

C L I N

Clinical
Laboratory
News

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REGULAR
CRP SATISFIES

91.1%

Agreement for
hs-CRP and CRP
in risk classification

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Inclusive Kidney Disease Care



IVD Market Predictions



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A few telltale signs of antioxidant interference may include delta flags without obvious clinical or technical explanation, nonphysiological results (e.g., negative values), and nonlinear dilutions.
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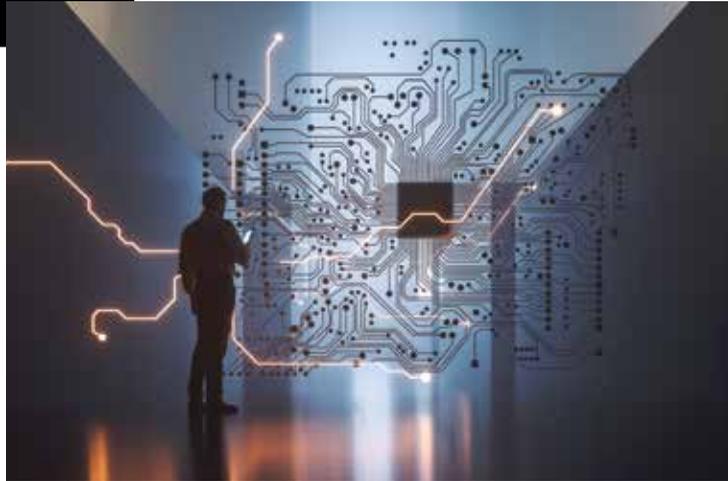
White House Issues Framework for Artificial Intelligence Bill of Rights

The White House Office of Science and Technology Policy has identified five principles to guide the design, use, and deployment of automated systems to protect the public in the age of artificial intelligence (AI).

“The Blueprint for an AI Bill of Rights: Making Automated Systems Work for the American People,” announced October 4, aims to provide a framework for anyone seeking to incorporate protections into policy and practice. The blueprint is designed around five principles intended to safeguard Americans from the adverse impacts of automated systems: 1) safe and effective systems, 2) algorithmic discrimination protection, 3) data privacy, 4) notice and explanation, and 5) human alternatives, considerations, and fallback plans.

Of interest to clinical laboratories, the blueprint addresses health and health insurance technologies, such as medical AI systems, AI-assisted diagnostic tools, algorithms, and predictive models used to support clinical-decision making.

Details about the framework, along with a technical companion on how the blueprint can be applied, can be found at www.whitehouse.gov/ostp/ai-bill-of-rights/.



HHS AWARDS FUNDS TO ENHANCE PREPAREDNESS FOR SPECIAL PATHOGENS

The Department of Health and Human Services' Administration for Strategic Preparedness and Response (ASPR) recently awarded \$21 million to 13 healthcare facilities to serve as leading providers of care within their regions to sustain and improve healthcare system preparedness for emerging special pathogens.

ASPR selected three new healthcare facilities to serve as Regional Emerging Special Pathogen Treatment Centers (RESPTCs), awarding \$3 million to each, and awarded an additional \$1.2 million each to the 10 existing RESPTCs.

RESPTCs are hospitals with enhanced capability and capacity to care for highly infectious diseases, such as Ebola or COVID-19. They serve as hubs for the National

Special Pathogen System and are continuously ready to care for special pathogen patients medically evacuated from overseas or diagnosed within the United States.

CBO IDENTIFIES APPROACHES TO REDUCE PRICES THAT COMMERCIAL INSURERS PAY FOR MEDICAL SERVICES

The Congressional Budget Office (CBO) has identified new policy approaches that federal lawmakers could adopt to reduce the prices that commercial insurers pay for medical services, thereby lowering health insurance premiums and the cost of federal subsidies.

According to the CBO, the prices that commercial health insurers in the United States pay for services provided by hospitals and physicians are much higher, on average, and have been rising more

quickly than the prices paid by public health insurance programs. Those rising prices, rather than growth in the per-person use of healthcare services, are an important driver of recent increases in premiums for commercial health plans.

Government policies can reduce commercial insurers' prices for providers by targeting the factors that contribute to high prices, says the CBO, which has identified three broad policy approaches available to Congress: promoting price transparency, promoting competition among providers, and capping the growth of prices.

Details about these proposals are discussed in the report, “Policy Approaches to Reduce What Commercial Insurers Pay for Hospitals’ and Physicians’ Services,” available at www.cbo.gov/system/files/2022-09/58222-medical-prices.pdf.



Type 1 Diabetes

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Bench Matters

How to Avoid Analytical Interferences in Trace Element Analysis



By Jessica Colon-Franco, PhD, DABCC, FAACC

Trace elements, also known as heavy metals, are found in the human body in very small concentrations, ranging from parts per million to parts per billion. Some trace elements (e.g., chromium, cobalt, copper, iron, manganese, molybdenum, selenium, zinc) are essential for biological processes in humans. Deficiencies in these elements can have adverse clinical manifestations that are reversed by supplementation. In excess amounts, some of these metals can be harmful.

Other metals, such as aluminum (Al), arsenic (As), beryllium (Be), lead (Pb), and mercury (Hg) do not have known biological functions and are toxic. Heavy metal poisoning may occur from occupational and environmental exposures, food and medicine, or lead-based paints.

For all these metals, clinical laboratories perform trace element testing in biological samples, either to assess patients' nutritional status or detect toxicity.

Sample Collection Is Critical

The validity of trace element results very much depends on taking steps to collect the sample adequately. To prevent contamination, laboratories list acceptable collection devices and procedures. The best practice for blood collection is to utilize certified trace metal-free tubes (i.e., royal-blue top, available with and without anticoagulant) or lead-free tubes (i.e., tan top).

Some laboratories may accept specimens in nontrace metal-free tubes if the preferred tubes are not available, such as during shortages. A recent example is utilizing EDTA lavender-top tubes for lead testing and adding a disclaimer in the result to alert that the container was not metal-free. Tube contamination and erroneous results due to this

practice have been reported numerous times. The Centers for Disease Control and Prevention (CDC) (www.cdc.gov/nceh/lead/lab) offers educational tools for proper venous and capillary sample collection.

For sample collection from children, elevated lead from a capillary collection is suspected of contamination and followed up by a second test from a venous sample. A sample should not be collected in patients receiving contrast material containing gadolinium (Gd), iodine (I), or barium (Ba) within 96 hours. Metal-based contrast agents interfere with trace metal analysis.

Selecting Trace Element Analysis Methods

The method of choice for trace element analysis is inductively-coupled plasma mass spectrometry (ICP-MS), due to its sensitivity and multi-element quantification. This method uses plasma heated at temperatures up to 10,000 K to ionize the sample, and specific isotopes that are detected by mass spectrometry.

Some clinical laboratories also perform elemental analysis by atomic absorption spectrophotometry (AAS).

In graphite furnace AAS, as a sample is heated by a flame, elements absorb light at a certain wavelength that is detected by a spectrophotometer. For context, participants of a recent proficiency testing survey by the College of American Pathologists mostly analyzed lead by ICP-MS (54%), followed by AAS (39%). Other heavy metals were universally reported using ICP-MS.

Despite the advantages of ICP-MS, this method has some shortcomings. ICP-MS is more expensive, requires higher technical expertise for method development, and is affected by spectral interferences (e.g., isobars, doubly charged or polyatomic species with the same m/z ratio as the element of interest). With modern instruments, we can overcome most spectral interferences, since ICP-MS instruments are equipped with a collision or reaction cell (CRC). Depending on the instrument, interferences may

be removed by promoting a reaction between a reactive gas (e.g., O_2 or H_2) and the interferent or analyte, or by combining a nonreactive gas, like helium, with kinetic energy discrimination, which will discriminate against large polyatomic species, among other approaches.

Technology developments to remove isobaric interferences in ICP-MS have continued. Most recently, ICP-tandem mass spectrometers (ICP-MS/MS or ICP-QQQ) have become commercially available. The first quadrupole (Q1) prefilters ions with a certain m/z ratio to enter the cell, and the other quadrupole (Q2) detects the target m/z ratio after the CRC reaction. Balcaen and colleagues have reviewed this technique in detail (*Anal Chim Acta* 2015; doi: 10.1016/j.aca.2015.08.053).

One current application of ICP-MS/MS in clinical laboratories is the accurate determination of

selenium, unaffected by gadolinium-based imaging contrasts. Gadolinium is doubly charged ($^{156}Gd^{2+}$) under ICP conditions, and it interferes with selenium assays using the ^{78}Se isotope. To accurately quantitate Se in the presence of Gd, Q1 filters the m/z ratio of 78, O_2 reacts with Se in the CRC, and the m/z ratio of 94 for $^{78}Se^{16}O^+$ is detected by the Q2.

The ICP-MS/MS technology is still relatively new and not widely used in clinical laboratories. Nevertheless, its robustness in removing interferences in biological and other complex matrices while maintaining sensitivity to detect trace elements is promising for clinical applications.

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The Sample

Some People More Prone to COVID-19 Vaccine Side Effects

Among individuals who have received COVID-19 vaccines, younger people, females, and those who got the second dose of the Moderna COVID-19 vaccine report more side effects from COVID-19 vaccines that may have led to moderate and severe limitations, according to a recent paper (Front Public Health 2022; doi: 10.3389/fpubh.2022.975781).

These observations from self-reported data might be explained by higher mRNA concentration in the Moderna vaccine, according to researchers. They added that increased side effects in these groups may be associated with additional protective immunity and fewer breakthrough infections, as other studies have shown.

In what the researchers believe is the first survey comparing side effects of Pfizer, Moderna, and Johnson & Johnson COVID-19 vaccines, the researchers surveyed 975 participants who attended the 2021 AACC Annual Scientific Meeting. General questions in the web-based Research Electronic Data Capture (REDCap) survey addressed demographics, past and present health conditions, smoking, exercise, and medications. COVID-19-specific questions covered SARS-CoV-2 vaccine status and type, vaccine side effects after each dose, and whether respondents had boosters, previous COVID-19 infections, diagnostic testing, and COVID-19 symptoms and their severity.

Participants were 47.1% male and had a median age of 50. Pfizer was the most administered vaccine, with receipt reported by 56.4% of respondents, followed by Moderna (32%) and Johnson & Johnson (7.1%). There were not significant differences in vaccine type received by age, health conditions, smoking, exercise, or type or number of prescription medications.

Side effects were reported more frequently after the second dose of the Moderna and Pfizer vaccine or the single-dose Johnson & Johnson vaccines. Males were significantly less likely to report side effects, while females were significantly more likely to report injection site reactions, fatigue, headache, muscle pain, chills, and nausea. In multivariate logistic regressions analyses, the second dose of the Moderna vaccine was associated with a significantly higher risk of side effects than both the second dose of Pfizer and the single dose of the Johnson & Johnson vaccine.

The researchers note the study is limited by a participant population that does not represent the U.S. population and by inability to determine whether patients had tested positive for SARS-CoV-2 before or after vaccination.



HIGH SENSITIVITY CRP TESTS NOT NECESSARY FOR SOME PATIENTS

Lower-cost C-reactive protein (CRP) tests for CRP values in lower ranges correlate highly with more expensive high-sensitivity (hs) CRP tests and can replace them to assess low levels of inflammation and evaluate cardiovascular risk, according to a recent retrospective observational cohort study (*J Appl Lab Med* 2022; doi: doi.org/10.1093/jalm/jfac069).

Because measurements of regular, lower-cost CRP have become very sensitive, with a lower detection limit of 0.3 mg/L, the researchers aimed to compare and explore the association between CRP and hs-CRP.

They retrospectively reviewed data from 607 consecutive patients referred for cardiovascular risk assessment with hs-CRP. The researchers analyzed data from 570 of the patients and assigned them to low-, medium-, and high-risk groups based on hs-CRP cutoffs of less than 1 mg/L, 1–3 mg/L, and more than 3 mg/L, respectively. The researchers assessed correlation between hs-CRP and CRP with the kappa statistic and visualized with a Bland-Altman plot. They also determined association between hs-CRP and occurrence of acute myocardial infarction, stroke, bypass surgery, or percutaneous coronary intervention via Cox regression analysis visualized with Kaplan-Meier curves.

The researchers saw total number reclassification in 8.6% of cases for CRP risk groups, demonstrating agreement of 91.4%. Correlation between CRP and hs-CRP was significant, with P more than 0.001 and Spearman regression of R2 of +0.98. A Bland-Altman plot displayed an average difference of 0.19 mg/L between CRP and hs-CRP. Cardiovascular events were more likely to occur in patients who were older, with hs-CRP more than 3 mg/L and a history of coronary artery disease.

Assessing inflammation markers alone may play a secondary role compared with other established

cardiovascular risk factors, the researchers said. They noted that elevated CRP appears helpful for determining patients with higher risk and for predicting further cardiovascular events and mortality.

Study limitations include its observational design and the fact that it was conducted at a single center, a tertiary care hospital at which some rare diseases may have been over-represented. Only 18.3% of patients in the study had multiple measurements of hs-CRP, which is preferred for correct risk group classification.

SINGLE-MOLECULE SEQUENCING MAY IMPROVE CANCER LIQUID BIOPSY

Single-molecule sequencing enables long cell-free (cf) DNA detection and direct methylation analysis for cancer patients, presenting new possibilities for liquid biopsy, according to recent research (*Clin Chem* 2022; doi.org/10.1093/clinchem/hvac086).

While circulating tumor DNA has become an important cancer care tool, previous research on circulating cfDNA has focused on short DNA fragments. Meanwhile, the conventional approach for methylation analysis, bisulfite sequencing, causes DNA degradation and is not ideal for assessing long DNA properties and methylation patterns.

In response, the researchers conducted a proof-of-concept study to determine whether single-molecule sequencing for cancer liquid biopsy via single-molecule real-time (SMRT) sequencing of plasma DNA could enable direct and concurrent assessment of both long cfDNA molecules and their methylation patterns.

For each molecule, the researchers performed fragment size and direct methylation analysis and computed a methylation score for single-molecule methylation patterns in 13 patients with hepatocellular carcinoma (HCC), 13 patients with hepatitis B infection, and 15 healthy controls.

The median percentage of plasma DNA molecules longer than 1 kb

was 15.7% in SMRT sequencing results in patients with HCC, which was 350-fold higher than that produced by short-read sequencing. The longest plasma DNA molecule carrying a mutant allele was 13,585 bp, demonstrating the existence of long tumor-derived cfDNA molecules in cancer patients. The researchers were able to generalize differential sizes to a broader size range of up to 3 kb. Patients with HCC tended to release more liver-derived DNA fragments into plasma compared with HBV carriers or healthy individuals.

The presence of long tumoral cfDNA might lead to a shift in the current focus of cancer liquid biopsy from short cfDNA molecules of 250 bp to 1 kb-long cfDNA molecules, the researchers wrote.



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Improving Chronic Kidney Disease Care

for All



How laboratories should consider transgender and nonbinary populations when updating and reporting renal function estimates.

BY DANYEL H. TACKER, PHD, AND MATTHEW D. KRASOWSKI, MD, PHD

Many laboratories are moving forward with implementing the updated 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations for estimated glomerular filtration rate (eGFR), which remove factors that adjust the resulting estimates for race (1). This update stands to benefit Black and mixed-race populations, while also eliminating the logistic challenges of either extracting information on race and

assigned at birth and gender identity. Transgender women were assigned sex as male at birth but identify as women; in contrast, transgender men were assigned sex as female at birth but identify as men.

There are also those who identify as something other than male or female, such as identifying with neither gender or with both genders. This group is often described with the umbrella term nonbinary, but other subterms such as gender fluid, genderqueer, and third gender are also used.

Transgender and nonbinary people may seek medical interventions that affirm their gender identity, known as gender-affirming therapy. Current standard of care for gender-affirming therapy includes hormone therapy (testosterone or estrogens and sometimes additional medications) and/or surgical procedures such as orchidectomy (removal of testes) or ovariectomy (removal of ovaries). Note that for a variety of reasons some transgender and nonbinary individuals do not use gender-affirming therapy.

EFFECTS OF GENDER-AFFIRMING THERAPY ON LABORATORY TESTS

A growing body of literature has documented the effects of gender-affirming therapy on the results of clinical chemistry and hematology tests (2). Early studies were predominantly either observational studies of transgender cohorts or retrospective analyses of laboratory data in individuals who received gender-affirming therapy.

More recently, a prospective research study determined reference ranges for chemistry analytes (including creatinine) in individuals who had been stably taking gender-affirming hormones for at least 12 months (3). In that study, the reference interval for transgender men and nonbinary individuals stably taking testosterone aligned with that for cisgender men (higher creatinine values) and not cisgender women. The observed shift to higher creatinine values with masculinizing therapy is consistent with previous retrospective studies.

One hypothesis is that use of testosterone increases muscle mass and thus production of creatinine. The results for feminizing hormones were more complicated. In the prospective study, transgender women and nonbinary individuals stably taking estrogen showed little difference in the creatinine reference interval from cisgender women (3), although the results of some retrospective and observational studies have varied.

ethnicity from electronic medical records (EMRs) or reporting two eGFR values (Black and non-Black). Institutions are realizing the value and improved equity such an update brings.

Although use of the updated equations is generally agreed to be a step in the right direction in the domain of laboratory medicine, a new consideration needs to be addressed: how eGFR differs for transgender patients, and how to address this difference in equations that still clearly depend on factoring for male or female gender. A broader challenge is how to interpret laboratory test results in transgender and nonbinary populations.

STANDARDS OF CARE FOR TRANSGENDER PATIENTS

Transgender people experience incongruence between sex assigned at birth and gender identity (personal sense of gender). Cisgender individuals are congruent between sex



With regard to eGFR, and a call for further review of the assessment of kidney function in the transgender population (9), a recent study by Fadich, et al., demonstrates the need for and value of addressing eGFR reporting in the transgender adult population (10). The authors retrospectively reviewed creatinine results obtained in transgender adults taking gender-affirming hormonal therapies—namely, testosterone or estrogens—before, during, and in maintenance phases of therapy. They also calculated estimated creatinine clearance (eCrCL, by using the Cockcroft–Gault equation) and eGFR (with the Modification of Diet in Renal Disease Study and CKD-EPI equations) and reported significant differences in these estimations over time.

These authors' findings in a relatively small transgender cohort are compelling preliminary data that issue a strong call for more prospective study, while reinforcing the ideas that creatinine significantly changes over time as a patient progresses through transitioning with gender-affirming therapy and then enters a steady-state phase of therapy, and current eCrCL and eGFR calculations are not adequate for expressing estimated renal function in the adult transgender population.

THE ELECTRONIC MEDICAL RECORD PROBLEM

In calculating eGFR, the challenge thus arises as to which sex or gender is appropriate for the calculations.

First is the issue of the “legal sex” used by the EMR for the main designation of a patient as male or female. By default, legal sex is usually sex assigned at birth unless intentionally changed later.

Recently, some EMR vendors have incorporated fields for sexual orientation and gender identity (SOGI) in patient records (4,5). These fields can capture information such as legal sex, sex assigned at birth, gender identity, and sexual orientation. Additional variables may include gender-affirming therapy and organ inventory. In current practice, the fields are typically voluntary for the patient to include.

One recent case example published by Fernandez-Prado and Ortiz illustrates the diagnostic challenges that may arise with creatinine and eGFR in the transgender population (6). In the case study, a transgender woman was classified in the EMR as male for legal sex until administrative change of her legal sex to female. With the use of female as the legal sex, the eGFR result was substantially lower than previous measurements when the individual was classified as male in the EMR. The fact that she was a transgender patient came to light only when clinicians investigated the abrupt shift in laboratory results.

HOW CLINICAL LABORATORIES CAN CLOSE CARE GAPS

Even if all the potential financial and basic-access barriers to health-care experienced by transgender persons are equalized or ignored, the situation described by Fernando-Prado and Ortiz exposes cultural and resource-related barriers to care for many transgender patients. Laboratories can and should consider addressing these barriers sooner rather than later. The constant narrative between a transgender patient and a new or unfamiliar care team can result in emotional triggers, recounting of past trauma, and the potential for discrimination on the part of the care team (7,8).

Clinical laboratories are an integral part of this care team and are poised to close care gaps by providing clinicians with better tools for laboratory-based testing and results reporting

and interpretation. In this way, health-care systems can streamline diagnosis and treatment for transgender and nonbinary individuals receiving gender-affirming therapies.

While laboratorians wait for evidence that can be incorporated into standardized renal function estimators, they must consider what to do in the meantime, particularly regarding reporting in EMRs. Whereas many institutions have sought to offer comparisons of legal and preferred gender in their EMRs, there is much variability in how these tools work and which reference intervals are posted to the EMR when testing is performed. In some cases, a patient's legal gender does not equal their preferred gender (5).

One major EMR vendor offers a calculation to determine whether all gender fields in a record are equal. If the fields are not equal, gender is categorized as “unspecified.” The easy answer appears to be to place both the cis-male and cis-female reference intervals in a result comment when gender is categorized as unspecified and to caution the provider that gender-specific differences need to be considered for key tests.

However, most EMRs do not place calculated, specific results in comments as part of standard functionality. Thus, the challenge becomes how to make comments and reference intervals more data-rich and flexible to give more guidance to providers handling results for patients taking gender-affirming hormonal therapy. Solutions will likely be most straightforward for tests with discrete measurements (e.g., hepatic enzyme or thyroid function tests).

The problem with eGFR in this scenario is that any calculated output still requires the selection of one or another gender. If the eGFR built into the EMR is designed to give only one output (most currently equate gender with male or female), the institution needs to carefully consider how to most accurately express eGFR for the transgender or nonbinary patient. Accurate reporting may require a discrete build that houses two outputs—a cisgender male equivalent and a cisgender female equivalent—for the provider



to review and consider while treating the patient. Such information can prove critical to eGFR results interpretation in transgender and nonbinary individuals, because the calculations applied likely assume that the patient will be taking gender-affirming hormonal therapy.

Currently, scientific reports on implementing such calculations for transgender and nonbinary individuals are lacking. Until studies reflect the best way to calculate eGFR for these individuals, we are left with room for creativity and information-sharing between institutions. Many institutions are choosing not to calculate eGFR in the interim for these individuals and to instead provide a creatinine or cystatin C result. The provider can then choose a result and calculate the eGFR using a preferred online tool. However, this approach lacks standardization and laboratory oversight, both of which could prove valuable as more research is published regarding eGFR estimations in these populations.

FUTURE RESEARCH NEEDS

The dialogue on gender and eGFR has only begun. First, increased adoption of EMR-based tools for documenting gender identity, gender-affirming therapy, and sex assigned at birth in addition to legal sex are clearly needed. Along with this, how these reporting fields are used by patients and providers should be studied, and any barriers or concerns relating to their use (e.g., discrimination, confusion with terms) should be addressed. A more detailed study of how gender-affirming therapy affects creatinine and eGFR, including the time course during hormone therapy, is also needed.

Research must also tackle cystatin C and other markers of renal function in transgender and nonbinary populations to clarify marker utility, reference intervals, and clinical decision points relating to renal function assessment in these individuals. Finally, clinical laboratories must standardize how to report laboratory values for tests such as creatinine to deal with discordance between legal sex, gender identity, and sex assigned at birth. ■

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REFERENCES

1. Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin c-based equations to estimate GFR without race. *N Engl J Med* 2021; doi:10.1056/NEJMoa2102953.
2. Goldstein Z, Corneil TA, Greene DN. When gender identity doesn't equal sex recorded at birth: The role of the laboratory in providing effective healthcare to the transgender community. *Clin Chem* 2017; doi:10.1373/clinchem.2016.258780.
3. Humble RM, Greene DN, Schmidt RL, et al. Reference intervals for clinical chemistry analytes for transgender men and women on stable hormone therapy. *J Appl Lab Med* 2022; doi:10.1093/jalm/jfac025.
4. Cahill SR, Baker K, Deutsch MB, et al. Inclusion of sexual orientation and gender identity in stage 3 Meaningful Use guidelines: A huge step forward for LGBT health. *LGBT Health* 2016;3:100-2. doi:10.1089/lgbt.2015.0136
5. Thompson HM, Kronk CA, Feasley K, et al. Implementation of gender identity and assigned sex at birth data collection in electronic health records: Where are we now? *Int J Environ Res Public Health* 2021; doi:10.3390/ijerph18126599.
6. Fernandez-Prado R, Ortiz A. A sudden decrease in serum creatinine and estimated glomerular filtration rate: Clinical implications of administrative gender assignment in transgender persons. *Clin*



Kidney J 2020; doi:10.1093/ckj/sfz152.

7. Safer JD, Coleman E, Feldman J, et al. Barriers to healthcare for transgender individuals. *Curr Opin Endocrinol Diabetes Obes* 2016; doi:10.1097/MED.0000000000000227.
8. Hostetter CR, Call J, Gerke DR, et al. "We are doing the absolute most that we can, and no one is listening": Barriers and facilitators to health literacy within transgender and nonbinary communities. *Int J Environ Res Public Health* 2022; doi:10.3390/ijerph19031229.
9. Collister D, Saad N, Christie E, et al. Providing care for transgender persons with kidney disease: A narrative review. *Can J Kidney Health Dis* 2021; doi:10.1177/2054358120985379.
10. Fadich SK, Kalayjian A, Greene DN, et al. A retrospective analysis of creatinine-based kidney function with and without sex assigned at birth among transgender adults. *Ann Pharmacother* 2021; doi:10.1177/10600280211050120.

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Where Does the IVD Market Go

After the Coronavirus

Testing Surge?

Industry experts say COVID-19 will have a significant impact over the next 5 years and predict its influence will drive new growth.

BY KIMBERLY SCOTT

In 2022, testing for SARS-CoV-2 is expected to add almost \$33 billion to the in vitro diagnostic (IVD) market, according to Kalorama Information, which recently published the 15th edition of “The Worldwide Market for In Vitro Diagnostic Tests.” Thereafter, SARS-CoV-2 testing is projected to decline about 6% per year to about \$23 billion in 2027.

“The SARS-CoV-2 virus has shown that it can adapt, and there are enough variants that it has staying power. At this point, it’s endemic,” said Bruce

Carlson, senior vice president of Kalorama, which is published by the Science and Medicine Group. “We do think that COVID testing will decline, but it won’t go away. COVID testing still will be a significant dollar contributor to the market.”

Donna Hochberg, PhD, a partner with Health Advances, a health-care consulting firm in Newton, Massachusetts, agrees. “We are out of the pandemic phase, so there is less surveillance, but COVID testing is still pretty high volume, especially over-the-counter antigen testing.”



Hochberg predicts that the SARS-CoV-2 testing market, combined with testing for influenza, will end up being two to three times the traditional flu testing market. Mini-panels, which include testing for SARS-CoV-2, flu, and respiratory syncytial virus (RSV), will help drive growth in this market.

“Patients have a lower threshold for what drives them to get tested now,” she said. “Before COVID, if you had a cold, you wouldn’t get tested or you wouldn’t go to the doctor, but now people are more likely to get tested for any cold- or flu-like illness.”

GLOBAL IVD MARKET TO REACH \$127.4 BILLION AS CONSOLIDATION CONTINUES

Overall, the worldwide IVD market is projected to reach \$127.4 billion by the end of this year, with \$94.8 billion originating from non-SARS-CoV-2 tests and \$32.6 billion from SARS-CoV-2 tests, according to Kalorama. By 2027, the market is expected to top \$140 billion. Not surprisingly, cancer testing is among one of the fastest growing segments, with in situ hybridization, molecular cancer markers, immunohistochemistry, and HPV

molecular testing among the strongest growth areas.

Molecular diagnostics (MDx) is continuing its upward trajectory, said Hochberg, who notes laboratories that adopted platforms for SARS-CoV-2 PCR testing can now use those platforms for other types of molecular testing. She predicts that non-SARS-CoV-2 MDx will grow by the mid to high single digits annually over the next few years.

COVID-19 reinforced rather than broke the consolidation trend in IVD companies, noted Carlson. “The pandemic brought a host of new,

smaller companies—yet larger companies had the distribution and production capacity, as well as credibility with labs,” he said.

In 2022, the top IVD companies account for about \$101 billion of IVD product sales, compared to \$97 billion in 2021 and \$47 billion in 2016. This represents an approximately 13.7% increase in top-tier revenues for 2016–2022.

For the first time, Abbott Diagnostics now leads the IVD market, according to Kalorama. In the last edition of the report, the top position was tied between Roche and Abbott. The reason, said Carlson, is Abbott’s position in point-of-care testing (POCT) from its Alere acquisition, the pandemic, and glucose test sales.

Other growth areas include drugs of abuse, immunoassays, cardiac markers, fecal occult blood, HbA1c POCT, tests for inherited diseases, and molecular testing for organ transplants.

Mass spectrometry, which can

Kalorama estimates that mass spectrometry will have a compound annual growth rate of 14% over the next 5 years.

offer higher accuracy than immunoassays, continues to be an important part of the market—and not just for microbiology. Kalorama estimates that mass spectrometry will have a compound annual growth rate (CAGR) of 14% over the next 5 years and exceed a billion dollars by 2027. Drivers in this area include HbA1c testing, vitamin D testing, and companion diagnostics.

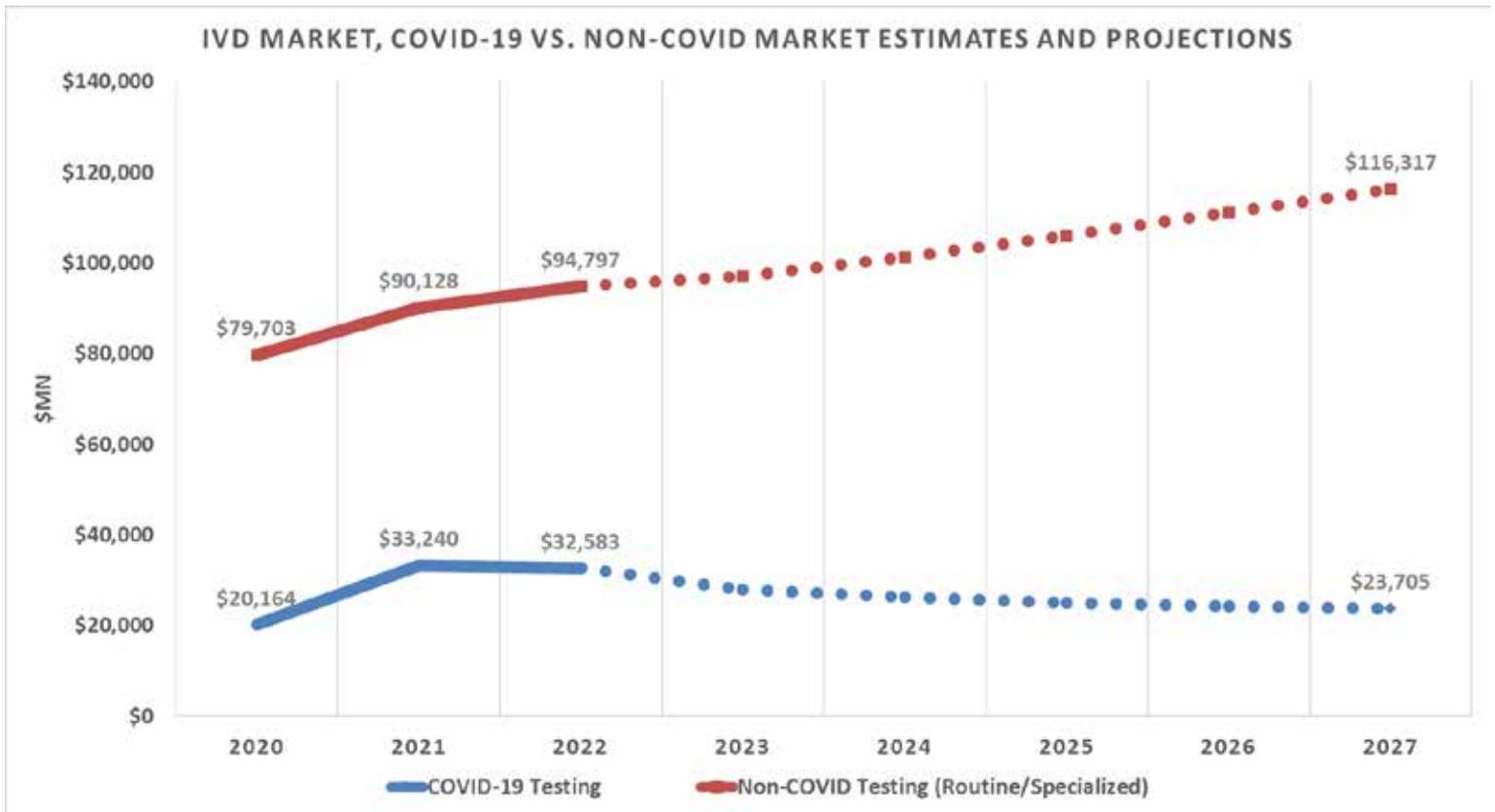
Automation also is helping drive growth in mass spectrometry, said Hochberg, who notes that Thermo Fisher Scientific’s Cascadion analyzer gives labs more ability to perform testing. “There are a lot of benefits to mass spectrometry, such as specificity and multiplexing, that will override

some of the technical challenges, particularly when you have automation in place,” she said.

Hochberg sees mass spectrometry being used to test difficult-to-measure analytes, such as estradiol, which is a complex molecule not measured well by immunoassay, and in therapeutic drug monitoring.

The continuous glucose monitoring (CGM) market also is experiencing rapid growth, with a CAGR of 6.6% between 2021 and 2027, according to Research and Markets, a research firm based in Dublin. The spike in the senior population and the increasing prevalence of diabetes have been essential factors driving the CGM market’s expansion, said the company.

Combined Performance in Coronavirus and Non-Coronavirus IVD Market Segments 2020–2027



Source: Kalorama Information



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Currently, more than 537 million adults worldwide are living with diabetes, and this number is projected to balloon more than 37% to 783 million people by 2045. In the U.S. alone, diabetes is the most common chronic condition, with more than 133 million people living with diabetes or prediabetes. The CGM market is highly competitive, with only a few companies competing. Abbott, Roche, Tandem Diabetes Care, Dexcom, and Senseonics are among the biggest players.

WHAT TO WATCH: 10-YEAR IVD TRENDS

Over the next decade, Kalorama is predicts a number of trends that will shape the IVD market, from increased participation by non-U.S. countries to increased collaboration between companies and evolution of sampling methods.

Among the trends discussed in the report:

Regions of market influence.

Korea and China are slated for higher overall growth in IVD. The Chinese market for IVDs is estimated at nearly \$6.6 billion and is expected to show annual growth of 3.8% to reach \$7.9 billion in 2027. Glucose monitoring is a major focus area for the Chinese IVD market, representing roughly 25% of the market's value. South Korea, which in 2020 initiated a fast-track procedure for

international patients with severe illness, has shown tremendous growth in medical tourism. The IVD market in South Korea is considered favorable for its regulatory process and foreign investment opportunities. Kalorama estimates the IVD market in Korea to be \$545 million in 2022 with 5.8% annual growth, reaching nearly \$721 million by 2027.

Collaboration, acquisitions. The future of the industry lies in the development of more sensitive, faster, user-friendly, information technology-capable devices for a host of new protein and molecular markers. No company owns all the technology needed to develop these new tests and systems, said Carlson. Thus, many companies are acquiring other IVD manufacturers to shore up their research and development. For example, in February 2022, BD, looking to broaden its flow cytometry segment for hematologic cancer and blood diseases, acquired Cytognos. In April 2022, bioMérieux acquired Specific Diagnostics to add to its critical infection sepsis line, and in June 2022, Fujirebio acquired ADx NeuroSciences and Qiagen acquired Blirt for additional growth in reagents.

New sample methods. Tests using blood, nasal fluid, and tissue dominate the IVD market, but the search for easier-to-collect samples

continues. The pandemic and the need for rapid, reliable testing has heightened interest in saliva as a convenient medium for infectious diseases. Recent studies have shown that saliva is just as effective as a nasopharyngeal swab for traditional SARS-CoV-2 PCR tests and useful in at-home rapid antigen tests. The Food and Drug Administration has issued more than 30 emergency use authorizations for saliva-based SARS-CoV-2 tests. Saliva is also increasingly being used to diagnose diseases affecting the mouth, esophagus, stomach, large and small intestines, kidney, and liver.

Hochberg noted that there is also work being done in using breath and capillary blood for diagnostic testing. Patient-focused testing services, such as Everlywell, Everly Health, and LetsGetChecked, are driving the market for finger-prick sample collection.

"Patient-focused testing services want to make sample collection as easy as possible," she said. "Point-of-care testing is also pushing sample collection in that direction."

FUTURE GROWTH

As the global population ages and new testing methods are developed, the worldwide IVD market will continue to grow. But which areas will grow the fastest will depend on a number of key factors, including potential future pandemics, lifestyle trends that might have an impact on chronic diseases, and consumer demand.

A consumer-oriented "democratization" of testing is sure to play a key role in growth of in vitro diagnostics, Hochberg said, especially as consumers have become more knowledgeable about testing during the COVID-19 pandemic. Automation also will help to drive growth in the IVD market.

"The pandemic really exacerbated the labor shortage in labs, which has made automation even more important," she said. "With more automation comes the ability to perform more tests, which will lead to an increase in development of new assays. Automation is a big growth driver." ■

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Many companies are acquiring other IVD manufacturers to shore up their research and development.



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New Guidance on Point-of-Care Testing for Reproductive Health

Experts give updated recommendations on testing for ovulation, pregnancy, and premature rupture of membranes.

BY JEN A. MILLER

In September, AACC issued new guidance for point-of-care testing (POCT) for fertility and reproductive health. This new document replaces previous guidance set out in 2007 and incorporates advancements in knowledge about the accuracy of these kinds of tests. It also addresses the fact that usage, acceptance, and even preference for this technology is surging.

“Point-of-care tests can be a powerful tool to help patients and their babies across reproductive and fertility medicine. They can help people better understand their menstrual and ovulation cycles, whether they’re trying to conceive or avoiding pregnancy,” said James H. Nichols, PhD, DABCC, FAACC, professor of pathology, microbiology, and immunology at the Vanderbilt University Medical Center, and editor of the updated guidance. “But if point-of-care tests are used incorrectly or inappropriately, they can lead to unnecessary treatment or put a patient’s life at risk. We hope these guidelines can help guide clinicians on the best way to use these kinds of tests.”



The guidance was developed by a committee of experts with interest and experience in POC and laboratory testing. The committee members created clinical questions related to the use of POCT in the assessment of ovulation, pregnancy, premature rupture of membranes (PROM), and evaluation of fetal distress. They then surveyed peer-reviewed literature that could address each clinical question, including publications on test performance, sensitivity, and potential interferences. They also reviewed guidance documents from other professional organizations such as American College of Obstetrics and Gynecology.

The new AACC guidance is also written with increased use, acceptance, and trust of POCT in mind, as patients have gotten used to doing things like testing for SARS-CoV-2 in a clinic or home setting.

“Point-of-care testing is popular because it’s convenient and easy to use. In some cases, it’s accessible directly by the patient,” said Zahra Shajani-Yi, PhD, DABCC, FAACC,

NRCC-CC, technical director of chemistry for Labcorp’s San Diego



regional laboratory and national codiscipline director of routine and esoteric immunoassays, and coauthor on the new guidance. “As that use has increased, it is incredibly important to know in what situations point-of-care testing should be used, and what these tests’ limitations are.”

That applies to POCT both in and outside of reproductive health.

THREE AREAS TO WATCH IN THE UPDATED GUIDANCE

Authors of the new guidance highlighted three key areas that have been updated and that laboratory medicine professionals should discuss with clinicians:

Testing for PROM. PROM is defined as rupturing of the amniotic sac prior to the onset of labor. It complicates 2%–3% of pregnancies in the U.S. and increases the risk of preterm birth, which is why POCT could be useful in helping clinicians to accurately diagnose PROM and deliver swift care. However, the new AACC guidance cautions that using commercial kits for PROM alone is not recommended without clinical signs that a patient’s water has broken, such as leakage of amniotic fluid from the cervical opening. “There needs to be clinical context, not just a test alone,” said Shajani-Yi.

The updated AACC guidance also includes tables on the

effectiveness of different POC PROM tests with respect to different clinical diagnostic criteria. “Having something like that is very useful for clinicians,” she added.

Use of urine luteinizing hormone tests for ovulation. Authors of the new guidance found that home tests accurately and reliably predict ovulation and can improve the likelihood of conception among healthy fertile women. These tests also can be used to time certain assisted reproduction procedures.

In addition, the guidance covers how POCT can pinpoint the day of ovulation, which may vary greatly between patients. For example, the average menstrual cycle is 22 to 37 days, with ovulation occurring at any point from day 8 to 26.

“These guidelines have been updated with new studies to show this range, and can be used in discussion about where point-of-care testing can be useful,” said Shajani-Yi. “Having this information demonstrates some of the nuances and background on how these tests should be used.”

Use of pregnancy POCT. While laboratory pregnancy tests are the gold standard in determining pregnancy, the new guidance urges healthcare providers to consider using pregnancy POCT in situations where rapid diagnosis is needed for

“As that use has increased, it is incredibly important to know in what situations point-of-care testing should be used, and what these tests’ limitations are.”

—Zahra Shajani-Yi, PhD, DABCC, FAACC, NRCC-CC

timely treatment decisions. For example, if a patient presents to the emergency department with unstable vital signs and symptoms of a ruptured ectopic pregnancy that might require surgery, a POC pregnancy test can give a result in minutes.

“We focused on the use of point-of-care testing in emergency management because time can really make a difference in these scenarios,” said Nichols. POC pregnancy tests can also ensure that any procedures that are potentially dangerous to a fetus, such as X-rays, are not performed on patients who could be pregnant, no matter what they came to the emergency department for. This is also why the new guidance should be shared not just with clinicians focusing on fertility and reproductive health, but also with emergency medicine healthcare professionals, he added.

POCT ON THE UPSWING ACROSS MEDICINE

The new AACC guidelines are especially important in a healthcare world where POCT has become more popular, and even expected, because of the pandemic. If someone is comfortable testing themselves for SARS-CoV-2 at home, they will be comfortable self-administering other kinds of tests.

And it’s just the start, said Nichols. “There will absolutely be more. This is not the end. We see requests for testing on the rise, and spreading out of the hospital into the community, so I think this is certainly an up-and-coming field.”

That’s especially true in reproductive and fertility medicine. According to the market research company Technavio, the fertility testing device market share is expected to increase to \$153.91 million by 2026, with an annual growth rate of 5.73%. Technavio considered ovulation predictor kits, fertility monitors, and male fertility testing devices in their report. And these devices represent just a piece of the expected POCT pie. By 2028, the global POC market is expected to reach \$65 billion, according to Research and Markets.

Nichols predicts that the next big wave of innovation will be molecular diagnostics. “With COVID, testing has moved outside of the hospital and microbiology laboratory and into the community,” he said. “We’re using it in the emergency department, in clinics, and patients are using SARS-CoV-2 antigen tests in their homes. We’re trusting those home diagnostics more.”

The trust with home tests has changed for both patients and physicians. “Before, when you walked into your physician and said my home pregnancy test is positive, they immediately redid it because they didn’t trust it,” he said. “Now if you walk in and say, ‘My COVID test was positive,’ they believe patients and the test and don’t necessarily redo it.”

Shajani-Yi said that this increased use and popularity of POCT means that guidelines like these and others from AACC will become even more critical to ensure the best patient care in the future. “It’s really

important that we continue to publish guidelines that clearly review the current literature and describe the clinical use benefits and limitations and nuances of each method,” she said. ■

Jen A. Miller is a freelance journalist who lives in Audubon, New Jersey.

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An interview with Elizabeth Palavecino, MD

How to Approach Antimicrobial Stewardship After COVID-19

BY JEN A. MILLER

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MOLECULAR DIAGNOSTICS

During the worst of the pandemic, clinicians threw everything at COVID-19 to try to save patient lives. That often included antibiotics. About 80% of patients hospitalized with COVID-19 received antibiotics between March 2020 and October 2020, according to the Centers for Disease Control and Prevention (CDC), even though fewer than 3% of patients showed any sign of a bacterial infection (www.cdc.gov/drugresistance/covid19.html). CDC noted this was likely due to difficulties distinguishing COVID-19 from community-acquired pneumonia when patients first arrived at a hospital. In addition, critically ill patients might have been treated for bacterial co-infections.

CDC is now devoting millions of dollars for local health departments to tamp down on improper antibiotic prescribing, including \$120 million to departments in New York City, Los Angeles County, and 60 other jurisdictions, according to *Bloomberg Law*.

Laboratory medicine professionals play a crucial role in antimicrobial stewardship programs (ASP), and in ensuring appropriate antibiotic use. We spoke to Elizabeth Palavecino, MD, professor of pathology at the Wake Forest University School of Medicine, about changes she's seen in ASP throughout her career, especially during the COVID-19 pandemic.

How have advances in molecular testing changed the approach to ASPs?

There is no doubt that molecular testing has improved antimicrobial stewardship. In our institution, when we started doing more molecular testing, we saw the impact of having results available to the clinicians much faster. They can decide on a therapy at almost the same time they are seeing patients.

We implemented the use of a multiplex panel for detection of organisms from positive blood cultures on a specific group of patients: those admitted to the hospital, especially the intensive care unit (ICU). The results were available shortly after growth was detected in the blood culture bottles 7 days a week, 24 hours a day.

Of course, if you send a result at 2 a.m., you really need somebody on the clinical side to evaluate the report and make a treatment decision. If the lab sent the result to the ICU, there was always a clinician available there who could make a therapeutic decision. That's why, at the beginning, we focused primarily on those patients who could benefit the most. In our hospital, the use of rapid molecular testing from positive blood culture has led to rapid diagnosis and appropriate treatment of bacteremia.

Our goal is to test the right patients at the right time to ensure appropriate use of antibiotics. If we do a lot of testing on patients who are not having an infectious process, we get more chances of a false positive, and then that patient is going to be treated for something they don't have.

How has COVID-19 affected ASP performance, and what have we learned for the future of ASPs?

COVID-19 impacted us a lot. At the beginning, we didn't have reagents. Manufacturers dedicated all their resources to producing coronavirus tests. For other tests—syndromic panels, molecular testing—we didn't have enough reagents, or we didn't have the disposables needed to perform testing. We really had to prioritize when to use molecular testing for infections other than COVID-19.

Later, COVID-19 impacted us due to how long patients were in the hospital. Some were hospitalized for a long time, in the ICU and on ventilators. All these things are risk factors for getting an infection of a multi-drug resistant organism. If you look at the surge of COVID-19, that same curve is seen in prescription of antibiotics in the hospital.

That made things more difficult for us and ASP. Remember, we didn't know a lot about COVID-19 at the time.

We have been focused on communication with providers and explaining how they can ensure appropriate use of antibiotics, and we are seeing significant improvement. We also know more about COVID-19 and how it behaves. For example, after people have a viral infection, they have a higher chance of getting a bacterial infection because the virus can damage tissue and interfere with the body's defense mechanisms and with immunity. This is true for other viruses as well as for the SARS-CoV-2 virus.

So we still are in the process, now that we have learned more about the behavior of this virus, of educating our clinicians.

How do the unique qualities of molecular testing, such as speed, affect how the lab collaborates with clinicians, nurses, and pharmacists?

Every time I do a lecture on ASP for microbiologists and technologists, I always emphasize that we need to collaborate with multidisciplinary clinical teams. To do that, we must spend more time outside of the laboratory and participate in different institutional committees designed to improve the care of the patient.

We know exactly the testing that we can do, and whether there are limitations to these tests. Typically,

other healthcare professionals understand results. It is difficult to educate everybody. We have a large number of clinicians throughout our healthcare system. Physicians must continually learn about their own specialties. They're not going to be as focused on laboratory medicine, so we need to translate what the results for a specific test mean. Adding comments in the reports has allowed us to provide education to a vast community of providers.

This is particularly important for those molecular tests performed for patients in ambulatory care settings. I don't worry as much about interpretation for patients in the hospital, because I have my ASP group review results, especially for blood cultures, and provide consultation to the clinical team if needed.

therapy but the right antimicrobial therapy, the patient has lower chances of survival.

Sometimes we have the identification of an organism coming from the blood culture, but we don't yet have all the susceptibility testing. So, we publish our antibiogram with the rate of antibiotic susceptibility for each organism seen in our hospital. That way, all our providers can select empiric therapy based on pathogen identification, until the full susceptibility report is available, so they don't have to start with a broad antibiotic.

What do you think will be the future ways that advances in molecular testing will improve patient care?

Years ago, I wrote an article about how we didn't expect to see molecu-

I ALWAYS EMPHASIZE THAT WE NEED TO COLLABORATE WITH MULTIDISCIPLINARY CLINICAL TEAMS. TO DO THAT, WE MUST SPEND MORE TIME OUTSIDE OF THE LABORATORY.

the pharmacists in my program are the ones who understand that first. We usually do preliminary studies with them when we want to implement a new panel, then the ASP staff and I decide whether to use it. Next, we offer education to providers throughout the hospital.

We have education programs designed for medical students, residents, fellows, general practitioners, and specialists—each of those groups has unique needs. We educate the nurses, too, particularly on the collection of samples, as we need a good sample to provide the right answer for the patient.

Does integrating molecular tests as part of ASP require different types of interpretation from the laboratory?

Clinicians, nurses, and pharmacists need to be educated about the advantages and limitations of tests. To help with the selection of the best treatment for a particular infection, the lab adds comments in the microbiology report to help

But for something like a gastrointestinal (GI) panel, we try to tell a provider not to order that unless the patient has been sick for more than 7 days, because most mild GI infections are self-limited and the patient is usually going to get better within that time frame. We leave specific comments for these situations so that at the time of ordering, the provider can see the requirement for ordering the test, and if the test is positive, a comment is added for an interpretation of those specific results. This has helped a lot in ambulatory clinics where it is otherwise very difficult to educate everyone working there.

What are some of the ways that you see molecular testing improving patient care in the context of ASPs?

No doubt having rapid results, particularly PCR testing for bloodstream infections, has been a huge help because every hour you delay administering not only antimicrobial

lar testing performed outside the main laboratory. I was afraid of people performing these tests without the right experience and that they could cause cross-contamination. But COVID-19 really changed my perspective. We didn't have any other choice but to provide molecular testing in other clinics. We trained them, validated the tests, then monitored how they were doing. We didn't have any problems during the pandemic with cross-contamination.

In the future, we need to have more molecular tests at the point of care. These tests could quickly diagnose some of the most frequently encountered infections and rule out things like SARS-CoV-2, group A *Streptococcus*, and influenza A and influenza B. Several test manufacturers have also added respiratory syncytial virus, as there has been an increase in cases of infection. Home testing also will continue. All of these advances can help decrease the likelihood of inappropriate antibiotic prescribing. ■

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MOLECULAR DIAGNOSTICS



An interview with Stella Antonara, PhD, D(ABMM)

How to Select Clinically Relevant Targets for Infectious Disease Panels

BY JEN A. MILLER

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ON

MOLECULAR DIAGNOSTICS

Designing infectious disease panels isn't as easy as picking a few targets off a list and sticking them into one test. Clinical laboratories must factor in many different considerations, from the pathogens physicians are already testing for, to available laboratory equipment, to inpatient versus outpatient status. Since the COVID-19 pandemic, physicians are also more aware of the power of molecular testing.

So how should clinical laboratories approach creating and evaluating infectious disease panels? We spoke to Stella Antonara, PhD, D(ABMM), medical director of microbiology at OhioHealth Laboratory Services, about this, and about how the changing role of point-of-care testing could affect infectious disease testing in the future.

When you build a molecular panel for infectious disease testing, what are the top considerations you have to weigh?

The first thing we do is review the list of the tests our providers send out the most. What are their needs? Do they test for a specific target? We also try to be good stewards of our resources and make sure results are informing care. If we bring a test on, we look at how results will be used, and if they're going to be acted upon in a reasonable amount of time. We also ask if we'll be able to have results for our providers with a fast turnaround time, which is usually another reason to bring a test in house.

Other important considerations include how the test complements the rest of the testing we perform in house, whether we can run the test on

a platform we already have, and—if yes—what other tests we can add on to this platform that we're already using. That goes back to being a good steward and utilizing resources we currently have available in the lab.

How would you advise others to approach making such decisions about these panels?

That goes back to your first question: What are you looking for when you're trying to make these types of decisions? It's utility and addressing patient needs. These decisions also depend on what kind of laboratory you are. If you're a reference lab, are you serving a big hospital system where a lot of different physicians can access the resources that you offer? Our microbiology laboratory acts as a reference laboratory for our hospital system. At the same time, we also have an extensive network of physicians' offices that we work with, so our panels would be available to them as well.

If you're an academic laboratory, you may have a niche area, and you may want to fulfill, not just clinical applications, but also research applications that dovetail with the clinical research your lab performs.

Did COVID-19 make clinicians more aware of the possibilities of molecular testing?

A silver lining of the COVID-19 pandemic is that information about clinical testing has gone out to everybody—not just to providers, but also to people in the community. People who are not laboratory oriented are using the term "PCR" left and right.

So yes, it goes without saying that COVID-19 brought a lot of awareness about molecular testing to providers.

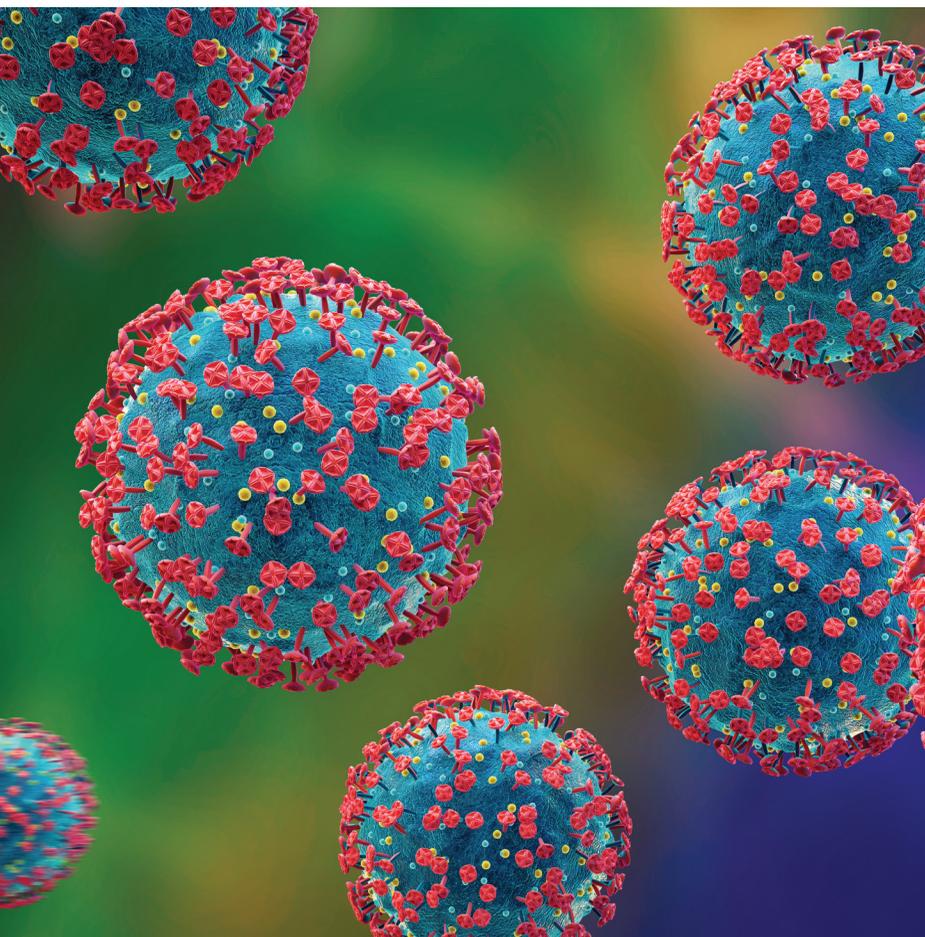
COVID-19 has also raised a lot of awareness with administrators about what we do, because they invested large sums of money to bring in new instrumentation to meet increased testing demands during the pandemic. So now everybody's looking into how we can utilize that equipment. We spent all this money—what do we do with these instruments now? How do we optimize available tests, and how do we optimize the platforms that we have. Could they be used for additional testing?

What is a clinical laboratory's role in helping clinicians evaluate panels they might have learned about elsewhere?

Clinicians now are very astute about what laboratories can offer. Diagnostic companies are targeting them with education on different available panels.

If someone comes to us with a test request, or we find a test we think might work for our patients, we test drive it with a few of our providers and see what they think of the results. We look at how those test results would fit in their practice and what the providers found helpful about them.

Sometimes we do a study and find that yes, a test is amazing. But we've also test driven a few where something that seemed so interesting and exciting in theory was not helpful at all in clinical practice, and we decided not to implement it.



How are all these considerations different for respiratory diseases versus gastrointestinal or other disease areas?

For respiratory panels specifically, when you design a panel for outpatient populations, you can just include the four or five pathogens most commonly found in the general population. But if you're designing panels for the inpatient population, especially for those who are immunocompromised, then you'd probably want to use a panel with a lot more targets. You'd have to have a larger panel so you can look for other things that are not so common and may not apply to the general population, but that may affect hospitalized patients.

When it comes to gastrointestinal panels, there are panels that detect bacteria, viruses, and parasites all together, but there's also an option to go piecemeal, i.e., let's test first for common bacteria, then go for viruses, especially if there's a known outbreak. If those are all negative, then go for the parasitic panel. It all depends on

how you approach diagnostics, and what patient population you're doing the testing for.

Regardless of what kind of panel you're using, it's important to educate providers on the large slew of organisms that can be analyzed. That's not necessarily needed for infectious disease providers, but it's important for your typical physicians' office.

Education around reimbursement is also particularly important. Insurance companies will ask why they should reimburse you for such a large panel, and what's the value if you have 15 targets versus if you have eight targets? Laboratorians can help clinicians make the right choice in these cases.

How do you collaborate with clinicians outside the laboratory when deciding on what targets/organisms should be in a panel?

In our healthcare system, we have groups that consist of each specialty who discuss best practices, not just

for treatment but also for diagnostic testing. We participate on those panels. That allows us to have a relationship with the representatives in each specialty, so we can hear what they want and what they need, and if those wants and needs change over time. It also helps us understand what they might want to test for in the future, so we can research and prepare for those upcoming requests.

How has COVID-19 changed these considerations in the lab for non-COVID testing?

There's been a lot of talk about how there's going to be an explosion of point-of-care testing. Whether that will happen or not, we'll see. For example, we thought we were going to have more flu point-of-care testing that could be done at home, and we haven't.

That's not to say COVID-19 hasn't changed point-of-care testing, but new point-of-care tests are being marketed more to physicians' offices than the general public. Yes, you can do testing at home, but from what I've seen personally at least, even people who home-tested a lot during the worst of COVID-19 are going back to the provider's office for respiratory illnesses.

As for how COVID-19 has impacted infectious disease panels, I see a lot of point-of-care testing and syndromic panels for respiratory illnesses that only have a few targets—three or four of the most common things that you see being marketed towards physicians' offices. We see this as part of a trend of decentralization, which makes sense.

How does that affect the central laboratory's role? It goes back again to diagnostic stewardship, and also healthcare systems having more equipment to run tests, especially molecular tests. I think that it does help to have more sensitive assays with faster turnaround times. But even with point-of-care tests, the bottleneck is still at helping our providers with interpretation of results. Having communication channels open and participating in panels and on specialty groups that can affect policy or guidelines that are going to be put forward is crucial. ■

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MOLECULAR DIAGNOSTICS

Regulatory Roundup

Emergency Use Authorization Granted to Quest Monkeypox Test

Quest Diagnostics has received Food and Drug Administration emergency use authorization for a lab-developed molecular diagnostic test to aid in the diagnosis of monkeypox virus infection. Known as the Monkeypox Virus Qualitative Real-Time PCR assay, the test detects monkeypox virus DNA from the West African clade and clade II, as well as non-variola Orthopoxvirus DNA in lesion swab specimens stored in universal viral transport media.

A September 2 Centers for Disease Control and Prevention (CDC) Lab Alert calls for CDC to confirm monkeypox test results from public health labs for certain highly suspicious cases with negative results; this is due to a

rare deletion in the tumor necrosis factor receptor gene of the virus. However, this alert does not apply to the Quest monkeypox test, the company said. In fact, Quest designed the test to detect both monkeypox virus and non-variola Orthopoxvirus DNA in order to help protect against false negatives.

Quest performs the test at its advanced laboratories in San Juan Capistrano, California, and Chantilly, Virginia. New York's Department of Health also has approved the tests from both laboratories, enabling access for patients living in the state.



COLLECTION TUBE FOR SARS-COV-2 TESTING RECEIVES 510(K) CLEARANCE AND CE MARK

MagBio Genomics recently announced Food and Drug Administration (FDA) 510(k) clearance and CE mark approval of its MagXtract Collection Tube, which is designed for sample collection and processing. According to the company, this is the first FDA-cleared collection tube with guanidine-free molecular transport medium that's available for SARS-CoV-2 testing. It will enable laboratory staff to comply with

FDA's advisory to avoid collecting SARS-CoV-2 samples in devices that use guanidine-based mediums, because cleaning these devices with bleach creates the highly toxic gas cyanide. In Europe, the MagXtract Collection Tube is available for testing for both SARS-CoV-2 and influenza and is validated for bacterial and fungal sample collection, as well as stabilization in research studies. The tube's medium directly lyses cells during transport and inactivates pathogens, eliminating the need for containment procedures. It also provides ambient temperature stability of RNA samples for up to 8

days, eliminating the need for cold storage and shipping.

ABBOTT'S TEST KIT FOR MONKEYPOX VIRUS GETS FDA EUA

The Food and Drug Administration (FDA) has granted emergency use authorization to Abbott Molecular's Alinity m MPXV test for monkeypox virus. The test uses lesion swab specimens in viral transport media from individuals suspected of monkeypox infections and is intended for use by CLIA-certified laboratories.

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- Hct
- Hb
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- Na
- K
- Cl
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- Lac
- Urea
- Creat/eGFR**
- tBil
- CO-Ox
- HbF
- MCHC**



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Mg⁺⁺ and Ca⁺⁺ Simultaneous disorders of Mg⁺⁺, Ca⁺⁺ and K⁺ are common among critically ill patients.^{1,2,3} All these electrolytes are critical in maintaining key physiologic functions including:

- Cardiac and skeletal muscle contractility
- Cardiovascular and respiratory smooth muscle tone
- Kidney function and fluid balance

Estimated Plasma Volume (ePV) The plasma volume status of a patient is one of the top priorities in treating critical conditions including CHF, ARDS, AKI, COPD, Surgery, and Sepsis.^{4,5} ePV monitoring allows clinicians to guide therapy for hyper- and hypovolemia in real time.

Creatinine/eGFR Over 50% of ICU patients will develop some degree of acute kidney injury (AKI).⁶ Creatinine/eGFR point-of-care monitoring provides an early indication of changes in kidney function and a guide for therapy to prevent AKI.

MCHC Mean corpuscular hemoglobin concentration (MCHC) provides insight into chronic low grade blood loss and autoimmune hemolysis.

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References

1. Cardaccio C et al. Multiple Electrolyte and Metabolic Emergencies in a Single Patient. Case Reports in Nephrol Vol 2017; Article ID 4521319:1-6.
2. Alabi FO et al. Multiple electrolyte imbalances and mixed acid-base disorder posing a diagnostic dilemma: a case report. J of Med Case Reports 2020;14(15):1-5.
3. Hypomagnesemic hypokalemia and hypocalcemia: clinical and laboratory Characteristics. Elisaf M et al. Miner Electrolyte Metab 1997;23(2):105-112.
4. Kobayashi M et al. Prognostic Value of Estimated Plasma Volume in Heart Failure in Three Cohort Studies; Clin Res Cardiol 2019;108(5): 549-561.
5. Metkus T et al. Estimated Plasma Volume is Associated with Mortality in Acute Respiratory Distress Syndrome. Crit Care Explorations 2021;3(9):1-9.
6. Mandelbaum T et al. Outcome of critically ill patients with acute kidney injury using the AKIN criteria. Crit Care Med 2011;39(12):2659-2664



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Although positive results from this test are indicative of the presence of monkeypox virus, FDA requires clinical correlation with patient history and other diagnostic information to determine patient infection status. Likewise, positive results do not rule out bacterial infection or coinfection with other viruses. Negative results must also be combined with clinical observations, patient history, and epidemiological information.

■ FDA FINALIZES GUIDANCE ON CLINICAL DECISION SUPPORT SOFTWARE

The Food and Drug Administration (FDA) has issued final guidance indicating the types of clinical decision support (CDS) software functions that are considered medical devices under the new definition of a device established by the 21st Century Cures Act. The guidance also clarifies the scope of FDA's oversight of CDS software intended for use as a medical device. It states that FDA's existing digital health policies continue to apply to software functions that meet the definition of a medical device, regardless of whether the software is intended for use by healthcare professionals or by patients and caregivers. The final guidance clarifies the types of CDS functions that do not meet the definition of a device, as well, and provides several related examples.

Additionally, it's worth noting that a section on the International Medical Device Regulators Forum's risk categorization that appeared in the 2019 draft version of this guidance is not included in the final version.

■ ROCHE GIVEN FDA CLEARANCE FOR SPACE-SAVING SYSTEM

The Food and Drug Administration has granted Roche 510(k) clearance for its cobas pure integrated solutions, which combines technologies for clinical chemistry, immunoassay, and

ion-selective electrode diagnostic testing on a single platform. With a footprint of about 21 square feet, the new compact, modular system is designed to help optimize space and resources for low- to mid-volume labs. The system also will provide access to a broad menu of more than 186 tests across a wide range of disease areas, including infectious diseases, oncology, and cardiology.

■ THERMO FISHER GETS FDA OK FOR CO-DIAGNOSTIC FOR CANCERS WITH RET MUTATIONS, FUSIONS

The Food and Drug Administration has approved Thermo Fisher Scientific's OncoPrint Dx Target test as a companion diagnostic to aid in the selection of patients who may be eligible for treatment with Lilly's Retevmo (selpercatinib). Patients who might benefit from this drug include those with RET-fusion-positive locally advanced or metastatic non-small cell lung cancer, RET-fusion-positive advanced or metastatic thyroid cancer, and RET-mutation-positive advanced or metastatic medullary thyroid cancer.

The test is also approved in Japan as a companion diagnostic for Retevmo with the same indications. With these approvals, the test is now authorized for use as a companion diagnostic in 17 countries for 15 targeted therapies. Using next-generation sequencing, it detects multiple alterations at once from a small sample size, helping to quickly match patients with the appropriate targeted therapy.

■ QIAGEN ADDS NEW CE-MARKED ASSAYS TO NEUMODX INTEGRATED PCR SYSTEM

The CE mark has been granted to Qiagen's new assays for Epstein-Barr virus (EBV) and human herpesvirus, which have been added to the company's NeuMoDx assay menu for organ transplant-associated viruses. The new assays support Qiagen's strategy of expanding the menu of tests available for use on

the NeuMoDx 96 and 288 molecular systems.

The new tests are intended to aid in viral load monitoring in the management of immunocompromised patients, such as organ transplant patients. Diseases caused by EBV can cause major complications in organ transplant recipients. Herpesvirus infections also remain a major cause of postoperative mortality in transplant patients.



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Ask The Expert

Mitigating Test Interference From Antioxidant Vitamins



EXPERT

By Vrajesh "Raj" Pandya, PhD, DABCC

Which vitamins have antioxidant properties?

A: Vitamins A, C, and E, as well as their precursors, all have antioxidant properties that reduce free radical-mediated cellular damage. Although vitamins A and E at high concentrations have the potential to cause serious health consequences, vitamin C has low toxicity potential. Its serum values in healthy persons range between 23 and

114 $\mu\text{mol/L}$. However, excess supplementation might result in concentrations as high as 30,000 $\mu\text{mol/L}$. These supraphysiological concentrations can interfere with a variety of lab assays.

Which lab tests are affected by vitamin C?

Redox reaction-dependent tests, including those for cholesterol, triglycerides, and enzymatic creatinine, are susceptible to interference by high-dose vitamin C. Because of its powerful reducing potential, vitamin C might artificially lower the chromogen signal dependent on peroxide generation. High vitamin C concentrations may also impact potentiometric assays, such as those for electrolytes.

Furthermore, the vast majority of vitamin C is eliminated in urine, and due to renal reabsorption of water, very high urinary vitamin C concentrations can be observed. Urinary vitamin C has been shown to affect dipstick testing for nitrites, bilirubin, glucose, and hemoglobin.

What indicators point to vitamin C interference?

A few telltale signs of antioxidant interference may include delta flags without obvious clinical or technical explanation, nonphysiological results (e.g., negative values), and nonlinear dilutions. Also, clinician inquiries calling results into question may raise suspicion of interference.

In such cases, laboratories may decide to measure vitamin C concentrations in the specimen. However, vitamin C concentration assays are expensive and often only available at reference laboratories. One potential alternative to these assays is to use test strips to detect vitamin C in a patient sample, an approach whose utility was demonstrated by our group in a recent case report (Clin Biochem 2021; doi: 10.1016/j.clin-biochem.2021.07.001). Although test strips are a straightforward and low-cost alternative to high-performance liquid chromatography-based assays, labs must still validate them before using them for clinical testing.

What can labs do to mitigate this interference?

Working in collaboration with

providers, laboratories can take a few steps to prevent vitamin C interference from affecting results:

Precollection questionnaires. Patients can complete these before their appointment at the clinic or collection site. The questions may ask about the type, amount, and frequency of any dietary supplements the patient may be taking. If the supplement intake appears to be excessive, the patient would then need to speak with a provider before specimen collection.

Clinician and patient education. Labs can identify the impacted tests and compile a list, which may then be shared with clinicians. To facilitate patient awareness, educational pamphlets explaining test interference in lay terms may also be posted at clinics and collection sites.

Chartable notes. Labs can determine the direction of change caused by interference in each of the affected tests. If the change in the result creates a delta flag, it may be reported with a chartable comment such as, "Antioxidants may interfere with this assay. Interpret the results in the clinical context."

Finally, labs may employ a few basic measures such as requesting a fresh specimen, performing serial dilutions, and testing on a different platform. When such approaches are not feasible due to limited volumes or the irretrievable nature of the specimen, storing the specimen at room temperature is another possibility, because vitamin C is temperature sensitive and its effectiveness declines with time.

The recent study performed by our group also showed the utility of a vitamin C-neutralizing enzyme called ascorbate oxidase (AO). Labs can treat patient specimens suspected of interference with AO prior to testing. Since this involves specimen manipulation, labs must perform a thorough validation taking into account regulatory aspects before trying this approach.

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