "Smaller companies might not have the technical support that the bigger companies offer, or their systems may not be engineered as well as the larger companies. The larger companies get more data for clearance from the FDA." Clearance from the U.S. Food and Drug Administration (FDA) does not guarantee the same performance as another brand.

For low volume labs, the Sysmex CA-104 and the Siemens BFT II would each have results within seconds of each other; just be familiar with bias and reference ranges for each.

Larger models have multiple technologies, such has having several wavelengths for coagulation, immunologic and enzymatic testing. Those are things the bench and table models might not do, and they may not connect with an LIS system; whereas, larger models may have the computer capability of connecting with LIS.

Models with a computer board, instead of a personal computer, may require changing a system upon upgrade. Embedding is a major change, as it allows for FDA notification. Some stand-alone models may still be using Windows 7 or 10. Trolio advises, "wait until the next generation of analyzers. If you buy one running on Windows 7, you might have five years. Newer models will have newer operating systems."

Lab should consider

"A coagulation analyzer brings its greatest value to the laboratory when coupled with an extensive best-in-class reagent menu for both routine and specialty assays," explained Chromczak. "Laboratories should determine the testing needs of their patient population based on healthcare provider ordering requests. The coagulation analyzer should support a robust testing menu to prepare for expanded testing needs. Reagent and consumable stability and quantity increase throughput and improve turn-around-times. Hands-on time required to maintain and run the analyzer should be aligned with the laboratory's workflow and demand. Maintenance activities should be limited, and the system should provide full traceability for all end-user activities."

"All available analyzers on the market are great systems," explained Jason Lam, Sr. Marketing Product Manager, Siemens Healthineers; still, he advised there may be questions worth asking when purchasing coagulation analyzers, such as, "how are the analyzers helping the techs be efficient and mitigating erroneous results?"

If the ultimate goal is maximizing and increasing productivity, testing, accuracy and reliability, while decreasing diagnostic errors, another question worth asking is, "how easy is it to run QC on the analyzer, and is it fully automated?"

Take into consideration response time for on-site support, remote support through software application, as well as how it can improve customer satisfaction.

Lam added, "the labs really need to evaluate what challenges in their own labs need to be overcome, and how the right fit system helps mitigate those challenges and provide the best patient results and care."

Table 1[4, 5, 6, 7]

Model	Clot Detecting Principles
Lower Volume Labs	
Bio/Data PAP-8E Platelet Aggregation Profiler	Optical
Haemonetics TEG 5000	resonance
Haemonetics TEG 6s analyzer	Viscoelastic hemostasis, resonance frequency
Siemens BFT II	mechanical and photo-optical
STA Satellite®	Viscosity (mechanical), Chromogenic, Immunoturbidometric
Sysmex CA-104	turbodensitometric photo-optical
Sysmex CA-620 and CA-660 Systems	620: opitcal; 660: optical, chromogenic, immmunologic
Total Thrombus Analysis System (T-TAS)® 01	Change in Microfluidic Pressure Waveform Gradient
Intermediate Volume Labs	
Abbott CELL-DYN RUBY	4 angle optical MAPSS Multiple Scatterplot Analysis
Instrumentation Laboratories ACL TOP 550 CTS	Optical
Hemosonics Quantra®	Viscoelastic hemostasis, Sonic Estimation of Elasticity via Resonance(SEER) Sonorheometry
STA Compact Max®	Viscosity (mechanical), Chromogenic, Immunoturbidometric
Sysmex CS-2500 System	PSI, optical, chromogenic, immunologic
High Volume Labs	
Abbott CELL-DYN Sapphire	Multi Angle Polarized Scatter Separation (MAPSS)
STA R Max®	Viscosity (mechanical), Chromogenic, Immunoturbidometric
Sysmex CS-5100 System	PSI, optical, chromogenic, immunologic

REFERENCES

1. University of Wisconsin Hospitals and Clinics Authority. Coagulation: Plavix VerifyNow Platelet Reactivity (PRU) test. UW Health. https://www.uwhealth.org/lab-test-directory/coagulation/name-125134-en.html. Accessed April 15, 2021.
2. PT/INR CARTRIDGE. PT/INR Test Cartridge | Abbott Point of Care. https://www.pointofcare.abbott/us/en/offerings/istat/istat-test-cartridges/PT-INR. Accessed April 15, 2021.
3. Diagnostics R. Roche introduces first self-testing device for Warfarin monitoring with built in Bluetooth technology. https://www.prnewswire.com/news-releases/roche-introduces-first-self-testing-device-for-warfarin-monitoring-with-built-in-bluetooth-technology-300662601.html. Published June 27, 2018. Accessed April 15, 2021.
4. TEG 5000. TEG 5000 Thrombelastograph Hemostasis Analyzer System| Haemonetics. http://teg.haemonetics.com/en-gb/teg-5000-thrombelastograph. Accessed May 3, 2021.
5. Hematology analyzers & systems. Hematology analyzers and systems | Abbott Core Laboratory. https://www.corelaboratory.abbott/us/en/offerings/category/hematology. Accessed May 3, 2021.
6. ACL TOP Family 50 Series: Instrumentation Laboratory. ACL TOP Family 50 Series | Instrumentation Laboratory. https://www.instrumentationlaboratory.com/us/en/acl-top-family-50-series. Accessed May 3, 2021.
7. cobas t 511 coagulation analyzer. Roche Diagnostics. https://diagnostics.roche.com/global/en/products/instruments/cobas-t-511.html. Accessed May 3, 2021.

	Menu/Test Parameters	Size	Weight	Maximum throughput
	Routine and Special Aggregation, Inherited Diseases; von Willebrand Factor, Ristocetin CoFactor Activity; Dual Anti-Platelet Therapy & Other Drug Induced or Acquired Dysfunctions	19.5 x 21.7 x 21.5-25.5 in	40 lb	9 tests/channel, 8 test channels
	Kaolin TEG, Kaolin TEG with Heparinase, RapidTEG™, TEG Functional Fibrinogen, TEG PlateletMapping®	11.4 in x 8.6 in x 7.0 in	12 lb	2 channels/analyzer, up to 8 channels/computer
	Viscoelastic hemostasis assessment; Kaolin TEG, Kaolin TEG with Heparinase, RapidTEG™, TEG Functional Fibrinogen, TEG PlateletMapping®	6.9 x 10.1 x 10.6 in	9.4 lb	Single patient cartridge, up to 4 channels/ cartridges
	PT; APTT; Fibrinogen; Thrombin Time, Test Thrombin, Thromboclotin®*; Factors II, V, VII, VIII, IX, X, XI, XII; LAs, LA 1, LA 2;* Thrombosis: ProC® Global*, ProC Global FV*, Protein C*	200 x 300 x 100 mm	3.8 kg	60 PT tests/hour, 30 APTT tests/hour
	PT, aPTT, Fib, D-dimer, TT, anti-Xa(UFH/LMWH), AT(functional/antigen)	27.4 x 21.1 x 25.5 in	32.6 kg	40 (test dependent)
	PT; APTT; Fibrinogen; Thrombin Time: Test Thrombin, Thromboclotin; Factors II, V, VII, VIII, IX, X, XI, XII	270 x 95 x 310 mm	2.9 kg	4 tests/run
	PT, PTT, Fib, TT, BT, Factors, Lupus, Pro C, Heparin, Antithrombin, D-dimer	22.5 x 19.5 x 19.5 in	94.6 lb	up to 60 tests/hour with simultaneous testing
	PL Chip—Platelet Function in Whole Blood	14.2 x 12.6 x 9.7 in	13.2 lb	12/Hour
	22 parameters, including WBC, RBC, HGB, MCV,PLT, HCT, RDW, PLT, MPV, RETC	19.25 x 34 x 30.25 in	232 lb	CBC + Differential: Up to 84 per hour
	RecombiPlasTin® 2G, PT-FIB HS Plus, SynthASil, APTT-SP, Fibrinogen; APS; FXIII; D-Dimer; Fibrinolysis; HIT-Ab(PF4-H)*; Antithrombin, Protein C, Free Protein S, FV Leiden (APC-R V); VWF; FVIII	43 x 32 x 29 in	324 lb	PT, 240 tests/hr; APTT, 180 tests/hr; PT/APTT, 180 tests/hr
	Clot initiation, likelihood of heparin influence, clot stiffness, fibrinogen contricution to clot stiffness, platelet contribution to clot stiffness	36 x 49 x 30 cm	16.5 kg	Single patient cartridge; complete results <15 min
	PT, aPTT, Fib, D-dimer, TT, anti-Xa(UFH/LMWH), AT(functional/antigen), dRVV screen/confirm, factor assay (intrinsic/extrinsic),vWF:ag, plasminogen, proteins C and S, reptilase	27.75 × 38.18 × 28.73 in	309 kg	140 (test dependent)
	PT, PTT, Fib, TT, BT, Factors, Lupus, Pro C, Pro S, Heparin, Antithrombin, D-dimer, Plasminogen, α2-Antiplasmin	30.6 x 35.2 x 27 in	242.5 lb	180 tests/hour, with simultaneous testing
	WBC, differential, NRBCs, PLT, RBC, Monoclonal, Reticulocytes, HGB, MCV, PLTo, RETC	30 x 48 x 32 in	375 lb	CBC: 105 per hour, CBC + RETC: 69 per hour
	PT, aPTT, Fib, D-dimer, TT, anti-Xa(UFH/LMWH), AT(functional/antigen), dRVV screen/confirm, factor assay (intrinsic/extrinsic),vWF:ag, plasminogen, proteins C and S, reptilase	49.8 x 48 x 31.6 in	238 kg	300 (test dependent)
	PT, PTT, Fib, TT, BT, Factors, Lupus, Pro C, Pro S, Heparin, Antithrombin, D-dimer, Plasminogen, α2-Antiplasmin	30.6 x 35.2 x 27 in	242.5 lb	400 tests/hour with simultaneous analysis

The role of plasma viscosity testing in managing COVID-19 disease

By Daniel Gleghorn

Plasma viscosity levels are significantly increased in patients testing positive for SARS-CoV-2, and an inexpensive, accurate test aids in identifying positive cases and monitoring disease progression. The emergence of a novel pneumonia-inducing condition was reported in Wuhan, China, in late 2019, resulting in an unprecedented global pandemic, infecting at least 140 million people and responsible for more than 3 million deaths worldwide.[1] Originally designated 2019 novel coronavirus (2019-nCOV), the World Health Organization (WHO) formally named the disease COVID-19 with the causative virus responsible being termed severe acute respiratory syndrome coronavirus (SARS-CoV-2).[2]

Symptoms range from cough, pyrexia and loss of taste/smell, to severe respiratory disorders, cytokine storm, microclot formation and multi-organ failure. Reports reveal that 20% of positive cases are asymptomatic, 14% are severe and needing medical attention, and 5% require critical care. At present, there is no blood test for virus severity.

Photo from Benson Viscometers

Traditional use of plasma viscosity

Prior to the emergence of COVID-19, plasma viscosity (PV) testing has been commonplace for many years, albeit in larger specialist referral laboratories.

Together with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), PV provides a measure of acute-phase response; essentially an early inflammatory response that is associated with an increase in plasma proteins and fibrinogen. These fundamentally provide an indirect measure of infection, inflammation and malignancy.

Plasma viscosity testing is useful in diagnosing and monitoring conditions, including temporal arteritis and polymyalgia rheumatica. In particular, it is essential to monitor PV levels regularly in cases of Waldenström macroglobulinaemia, which is attributed to an elevated production of paraproteins and can escalate to what is known as 'hyperviscosity syndrome.' This syndrome presents with neurological abnormalities, visual aberration, and mucosal bleeding. Myocardial infarction can occur if left untreated.

Hyperviscosity causes damage to the endothelium and is a known contributing risk factor for thrombosis. Determining PV levels in these patients allows for monitoring of disease progression and/or treatment success, making it vital.

Plasma viscosity versus ESR

Plasma viscosity testing has many advantages over the traditional ESR (erythrocyte sedimentation rate). Unlike ESR, PV is unaffected by anemia and polycythemia, can differentiate between protein abnormalities and inflammatory processes, and is less susceptible to pre-analytical and physiological variables. Plasma viscosity is also more stable and can be measured up to seven days after venipuncture, compared to ESR, which ideally needs to be analyzed within four hours at room temperature, or 24 hours at 4°C. This can make a huge difference for rural locations or in less-developed countries where transportation links may not be as well established. The majority of modern clinical viscometers are semi/fully automated methods, with testing taking as little as 10 minutes when the centrifugation step is taken into account. In the traditional Westergren method, analysis can take over an hour inclusive of sufficient mixing prior to analysis.

Plasma viscosity analysis also has the advantage of a uniform reference range for both sexes (1.5–1.72 mPas). Most modern viscometers perform a serum viscosity with no additional changes to the system or reagents. This can be beneficial if clinicians want to exclude the effects of fibrinogen from the result. Some also have the potential to perform a whole blood viscosity.

Plasma viscosity in critically ill patients with COVID-19

Very few publications have described the correlation between COVID-19 and its effect on the viscosity of the patient's plasma. A recent study conducted by Maier et al.[3] showed that in a small cohort of 15 critically ill COVID-19 patients admitted to an intensive treatment unit, all displayed a significantly raised PV level of 1.9–4.2 mPas (reference range 1.5–1.72 mPas).

It was also shown that there was a strong correlation between the viscosity of the patient's plasma and their sequential organ failure assessment score ($P<0.001$), which provides a prediction of mortality based on the severity of organ dysfunction.[3]

A second study conducted by Truong et al.[4] looked at the use of therapeutic plasma exchange in six patients critically ill with

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COVID-19. The pre-treatment PV levels in their selected patients were 2.6–4.2 mPas, with a median of 3.75 mPas.[4] Both of these studies show the relationship between severity of COVID- 19 and the significantly raised viscosity of the patient plasma.

Diagnostic value of PV testing for patients with COVID-19

Two of the major limitations of the previous studies were cohort size and restricting the PV measurements to only critically ill COVID-19 patients. To address these limitations, we wanted to measure the PV of all hospitalized COVID-19 patients who displayed a broad range of symptoms. The set-up was simple: measure the PV of all patients presenting to hospital with COVID-19 symptoms, then separate patients into a positive and negative group, once the polymerase chain reaction (PCR) results of their upper respiratory swabs were known. We did not want to measure the positive group against a 'normal,' healthy population.

Essentially, the question was: Could the PV alone differentiate between two unhealthy patient cohorts?

We analyzed these patients. Those patients testing positive for COVID-19 had a mean PV of 2.00 mPas, compared to the negative group having a mean PV of 1.62 mPas, which was statistically significant ($P<0.0001$).[5] We were also able to determine a cut-off PV of 1.83 mPas, which has a sensitivity of 69.6% and specificity of 98.7% for COVID-19.[5] Using plasma viscosity[5] alone, we can clearly distinguish between these two patient cohorts with relative accuracy.

Future research

There are many possible avenues for future research. Performing serum viscosity testing would eliminate the interference of fibrinogen and hopefully, provide a more sensitive method of measuring the paraprotein level in these patients. This may have the potential to measure the level of antibody titers, and act as an indirect measure of patient immune response. If so, can we predict if a patient is recovering favorably, or is disease progression worsening?

A multi-center study would enable us to understand any geographical variations, not just in respect of the ethnicity of the patient population, but also in the effect potential SARS-CoV-2 variants have on plasma viscosity levels. For example, we could address the question: Do different variants affect the viscosity of plasma in the same way, and to what extent?

It would also be beneficial to determine the PV levels of COVID-19 patients in their respective categorized symptomatic groups (i.e., mild, moderate, and severe) and, if possible, also the asymptomatic cases. Determining a PV cutoff or reference range for each group could provide clinicians with addition information as to whether the patient condition is improving or deteriorating.

Conclusion

Plasma viscosity has a role to play in the diagnostic triage of suspected COVID-19 patients, as increased serum proteins contribute to the reported hyperinflammatory and prothrombotic states. This test has the potential to be incorporated into a patient's pre-admission diagnostic workup with little additional burden to labs. For those critically ill, routinely measuring the plasma viscosity may provide additional evidence to the clinical teams on the direction the disease is taking. This may provide supplementary evidence that prompts earlier intervention or cessation of certain treatment.

REFERENCES

1. Coronavirus Resource Center. Johns Hopkins University. https://coronavirus.jhu.edu/. Accessed April 27, 2021.

2. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RD. Features, *Evaluation, and Treatment of Coronavirus (COVID-19)*. Treasure Island (FL): StatPearls Publishing; 2021. [Internet]. http://www.ncbi.nlm.nih.gov/books/NBK554776. Accessed April 27, 2021.

3. Maier CL, Truong AD, Auld SC, Polly DM, Tanksley CL, Duncan A. COVID-19- associated hyperviscosity: a link between inflammation and thrombophilia? *Lancet*. 2020; 395 (10239): 1758–9. doi: 10.1016/S0140-6736(20)31209-5.

4. Truong AD, Auld SC, Barker NA et al. Therapeutic plasma exchange for COVID-19-associated hyperviscosity. *Transfusion*. 2021; 61 (4):1029–34. doi: 10.1111/trf.16218.

5. Gleghorn DM, Orisadare O, Omer A, Lynn R, Norcliffe D, Robinson M. Diagnostic value of plasma viscosity testing for patients with COVID-19. *Int J Lab Hematol*. 2021 Apr 4. doi: 10.1111/ijlh.13532.

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Could Testing Plasma Viscosity Help Us Reduce The Impact Of COVID-19?

COVID-19 is causing the worst global pandemic in living memory. It is putting huge strain on health services around the world and has currently caused the deaths of over 3.[illegible] million people (as of [illegible]).

Research shows Plasma Viscosity (PV) is significantly increased in patients suffering with COVID-19. The inflammation caused by COVID-19 leads to hyperviscosity - a known risk factor for thrombosis. PV can be elevated as 6% above normal in severely ill patients and can also increase the risk of pulmonary embolism, stroke, heart attack and heart/organ failure.

PV has been shown to have the potential to aid clinicians in quickly categorising COVID-19 patients into groups of high and low risk of complications associated with the disease. This early warning could enable quicker intervention where needed and reduce the strain on hospital ICUs [illegible].

How Can Plasma Viscosity Help...?

PV needs a positive, predictive indicator for COVID-19?

PV needs to determine the likelihood of a patient's one day improving or deteriorating?

PV needs early warning of patients who will require severely ill, critical care treatment?

PV needs to be part of the diagnostic algorithm and to support the triage of patients?

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The need for early detection in ovarian cancer

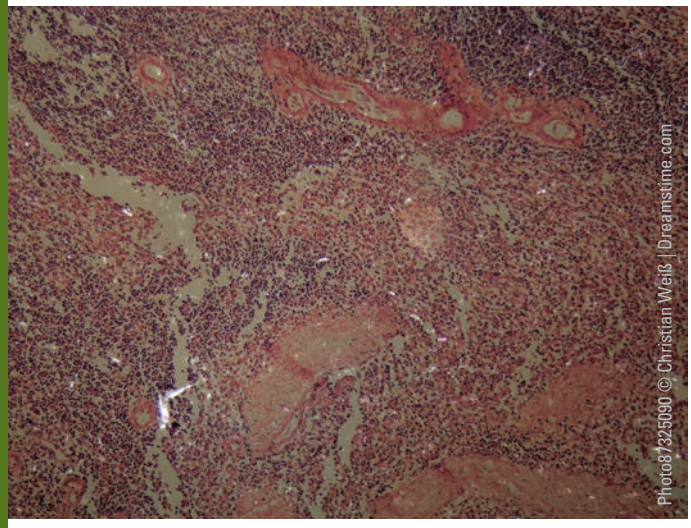
By Francesca I. De Simone

According to the American Cancer Society, it has been estimated that in 2021, in the United States alone, about 21,410 women will receive a new diagnosis of ovarian cancer (OC), and about 13,770 women will die from this disease. OC ranks 5th in cancer deaths among women, with a 1 in 78 chance of women developing this disease during their lifetime and a 1 in 108 chance of dying from the disease.[1]

While OC can affect women of all ages, it is rare in young women (under the age of 30), as it is most commonly diagnosed in women over the age of 50 (average diagnosis between 50 and 70).

OCs can be classified into three large groups: epithelial (circa 90% of tumors), germ cell (circa 5% of tumors), and specialized stromal cell (comprising the remnants). Interestingly, germ cell tumors are more common in women in their early 20s, while epithelial (EOC) tumors occur primarily in postmenopausal women, and sex cord-stromal tumors are most common in women in their 50s.

OC has been referred to as the silent killer, since most women are asymptomatic, or present with vague symptoms, including abdominal distention, urinary frequency and pain on surrounding organs from the pressure caused by the tumor mass. These symptoms are easily mistaken for other benign conditions and are, therefore, often dismissed by women as being related to aging, menopause or previous pregnancies. Because of this, more than 70% of OCs are diagnosed only once the disease is already widespread and has progressed to later stages (stage III or IV).



Cells of a human ovary with Ovarian cancer cells under the microscope.

There is a direct correlation between OC stage at presentation and survival. In stage I, when OC is limited to the ovaries, currently available surgery and chemotherapy can cure this disease in up to 90% of cases. Similarly, when the cancer has spread to the pelvis (stage II), 5-year survival reaches 70%. When the cancer has spread to other organs, such as the abdominal cavity in Stage III or outside the abdominal cavity and/or into the liver parenchyma in Stage IV, the cure rate drops to 20% or less.

It is, therefore, evident that early detection of OC could significantly reduce mortality rates and impact long-term disease control.

Diagnosis of ovarian cancer

As previously mentioned, the early detection of OC is, indeed, a crucial element for improving the patient's survival rate. According to the guideline from American College of Obstetricians and Gynecologists (ACOG) in 2016, the individual patient characteristics, physical examination findings, imaging results (including transvaginal ultrasound and Computed tomography (CT) scans), and serum marker measurements should all be used in combination for the evaluation and management of adnexal masses.

The annual or semiannual pelvic examination of women with suspected OC (from ages 25-35 years) allows physicians to feel the size, shape and consistency of the uterus. This approach may be limited due to the physician's difficulty (or sometimes impossibility) to feel any change in the uterus in early stage ovarian cancers.

Transvaginal ultrasound (TVUS) is the most common imaging test used to evaluate adnexal structures, and it helps in identifying the cancer through morphological changes associated with OC. This approach can help find a mass in the ovary, but it is not capable of differentiating between a benign mass or a cancerous one. CT scans, on the other hand, are not capable of identifying small masses, but only larger tumors.

Given the importance of early diagnosis and the promising effectiveness of biomarkers in OC triage, there has been a great effort to develop novel serum biomarkers and triage serum marker algorithms, with the precise goal of detecting OC at earlier stages, as well as improving the accuracy of referral to specialty care.

Clinical blood biomarkers currently available in the U.S. market have been shown to improve triage of women with suspected OC and, therefore, reduce mortality rates. The table below (Table 1) shows the serum protein biomarkers and algorithms currently available in the United States.

CA125

Cancer antigen 125 (or MUC16) is the most widely used biomarker for OC detection, and is often considered the "gold standard."[2] First identified in 1981, CA125 was FDA approved in 1997 as a cancer surveillance biomarker for women with a known diagnosis of OC. CA125 is, in fact, clinically used for monitoring chemotherapy responses, for detection of recurrence, and for improving clinical trial design.[3]

Interestingly, recent studies have also indicated that changes in CA125 levels may occur 18 months before clinical diagnosis, thus supporting the use of CA125 as a biomarker for early detection of OC.[4] However, there are limitations to the use of CA125 as an early detection biomarker. Specifically, although high levels of CA125 are present in 80% of advanced stage OCs and strongly correlate with specific subtypes of OC (including serous and endometrioid),[5] serum CA125 appears to be elevated in only 50% of patients with Stage I ovarian cancer.[6] Furthermore, CA125 is also elevated in common benign gynecological conditions (such as endometriosis, follicular cysts, cystadenomas, ovulatory cycle, and pregnancy), especially in premenopausal women.[3] All of these factors significantly affect CA125's sensitivity and specificity as a useful stand-alone biomarker for the early detection of OC. As a result, CA125 should be used in combination with patient data

and imaging.[7] CA125 may be more useful in conjunction with one or more other tumor biomarkers. Additional markers could play a role if, when used with CA125, they identify some carcinomas missed by CA125 (i.e., they improve sensitivity).

HE4

In 2009, the U.S. Food and Drug Administration (FDA) approved the Human epididymis secretory protein E4 (HE4/WFDC2) as a biomarker for monitoring both recurrence (HE4 detects EOCs 2 to 3 months earlier than CA125[8]), as well as disease progression.

As with most biomarkers, HE4 is expressed in both normal and malignant tissues. Specifically, its expression has been observed in the epithelium of fallopian tubes, endometrium and in the endocervical glands, as well as the epithelia of the respiratory tract, renal convoluted tubules and salivary glands.[9]

High levels of HE4 have been observed in specific subtypes of OC, such as serous (93-100%), endometrioid (80-100%), and clear-cell carcinomas of the ovary (50-83%), while it is absent in mucinous OC.[9] This may suggest the role of HE4 in differentiating and better characterizing specific histological OC subtypes.[10] Besides OC, HE4 is also elevated in other malignancies, including mesothelioma, lung, endometrial, breast, gastrointestinal, renal and transitional cell carcinomas.[11]

Interestingly, HE4 is less frequently elevated in benign ovarian tumors (both in pre- and post- menopausal women), serous cysts, teratomas, fibromas and inflammatory lesions, compared to CA125.[9]

Furthermore, HE4 (as well as ROMA) have shown to be very useful tools to exclude malignancies in endometriosis.[12]

Several studies have reported that HE4 alone is a better biomarker than CA125 alone in the diagnosis of OC.[13] Specifically, the higher sensitivity of HE4, compared to CA125, in premenopausal women[14] allows for better diagnosis of early-stage OC and borderline tumors.[15] Moreover, the higher specificity also allows the use of HE4 in monitoring OC recurrence.[16]

Interestingly, HE4 used in conjunction with CA125 yielded significantly greater sensitivity (at a set specificity) than either marker alone, or any other dual combination of markers.[15]

OVA1

Over the past few years, several algorithms have been developed to help with risk assessment of adnexal masses.

In 2009, OVA1 was approved by the FDA as a new algorithm that combines data from imaging, menopausal status, and a panel of 5 biomarkers: CA125, ApoA1, TTR, Tf and β2-macroglobulin. In 2016, the FDA cleared a second-generation multivariate index assay called OVERA, which combines CA125, HE4, ApoA1, follicle stimulating hormone (FSH) and Tf. Because FSH is part of the panel, there is no need to determine menopausal status. Overall, OVERA presents similar sensitivity and NPV to OVA1 (specifically 91% vs 94% sensitivity respectively and 97% NPV), although performing better for specificity (69% vs 54% respectively) and PPV (40% vs 31%).[17]

Risk of ovarian malignancy algorithm (ROMA)

In 2011, the FDA approved the ROMA score as a qualitative serum test designed to assess the likelihood of finding malignancies during surgeries in women with an adnexal mass and, thus, allows for better patient triage to centers of excellence.

The ROMA algorithm combines measurements of serum HE4 and CA125 to the menopausal status of the patient (defined by lack of menstruation or clinical signs of menopause for 6 months). The creators of this algorithm revealed a sensitivity of 93.8% (88.9% for pre-menopausal and 94.6% for post-menopausal women) and a specificity of 75% for the diagnosis of EOC.[18] Based on their result, the ROMA algorithm successfully classified patients into high and low risk groups with 93.8% of EOC correctly classified as high risk.[18]

Conclusion

The biggest challenge healthcare providers face when presented with women with adnexal masses, is to correctly assess the risk for OC as early as possible, despite the vagueness (or lack) of symptoms. Currently, there are no recommended screening tests for OC in the United States, due

Table 1. Serum protein biomarkers and algorithms available on the US market

	Year of availability on US market	Sensitivity	Specificity	Clinical Use
CA125[a]	1997	79%* 69%**	82%* 93%**	Monitoring disease progression, detection of residual or recurrent OC
HE4[b]	2008	47%	84%	Monitoring recurrence or progressive disease
OVA1[c]	2009	92%	54%	Prediction of likelihood of Malignancy found upon surgery
ROMA[d]	2011	94%	75%	Prediction of likelihood of Malignancy found upon surgery

CA125 cutoff value: *65 U/mL; **150 U/mL
HE4 cutoff value: 20% change in CV

a) LabCorp Cancer Antigen (CA) 125. https://www.labcorp.com/tests/002303/cancer-antigen-ca-125.
b) ELECSYS HE4, Epithelial Ovarian Tumor Associated Antigen (He4) test 510K. Roche Diagnostics.
c) Bristow RE, Smith A, Zhang Z, Chan DW, Crutcher G, Fung ET, Munroe DG. Ovarian malignancy risk stratification of the adnexal mass using a multivariate index assay. Gynecol Oncol. 2013 Feb;128(2):252-9. doi: 10.1016/j.ygyno.2012.11.022. Epub 2012 Nov 21. PMID: 23178277.
d) Moore RG, Miller MC, Disilvestro P, Landrum LM, Gajewski W, Ball JJ, Skates SJ. Evaluation of the diagnostic accuracy of the risk of ovarian malignancy algorithm in women with a pelvic mass. Obstet Gynecol. 2011 Aug;118(2 Pt 1):280-288. doi: 10.1097/AOG.0b013e318224fce2

to high false positive and false negative rates, resulting in unnecessary surgeries or delayed treatment.[19]

In order to overcome this diagnostic challenge, blood biomarkers and algorithms have significantly contributed to overcoming this issue and improving the referral of women with suspected OC to specialized centers.

REFERENCES

1. Key statistics for ovarian cancer. American Cancer Society. Published 2021. https://www.cancer.org/cancer/ovarian-cancer/about/key-statistics.html. Accessed May 4, 2021.
2. Høgdall E. Cancer antigen 125 and prognosis. *Curr Opin Obstet Gynecol.* 2008;20(1):4-8. doi:10.1097/GCO.0b013e3282f2b124.
3. Sarojini S, Tamir A, Lim H, et al. Early detection biomarkers for ovarian cancer. J Oncol. 2012;2012. doi:10.1155/2012/709049.
4. McIntosh MW, Drescher C, Karlan B, et al. Combining CA 125 and SMR serum markers for diagnosis and early detection of ovarian carcinoma. *Gynecol Oncol.* 2004;95(1):9-15. doi:10.1016/j.ygyno.2004.07.039.
5. Bast RC, Lu Z, Han CY, et al. Biomarkers and strategies for early detection of ovarian cancer. *Cancer Epidemiol Biomarkers Prev.* 2020;29(12):2504-2512. doi:10.1158/1055-9965.EPI-20-1057.
6. Chandra A, Pius C, Nabeel M, et al. Ovarian cancer: Current status and strategies for improving therapeutic outcomes. *Cancer Med.* 2019;8(16):7018-7031. doi:10.1002/cam4.2560.
7. Kumarasamy C, Madhav MR, Sabarimurugan S, et al. Diagnostic and prognostic role of HE4 expression in multiple carcinomas: A protocol for systematic review and meta-Analysis. Med (United States). 2019;98(28):1-6. doi:10.1097/MD.0000000000015336.
8. Ueland F. A Perspective on ovarian cancer biomarkers: Past, present and yet-to-come. *Diagnostics.* 2017;7(1):14. doi:10.3390/diagnostics7010014.
9. Nowak M, Janas Ł, Stachowiak G, Stetkiewicz T, Wilczy ski JR. Current clinical application of serum biomarkers to detect ovarian cancer. *Prz Menopauzalny.* 2015;14(4):254-259. doi:10.5114/pm.2015.55887.
10. Nguyen L, Cardenas-Goicoechea SJ, Gordon P, et al. Biomarkers for early detection of ovarian cancer. *Women's Heal.* 2013;9(2):171-187. doi:10.2217/whe.13.2
11. Galgano MT, Hampton GM, Frierson HF. Comprehensive analysis of HE4 expression in normal and malignant human tissues. *Mod Pathol.* 2006;19(6):847-853. doi:10.1038/modpathol.3800612.
12. Zapardiel I, Gorostidi M, Ravaggi A, et al. Utility serum marker HE4 for the differential diagnosis between endometriosis and adnexal malignancy. *Int J Gynecol Cancer.* 2016;26(1):52-55. doi:10.1097/IGC.0000000000000579.
13. Bristow R, Jordan. Ovarian cancer biomarkers as diagnostic triage tests. *Curr Biomark Find.* Published online 2013:35. doi:10.2147/cbf.s30228.
14. Holcomb K, Vucetic Z, Miller MC, Knapp RC. Human epididymis protein 4 offers superior specificity in the differentiation of benign and malignant adnexal masses in premenopausal women. *Am J Obstet Gynecol.* 2011;205(4):358.e1-358.e6. doi:10.1016/j.ajog.2011.05.017.
15. Moore RG, Brown AK, Miller MC, et al. The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass. *Gynecol Oncol.* 2008;108(2):402-408. doi:10.1016/j.ygyno.2007.10.017
16. Langmár Z, Németh M, Vleskó G, et al. HE4 – a novel promising serum marker in the diagnosis of ovarian carcinoma. *Eur J Gynaecol Oncol.* 2011;32(6):605-610.
17. Coleman RL, Herzog TJ, Chan DW, et al. Validation of a second-generation multivariate index assay for malignancy risk of adnexal masses. *Am J Obstet Gynecol.* 2016;215(1):82.e1-82.e11. doi:10.1016/j.ajog.2016.03.003.
18. Moore RG, McMeekin DS, Brown AK, et al. A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass. Gynecol Oncol. 2009;112(1):40-46. doi:10.1016/j.ygyno.2008.08.031
19. Stacy Simon. FDA warns against ovarian cancer screening tests. American Cancer Society. 2016. https://www.cancer.org/latest-news/fda-warns-against-ovarian-cancer-screening-tests.html. Accessed May 4, 2021.

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Laboratory training and competence assessment in the era of COVID-19

By Luann Ochs, MS

COVID-19 brought many challenges to the laboratory in 2020 and will continue to do so in 2021. The SARS-CoV-2 tests currently being used under emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) will evolve to have improved performance, and the manufacturers will obtain official regulatory clearance or approval. Other tests may no longer be available once their EUA expires, and laboratories using those tests will have to implement different tests. With these and other changes coming, it is as important as ever to have a robust, efficient, and effective training and competence assessment program for current and new laboratory staff members.

This article provides information on best practices for training and competence assessment, detailing a structured approach that can help laboratories establish a planned and systematic culture of training and competence assessment that meets regulatory and accreditation requirements. Given that people are the most valuable resource in an organization, an effective training and competence assessment program will ensure that the personnel are knowledgeable and competent to do their assigned jobs. Effective training[1] and competence assessment programs:

- Ensure personnel performance results in consistent, predictable, and high-quality outcomes.
- Ensure performance of assigned job tasks remains constant.
- Verify that staff members have and can demonstrate the necessary knowledge, skills, and behaviors to perform their respective duties.

Training and competence assessment are two separate and distinct activities. Training focuses on teaching the skills needed for a job, along with the work processes and procedures for job tasks, including quality, safety, IT systems, and other responsibilities. Competence assessment, on the other hand, follows training, and assesses whether the training was effective, and the trainees are ready to function in their work environment. Ongoing competence assessments ensure that personnel continue to demonstrate the necessary knowledge, skills, and practices to remain effective in their jobs. **Figure 1** shows the relationship between training and competence assessment.

Training programs

Training cannot typically be merely having a person read a procedure and sign off on a checklist. Procedures do not happen in isolation and are part of a process of many interlinked procedures for distinct activities that need to occur in a specific order. Training needs to be provided on work processes and include all the procedures that apply to any given process. Laboratories need to identify their various processes and associated procedures for all the work that is performed in the lab. They need to understand how many people are involved in each process and who performs each task. Once the processes, procedures, and people are understood, a training plan can be developed that takes into account the current knowledge and skill level of the personnel involved with any given process.

Determining the learning objectives is a very important first step. These objectives identify what needs to be learned and the activities that need to be demonstrated

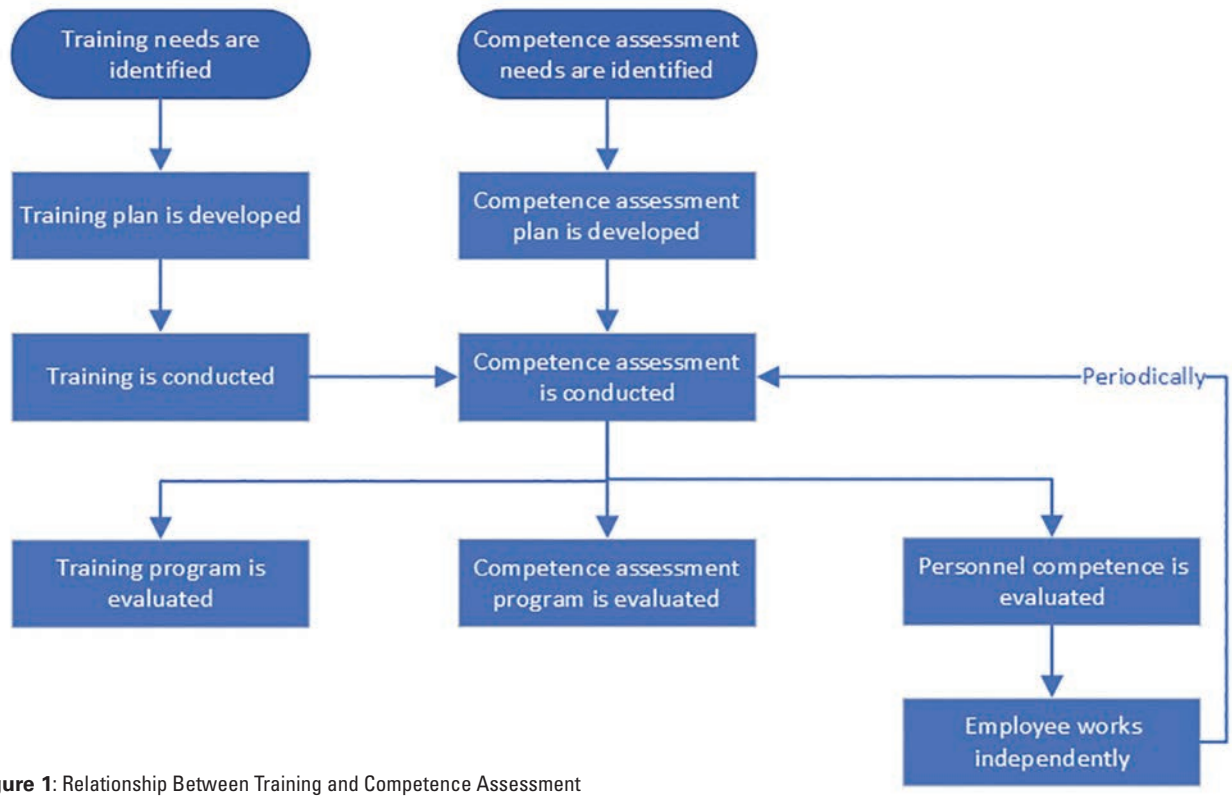

Figure 1: Relationship Between Training and Competence Assessment

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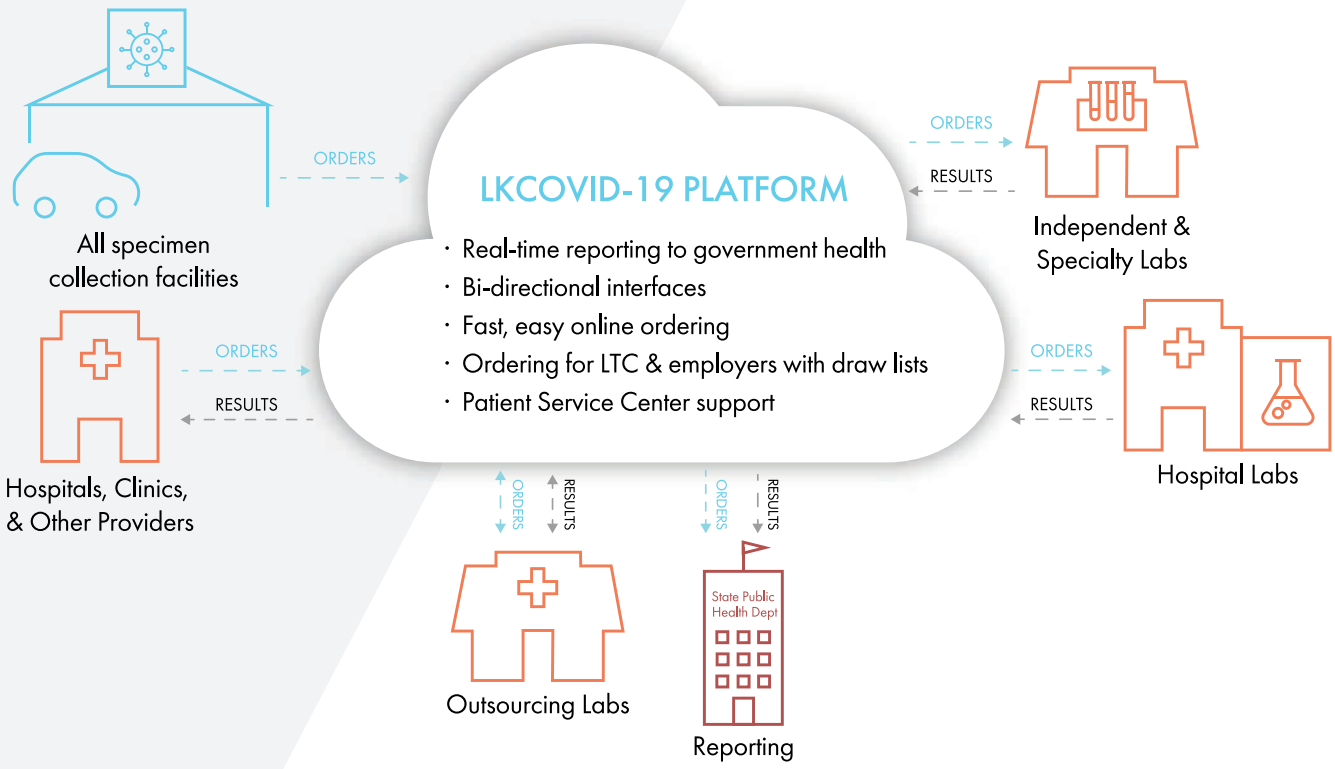

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Training Event Information	Function
Learning objectives	State the outcome expectations for the learner
Training methods	Describe the various training methods to be used
Training materials	List the training event materials and resources needed
Trainer instructions	Provide trainer preparation and presentation information
Learner instructions	Provide the learner with training event information
Training checklists	Describe the function of a training checklist
Learner assessment methods	Describe and provide the competence assessment methods and tools
Means for the learner to evaluate the training event	Identify tools for learners to evaluate the training experience

Table 1-shows the elements of a training plan.

by the learner after the training session. The objectives should define specific, observable, or measurable behaviors.

Multiple training methods can be used, as deemed appropriate for each objective. Methods can include, for example, self-study materials, demonstrations, lectures, videos, computer-based exercises, supervised practice sessions, and testing of samples.

Training materials can include items such as operator's manuals, procedures, handouts, practice materials, and others as needed for the specific training. Instructions for trainers and learners should be created to minimize any variability between instructors and to guide learners as they proceed through the training. The instructions should also include a list of materials needed for any demonstrations or practice sessions for learners. Using training checklists can help a learner complete each training activity successfully and serve as a record of completed training.

At the completion of the training, a learner's knowledge can be assessed by quizzes (oral or written), observation of activities, or a record review. And finally, a learner should have an opportunity to evaluate and provide feedback on the training event. It is important to capture whether a learner's expectations for the training have been met and whether the learning objectives have been achieved.

The training environment must be conducive to learning, and the learner needs to practice in a "safe" environment, where they are not punished for mistakes, they have time to learn and reflect, and they can make conclusions from the information and activities learned. Whenever possible, the training should take place in the work area. For nontechnical training, a conference room will suffice. No matter where the training is conducted, the learner needs access to private conversation space for asking questions and expressing concerns.[1]

Competence assessment programs

Competence assessment is required by regulatory and accrediting organizations; it is a good quality practice that should be an ongoing part of a laboratory's culture. As with most programs, the first step is to develop a comprehensive plan. In the case of planning for competence assessment, the plan needs to be based on and include activities for each job title, including quality management activities as appropriate. Criteria that define acceptable performance or a passing score need to be determined before implementing the program. All materials used in the competence assessment are subject to document control.

Competence assessment best practices include, as appropriate for each work process or procedure:[1]

- Directly observing routine work processes and procedures, including applicable pre-examination and post-examination processes and applicable safety practices. This is an objective means of assessing performance, especially for routine work, which should focus on high-risk process activities and procedure steps.
- Directly observing equipment maintenance and function checks.
- Monitoring the recording and reporting of examination results, including identifying any critical results, errors, or other possible issues. Such monitoring should include reviewing test results, QC records, calibration records, preventive maintenance records, any troubleshooting records, proficiency testing results, and any corrected or amended reports.
- Reviewing work records, such as work cards, log sheets, and computer data entry.
- Examining specially provided samples, such as previously examined samples, interlaboratory comparison (i.e., proficiency testing [PT]) materials or split samples, and in some cases, QC material.
- Assessing problem-solving skills, especially through simulations that can determine whether staff members problem-solve within their knowledge and skill level, escalating issues when appropriate.

Once the competence assessment plans are developed and approved, the assessments can be conducted. Assessments should be scheduled periodically based on requirements from regulatory or accrediting organizations. The best practice is to build ongoing competence assessment schedules into the laboratory routine, with consideration of the usual path of workflow. Not all personnel need to be assessed at the same time. Schedules should allow the daily workflow to continue without being disrupted by the assessments.

Records of all competence assessment activities need to be retained in individual personnel files. These records should include the names of the assessor and the person being assessed, as well as indicating what was reviewed or observed, when it occurred, and the outcome. The objective evidence of passing the competence assessment must be retained (direct observation checklists, testing data, etc.). It is important to ask the people who

Personnel Type	Basis of Competence Assessment Plan[1]
Non-testing personnel	All processes and procedures that relate to: • Laboratory test results, reports, and other services • The quality management system.
Testing personnel	• Describe the various training methods to be used
Other technical personnel	• List the training event materials and resources needed
Management personnel	• Provide trainer preparation and presentation information

Table 2 -Competence Assessment Plans

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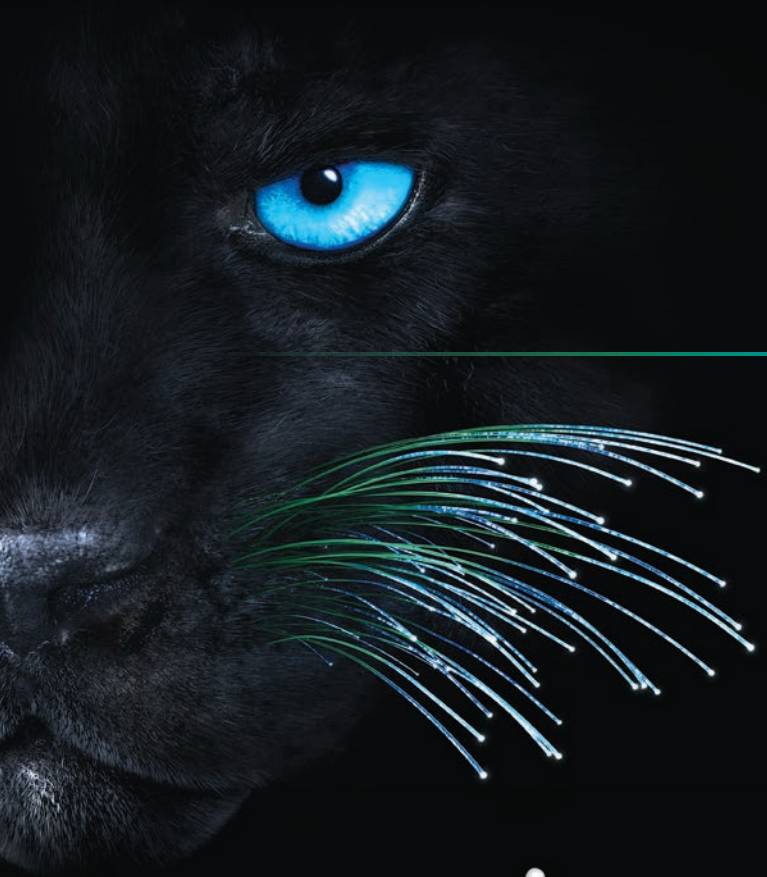

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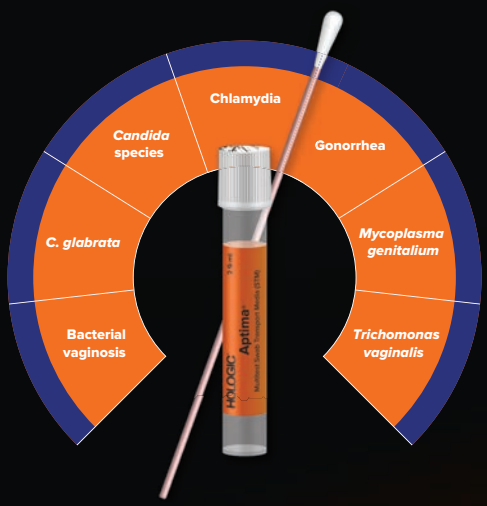

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References: 1. Aptima Combo 2 Assay [package insert] #502446-IFU-PI_012 San Diego, CA; Hologic, Inc., 2021. **2.** Aptima Mycoplasma genitalium assay [package insert] #AW-17946_002, San Diego, CA; Hologic, Inc., 2021, **3.** Aptima CV/TV assay [package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

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Methods for Assessing Problem Solving Skills [1]

Problem solving skills can be assessed by reviewing daily work, such as:

- Handling of results that are inconsistent with a patient's condition
- Resolving equipment and other technical or testing problems recorded in problem or troubleshooting logs
- Handling emergent situations
- Meeting a specific customer's needs
- Knowing when to escalate a problem that cannot be solved at that person's job level

Other ways to assess problem-solving skills include:

- Mock events
- Peer review
- Discussion/reflection groups
- Presentations

Methods for Assessing Problem Solving Skills

pass a competence assessment to sign a statement in which they commit to using the skills needed to perform their duties in the workplace. The assessment is not a group activity, as it is assessing individual skill, not group knowledge.

How to begin

A new training program is more likely to be accepted when a new change is occurring because staff has not already been trained by an older training method.

New training programs are best started when, for example, any of the following changes occur:

- A new or changed process is implemented.
- New instrumentation or tests are brought into the lab.
- Regulatory or accreditation requirements change.
- A process is problematic and needs to be improved.
- New quality improvement tools are implemented.

COVID-19 specific training

Training programs for COVID-19 testing need to include instruction about sample collection, storage, and transport; performing a test properly; and reporting the results. Each of these activities are likely to be performed by different people, and the development of a comprehensive training plan to ensure all personnel receive their appropriate training is needed. Training in this circumstance can be especially challenging due to the number of people needing training in a short amount of time.

Sample Collection:[2] It is important to collect, transport and store a sample properly for accurate and reliable test results, and training for personnel performing sample collection is essential. When providing collection of nasal swab samples for viral testing, laboratories need to be sure they follow their test manufacturer's instructions.

The manufacturer's package insert for the SARS-CoV-2 test contains specific information about the swab types authorized for use with the test. For viral testing, rayon or synthetic polyester fiber-tipped swabs are recommended, and calcium alginate or cotton swabs are not recommended. Nasopharyngeal samples are typically collected using swabs with fine, flexible wire shafts. Wooden-shafted swabs are not recommended because they can contain toxic or inhibitory materials and can also absorb some of the specimen volume.[2]

1. Typical directions for use of a nasal swab are:[2]
2. Pass a flexible, fine-shafted swab into the nostril.
3. Rotate slowly for five seconds to absorb secretions.
4. Immediately place swab into a vial of the appropriate viral transport media. (Drying will result in loss of viral viability.) Repeat for the other nostril using a fresh swab. Place both swabs into the same transport tube.

Sample Storage and Transport: All sample storage and transport instructions are given in the manufacturer's package insert and need to be followed to ensure accurate test results. Training on these procedures should be given to all personnel who handle the samples.

Testing: Whether the tests are performed at the point-of-care or in the laboratory, laboratory management should ensure that all staff members who perform testing receive proper training. They need to be trained on:

- Setting up instruments and reagents before testing
- Calibrating instruments and running QC samples
- The testing procedure
- Obtaining and reporting the test results in the laboratory information system or patients' charts
- Knowing if the test worked properly
- Knowing what could go wrong with the test and how to avoid errors
- Performing any necessary maintenance
- Proper reagent, calibrator, and QC handling and storage

Rapid tests[3] are typically simple to use and provide results within 30 minutes or less. A number of point-of-care tests for SARS-CoV-2 have been authorized for use, with varying sensitivity, specificity, and turnaround time. Users should be aware of a test's sensitivity and specificity and ensure that providers report results accordingly. Rapid test accuracy depends greatly on specimen quality and test performance. Low test sensitivities can make false negatives common, and negative rapid test results may require confirmation by a more sensitive test method.

Nucleic acid amplification tests are more sensitive but also easily subject to contamination. It is very important that personnel performing these tests are trained in all aspects of testing, sample handling, and how to avoid potential cross-contamination.

Reporting requirements for COVID-19 tests can include reporting not only into the laboratory information system or patient's chart, but also to local or regional health authorities for infection rate tracking. Training of each of these requirements needs to be provided for the appropriate personnel.

Summary

In summary, training for COVID-19 testing can certainly seem daunting at first, especially since it affects every area of the laboratory and all levels of laboratory workers. If the laboratory has a well-functioning training and competence assessment program already established, it is a matter of developing the specific materials needed to train staff members in the processes and procedures for each job function. While this remains a big task to undertake, a systematic approach can ensure that people are properly trained in the activities that they need to do for their job. Many test manufacturers have developed training programs and materials specific for their tests, and laboratory managers should not hesitate to reach out to test manufacturers for assistance with developing training programs.

REFERENCES

1. Clinical and Laboratory Standards Institute. Training and Competence Assessment – Fourth edition. Wayne, PA: Clinical and Laboratory Standards Institute; 2016. CLSI document QMS03.

2. Clinical and Laboratory Standards Institute. Viral Culture – First edition. Wayne, PA: Clinical and Laboratory Standards Institute; 2006. CLSI document M41.

3. Clinical and Laboratory Standards Institute. Point-of-Care Testing for Infectious Diseases – First edition. Clinical and Laboratory Standards Institute; 2020. CLSI document POCT15.

Luann Ochs, MS, is Product Development Manager at the Clinical and Laboratory Standards Institute.

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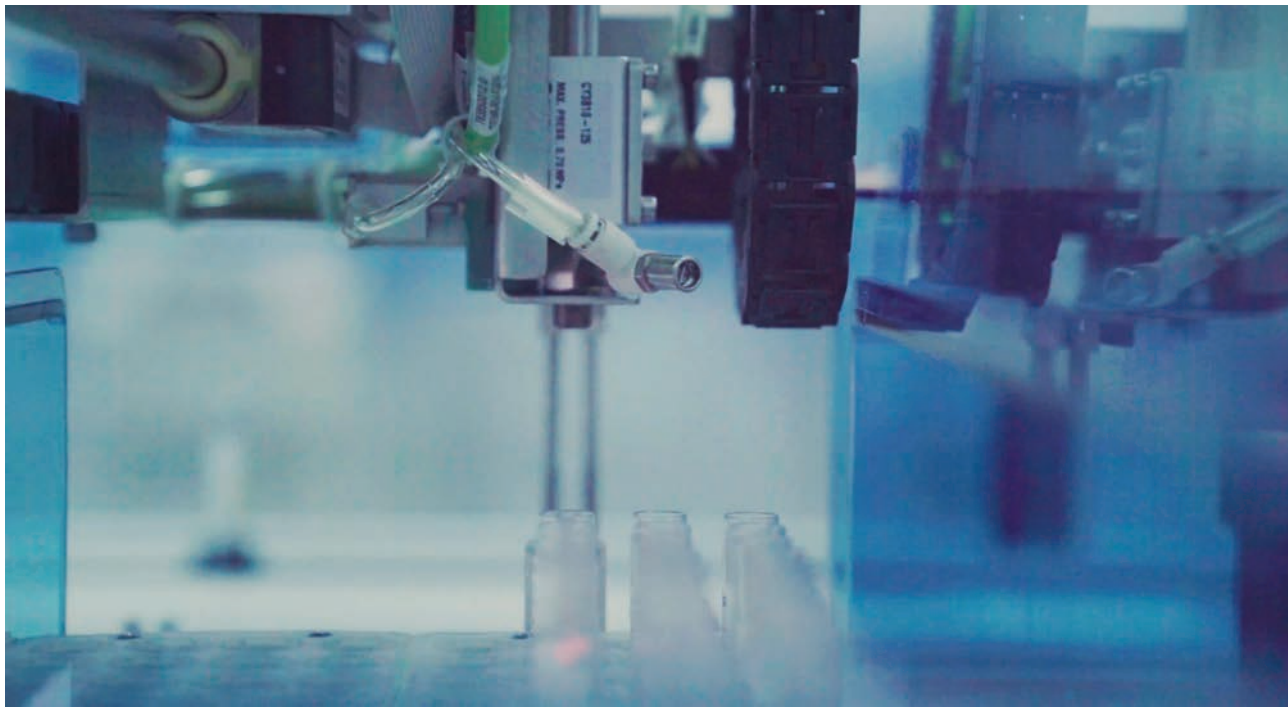

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From manual beginnings to an automated revolution – the past, present and future of chemistry testing

By Christopher Liddle, BSc

Clinical chemistry encompasses centralized analytical activity concerning the chemical composition of biological material necessary for the diagnosis and treatment of research into diseases.[1] The discipline, which originated in small laboratories with relatively few manual tests performed, now requires highly automated and integrated laboratories to produce hundreds of thousands of body fluid specimens every day to be analyzed, with the data obtained being interpreted with the end goal of assessing the health of patients.[2]

The transition from manual to automated testing began in 1875, when Thaddeus M. Stevens, MD, Professor of Analytical Chemistry at the College of Physicians and Surgeons of Indiana, created the first semi-automated device to be mentioned in American chemical literature. The device was designed to drip water through a piece of filter paper at a controlled rate to wash a filtrate and was an introductory insight into the ideas and techniques that would revolutionize clinical chemistry over the next century.[3] Furthermore, in 1956 Leonard Skeggs developed the AutoAnalyzer, the first practical and completely automated system designed to meet the specific needs of a clinical chemistry laboratory. The system performed blood analysis from start to finish without manual intervention by a technologist and provided new advantages, such as less labor, fast analysis, and the use of screening panels.[4]

Since the launch of the AutoAnalyzer, successful generations of stand-alone analyzers have continued to be popular within the clinical chemistry industry. The variety of systems available, many of which differ in terms of throughput volume, physical features, analytical speed and size of test menu, means that there is now an automated system widely available to suit the needs of the vast majority of laboratories worldwide.

Why automation transformed clinical testing

In modern times, automated testing systems have become increasingly popular, allowing users to transform their output amongst other perceived benefits, such as less labor required, decreased preparation time, and fewer input errors. Ultimately, the primary difference between automatic and manual systems is that in a manual system, a human tester is required on-site to provide the input for processes to run successfully.[5]

When considering the effectiveness of some of the above perceived benefits, I will refer to research carried out by Danyel Hermes Tacker, PhD, who completed a study, which involved processing 20 batches containing 5-90 specimens, each using both methods in parallel and randomly across a 4-week period.[6]

In Tacker's study, he identified 45 steps involved in the entire specimen-testing process. Of the multitiude of manual steps, Tacker believed that a vast majority of the manual steps could easily become automated if an up-to-date system was used. This emphasizes the ability of an automated system to take on more of the workload during the testing process, which as a result, reduces the requirement for as much human labor within the laboratory setting. Therefore, if the machinery can share a greater amount of the task, laboratories will be able

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Primary Presenter

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to reduce labor costs due to a decrease in demand for human expertise on-site.

Furthermore, Tacker's study also found a significant reduction in batch preparation time when an automated system was used in comparison to a manual testing system. In a batch containing 60 specimens, technologists took 145 minutes to prepare the specimens for testing, while the automated system took just 97 minutes. Following a similar pattern, a batch of 90 specimens took 184 minutes when prepared manually, compared to 97 minutes when automated. If a batch can be prepared for testing at a faster rate, this will allow for greater levels of operational efficiency and productivity. This means the laboratory can produce more test results each day because less time is being taken to prepare each batch.

Finally, a major advantage of automated systems is that, as a result of less human interaction with the process, there is likely to be a reduced number of errors. During Tacker's study, the technologists involved reported fatigue caused by moderate and persistent discomfort in the hands, neck and shoulders when processing high batch numbers. In addition to this finding, it was the multitude of tedius steps, which can be automated, that caused technologists the most discomfort. Therefore, it can be concluded that during a manual testing process, physical fatigue limits the ability to efficiently process batches containing a high quantity of specimens. As an automated system limits human input, fatigue will be reduced to the point whereby it may be non-existent, meaning that more reliable results can be produced.

The future of testing

One thing that is for certain is that automation continues to be the future of chemistry testing. Those within the science industry are constantly seeking to further innovate new technologies to improve productivity and efficiency within laboratories that strive to produce accurate results as fast as possible. Furthermore, as technology develops and fresh ideas enter the market, the automation of today will likely filter down into smaller laboratories, thus continuing the growth of an automated world of testing.

Perhaps the most common assumption regarding the future of testing within the laboratory is the birth of robotic lab assistants (robots). This shift began at the start of the millennium, with robots being introduced to laboratory settings to carry out previously manual tasks, such as manipulating samples, applying chemicals that aid the process of breaking up DNA into measurable segments, analyzing results, and feeding these results into a computer.[7] A study by the University of Liverpool in 2020, where a robotic lab assistant machine was created, found that a robot operated approximately 1,000 times faster than a human over the course of a working week.[8] The robot was in operation for 22 hours on each of the seven days, something that is simply not feasible when using human input without the uptake of high labor costs. Although robotic assistants create a common fear that there will no longer be a requirement for any human input, this is not true. The machine created by the University of Liverpool required programming and couldn't physically set up its own experiments.[8] This development will act as a major benefit within laboratories in the future, as while the robotic assistant carries out the tedious, time consuming tasks, scientists will have more time to carry out new research, which would not be possible in the present time.

As new automated technology becomes available in the future, it is likely that we will see a 'trickle down' effect with systems becoming more accessible and affordable to laboratories that differ in size and budget. In the past, limited supply and high costs meant that automated technology was often reserved for the benefit of the best funded laboratories around the globe.[9] However, as the demand for automated machinery continues long term, an increase in supply – in addition to the larger laboratories seeking the latest innovations – will result in an increasingly wide range of automated testing across smaller laboratories, medical centers, schools and universities. As this occurs, the number of laboratories depending solely on manual testing will further decrease, continuing the automated revolution to clinical testing.

Conclusion

In conclusion, we have witnessed a monumental shift in favor of automation since the work of Leonard Skeggs in 1956. Although this shift is not unique to the science industry, with much of the world favoring new technology over techniques and processes of the past, automated systems offer a range of benefits to both laboratories and the scientists who work there. Less preparation time, faster throughput and reduced human error mean that testing is now more efficient than ever before, improving results in faster times and, in-turn, making testing a more profitable exercise due to increased output. While some see the introduction of robotic assistants as a threat to employment, it is deemed highly unlikely that laboratories will ever be fully able to function without human input. Therefore, the additional helping hand will reduce fatigue and bodily strain amongst those working in the laboratory, allowing for more time to conduct new research, which will again lead to new findings and further develop capabilities in the future.

REFERENCES

1. Reeve, J, Twomey, P and Borovickova, I. 2021. The role of the clinical chemistry laboratory in facilitating earlier diagnosis of dyslipidaemia-associated inherited metabolic disease. *J Clin Pathol.* 2020;73(7):363-365. doi:10.1136/jclinpath-2019-206254.
2. Kricka, L. and Savory, J., 2011. International year of chemistry 2011: A guide to the history of clinical chemistry. *Clin Chem.* 2011;57(8):1118-1126. doi:10.1373/clinchem.2011.165233
3. Olsen, K., 2012. The first 110 years of laboratory automation. *J Lab Autom.* 2012;17(6):469-480. doi:10.1177/2211068212455631.
4. Armbruster DA, Overcash DR, Reyes J. Clinical chemistry laboratory automation in the 21st century - Amat Victoria curam (Victory loves careful preparation). *Clin Biochem Rev.* 2014;35(3):143-153.
5. Guru99.com. 2021. *Automation testing vs. manual testing: What's the difference?* https://www.guru99.com/difference-automated-vs-manual-testing.html. Accessed 29 April 2021.
6. Tacker D, Topardo J, Mahaffey C, Perrotta P. Workflow analysis comparing manual and automated specimen processing for mass spectrometry–based Vitamin D testing. *Lab Med.* 2014; 45(4), pp.361-367. doi: 10.1309/LMZL47EN6KDODMXJ Abstract
7. Edwards C. Medical robotics: the end of the lab technician? E&T. https://eandt.theiet.org/content/articles/2014/11/medical-robotics-the-end-of-the-lab-technician/. Published November 10, 2014. Accessed April 29, 2021.
8. Vincent J. Robotic lab assistant is 1,000 times faster at conducting research. The Verge. https://www.theverge.com/21317052/mobile-autonomous-robot-lab-assistant-research-speed. Published July 8, 2020. Accessed April 29, 2021.
9. Valinreja. The Past, Present & Future of Lab Automation. Bio Molecular Systems. https://biomolecularsystems.com/the-past-present-future-of-lab-automation/. Published March 9, 2021. Accessed April 29, 2021.

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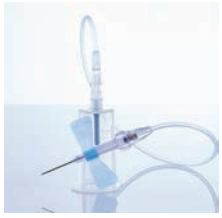

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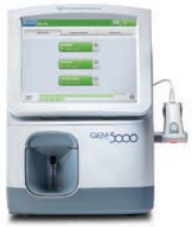

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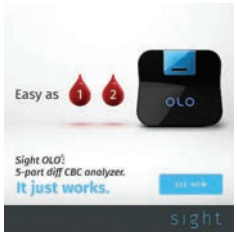

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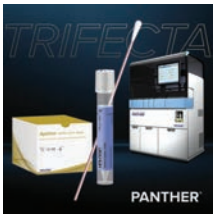

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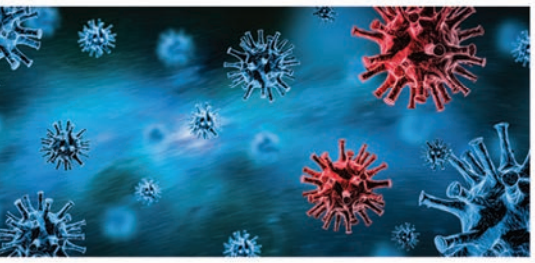

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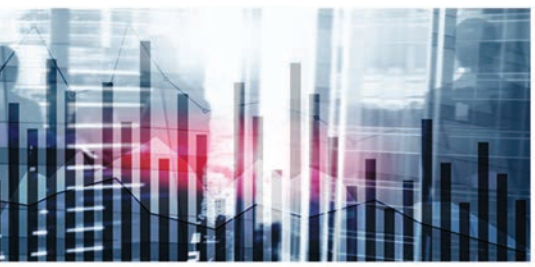
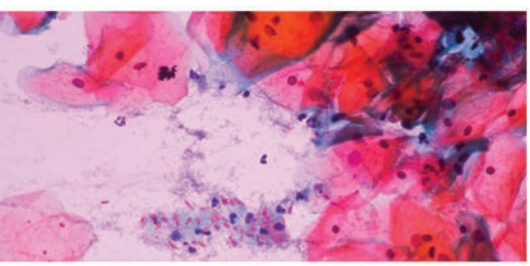
COVID-19 and the Lab: Testing, Supplies & Management

Visit first of our 2021 Forums featuring discussions on the latest in COVID-19 testing, supplies, and related operational processes. MLO editors presented our report on updates to the COVID-19 laboratory process, highlighting the latest test types, mediums, regulatory updates and reimbursement strategies.



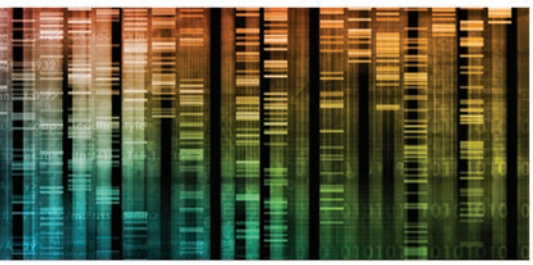
June 17
Clinical Analytics and Data Management

Our editors will present findings from our special report on Informatics in the Laboratory, with its focus on using valuable clinical analytics to inform the decision-making process in the lab. The presentation will include additional information on valuable solutions for healthcare laboratories.



August 17
Disease Management

MLO will explore how clinical laboratory professionals can help with disease management programs (DMPs) developed at their facilities. According to the CDC, clinical laboratories provide the foundation for accurate and timely disease diagnosis, prevention, and control to improve the health and safety of patients.



December 1:
Molecular Diagnostics for the Future Clinical Lab

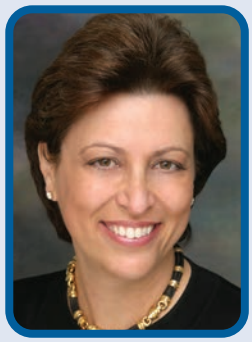
Using data gathered from our exclusive State of the Industry report on Molecular Diagnostics published in the November issue of MLO, we will explore the increasing roles of MDx and its use in the clinical laboratory.

https://endeavor.swoogo.com/mlo_forum/about

LABORATORY INNOVATOR

Using information technology to improve lab operations

By Linda Wilson



Lâle White, MBA, is Executive Chairman and CEO of **XIFIN**, which markets revenue cycle management software and a laboratory information system. White launched XIFIN in 1997. She has a BA in finance and an MBA from Florida International University.

Why did you decide to leave your position as Vice President of Finance at Labcorp in 1997 to launch XIFIN?

Lacking a commercially viable product to manage receivables for low balance, large volume, complex diagnostic labs; like many others in the industry, we had to create our own in-house solution. Over 15 years, I developed the last three progressively enhanced revenue-cycle management (RCM) products internally used by the lab, albeit with the limitations of the programming capabilities and standards developed by an in-house IT staff also servicing various higher priority needs of the company. Knowing that IT infrastructure technology was rapidly changing and with a keen understanding that real time, bi-directional integration to numerous process points and stakeholders was the primary solution to optimizing the accounts receivable process, I was determined to create the first commercial solution to the integration and communication problem in managing the entire revenue cycle for a diagnostic lab.

Will you briefly describe the changes to PAMA (Protecting Access to Medicare Act of 2014) reporting requirements and payment cuts that were enacted in the Coronavirus Aid, Relief, and Economic Security Act?

As a result of the pandemic, on March 27, 2020, the Cares Act was passed with provisions that delayed the scheduled 2021 fee reduction until 2022. The act also capped reductions from 2022-2024 at 15%. (It was previously capped at 10%, 2018-2020, rising to a 15% cap in 2021). Additionally, the next data reporting period was delayed until Q1 2022, while the collection period remained the same (January 1, 2019-June 30, 2019). This provided the lab industry with much needed reimbursement reduction relief. Previously the Lab Act (passed in 2019) had also authorized MedPAC to review the methodology used for PAMA data collection by CMS to provide some relief regarding the data collection burden. That report is expected to be out in June of this year.

What steps do you recommend that lab managers take to prepare for the upcoming cut to reimbursement for clinical diagnostic laboratory tests that is now set to be implemented Jan. 1, 2022?

The fee calculation from the original data set represented approximately a 30% cut on the top 25 tests taken over a three-year period because of the 10% cap on cuts for the first three years. Even though the cap will be 15% in 2020, the cuts are expected to be less than 10%. Lab managers need to make sure that they are optimizing returns and minimizing costs through greater automation and more efficient processes; or potentially outsourcing this administrative function to achieve better results, while providing them with a variable cost structure that will immediately adjust to volume fluctuations.

How do you expect federal payment policy for laboratory services to evolve in the future?

The upcoming MedPAC report is likely to streamline the data collection methodology for data collection related to PAMA. At the same time, Office of the Inspector General reports and MedPAC observations will shift focus to molecular/genetic testing, which represents the highest growth in our industry. Separately, the pandemic has resulted in a much-needed state- and federal-government focus on the health of the diagnostic network in the U.S. and an understanding of the impact of excessive rate cutting on lab capacity. This has enabled dialogue between legislators and the industry to review, and perhaps modify, some of the PAMA guidelines that have resulted in a race to the bottom from a reimbursement perspective, instead of establishing a true market price. This may result in modifications in the PAMA language that would bring more balance to the pricing exercise.

What overall approach to laboratory reimbursement have commercial payers taken, and how do you expect this to evolve in the future?

Commercial payers have followed published Medicare rates in their own rate structures for the most part, which is one reason why the PAMA exercise could not produce legitimate market rates that reflected the true cost structure of performing individual tests. As was expected, once the PAMA rates were published, many of the major payers followed suit in cutting rates all the way to the PAMA rate, without capping their cuts at the 10% level that PAMA required for Medicare. Payers have now shifted greater focus to narrowing the number of providers in-network, establishing restrictions on coverage by limiting payment of tests to certain conditions, creating pre-authorization requirements, contracting with lab benefits managers to further limit payment and establishing internal criteria, as we see with organizations like UHC. Some of these shifts include a preferred lab network or designated diagnostic provider criteria to limit in-network labs to those with best pricing and technical capabilities.

You have been active in the California Clinical Laboratory Association for many years. What is your role at the organization, and how does it fit into the overall mission of the organization?

I have chaired the state and federal contractor committees for CCLA for years, maintaining a working relationship with the Department of Health and Human Services. I was recognized by the association with a Lifetime Achievement Award.

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