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CONTINUING EDUCATION

8 Bedside blood glucose testing in critically ill patients
By T. Scott Isbell, PhD, DABCC, FACB

14 Understanding diabetes testing: Where are we, and where are we going?
By Jack Zakowski, PhD, FACB

21 CE Test
Tests can be taken online or by mail. See page 21 for testing and payment details.

DEPARTMENTS

4 From the editor

6 The observatory

48 Washington report
Smart steps for labs and hospital outreach as CMS prepares to cut Medicare fees
By Jeffrey H. Myers, CPA

50 Product focus: virology

MARKETPLACE

53 Advertiser index

EXECUTIVE SNAPSHOT

54 Fostering a culture of innovation in laboratory diagnostics
Andy Hay
Executive Vice President
Sysmex America, Inc.

LAB MANAGEMENT

52 Transforming the microbiology laboratory to address the Triple Aim in healthcare
By Irene K. Dusich, MT(ASCP)SM

CLINICAL ISSUES

44 Summer’s coming: What’s new with Zika?
By MLO Staff

MANAGEMENT MATTERS

46 A system-wide movement to improve patient care and reduce unnecessary laboratory testing
By Pradhia Samaranord, MD, MPH; Megha Joshi, MD; Insha Haque, DO; Alison Scary, MS; H. BBA/ASCP; Stephan Geary, MLS(ASCP)SH, and Brian Collins, BS

FUTURE BUZZ

40 LDTs and the FDA: The saga continues
By Anna Longwell, JD, MBA, MS

EDUCATION

36 Assessing the suitability of NGS panels for clinical sequencing
By Kristina Giorda, PhD

38 Long-read sequencing: An alternative to Sanger-based instruments
By Kathryn Kaho

THE PRIMER

42 Metrics of assay accuracy
By John Brunstein, PhD

LAB OF THE YEAR

22 MLO’s 2017 Lab of the Year: David Grant Medical Center Laboratory

28 First runner-up: Cedars-Sinai Medical Center

29 Second runner-up: UKHC Enterprise Laboratories

SPECIAL FEATURE

30 Using strategic marketing approaches in lab outreach
By Peter Frances

32 A practical checklist for creating lab value with your physicians
By Linda Newman, MT(ASCP), MBA
AUTOMATION + INFORMATICS: KEYS FOR QUALITY-BASED HEALTHCARE
How El Camino Hospital Is Meeting Today’s Healthcare Challenges Head-On

The shift from a fee-for-service (FFS) reimbursement system to a value-based system is here—and the transition continues to affect healthcare institutions everywhere. Now more than ever, today’s hospitals need to measure quality and performance on a continuous basis. And if they aren’t meeting their quality standards, they need to pinpoint the cause. Here’s the story of how one facility recently tackled the challenge.

El Camino Hospital’s Mission: Streamline Workflow to Improve Patient Care
For more than a decade, El Camino Hospital (Mountain View, Calif.) has been a leader in laboratory process improvement. During that time, they have achieved a 95% autoverification rate and eliminated unnecessary draws through the implementation and use of integrated automation, LEAN processes and, most recently, truly advanced healthcare informatics solutions. El Camino Hospital’s two campuses continually enrich their experiences and contributions to their network by incremental improvements.

Initial Gains Through Automation and Information Technology
Working in partnership with Beckman Coulter, El Camino Hospital first automated its core laboratory in 2003. Since then, the organizations have continued to partner, implementing multiple workflow optimizations and solution upgrades, building a progressively stronger, more profitable and more efficient laboratory operation at every step of the way.

In terms of information technology, the laboratory’s transformation began in 2009, when it upgraded from the DL2000 Data Manager to the REMISOL Advance data management system with Command Central. First, they implemented standardized verification rules—thus eliminating subjective interpretation of results—and added the ability to view information from multiple analyzers remotely from a central location. The REMISOL Advance servers are configured with data redundancy features and automatic backup functions to ensure data integrity.

“In the past, we would occasionally turn out results for five or six hours before we realized the QC was out,” explained Abbott. “That meant we had to rerun all those patient samples and re-run the tests, which could be verified. This often added 15-20 minutes to our overall turnaround time.”

Adding Extended Quality Control (EQC)
In 2013, the laboratory’s quality and efficiency took another step forward when it added the optional Extended Quality Control (EQC) module to its REMISOL Advance systems.

“Prior to adding EQC, we had to delay placing patient samples on the instruments every morning until quality control, for all the tests, could be verified. This often added 15-20 minutes to our overall turnaround time,” said Abbott. “With EQC, however, we don’t have to wait for all QC to finish before loading specimens. Now our operators have full confidence that if any single test’s QC value is out, the patient results for that test will be blocked from autovalidation, so nothing gets reported erroneously. This enables us to bring patient specimens onto the instruments sooner, reduce TAT and increase workflow.”

The EQC patient protocols also feature exponentially weighted moving averages (EWMA), which adds another layer of assurance. This feature continuously monitors patient results between QC runs. If QC values start to drift, it alerts the reviewing technician in real time, stopping autoverification of those affected results.

“At the time, we didn’t know it,” revealed Abbott. “However, we had implemented a lot of things either in tandem with REMISOL or autoverification. Now our operators have full confidence that if any single test’s QC value is out, the patient results for that test will be blocked from autovalidation, so nothing gets reported erroneously. This enables us to bring patient specimens onto the instruments sooner, reduce TAT and increase workflow.”

Thanks to data-driven software and valuable new process insights, El Camino Hospital is focusing on bold, new LEAN initiatives that help bolster system-wide efficiency and improve patient satisfaction. The core laboratory has also received a lot of help from Beckman Coulter’s Continuous Process Improvement (CPI) Team, who has been instrumental in providing LEAN training and guidance.

“Over the years, Beckman Coulter has proven its excellence in all areas from sales to service,” said Abbott, “but these value-added resources like the business intelligence software and the LEAN expertise we’ve received in recent years really put our hospital way ahead.”

REMISOL Advance is a trademark of Normand-Info SAS.
The diabetes “epidemic” takes its toll

Historically, the term “epidemic” has been generally used for communicable or infectious diseases, so when we began to hear about the “diabetes epidemic” a number of years ago, some of us may have thought the term was being used for dramatic effect. Today, few would deny that type 1 and type 2 diabetes do indeed constitute an epidemic in North America and the world.

The raw numbers, as reported by Dr. Jack Zakowski in one of this issue’s two Continuing Education stories (pp. 8-18), tell the story in stark terms. The number of people with diagnosed diabetes in North America is projected to increase from 44.3 million in 2015 to 60.5 million in 2040.

In the world, the number is expected to increase from about 415 million in 2015 to almost 642 million in 2040. Aside from the incalculable human cost, this has the potential to disrupt the health systems— and economies—of even prosperous, developed nations. It might overwhelm developing nations, and it could add to social and political unrest in vulnerable societies.

A recent article by Claudia Buck in the Sacramento Bee contained some sobering, if not shocking, statistics about diabetes in California. She reports that as many as 55 percent of California’s adults either have diagnosed diabetes or blood-sugar levels that put them at risk. One-third of adults between 18 and 39 in California either have diabetes or prediabetes.

Buck also reports that the rising prices of insulin are forcing low-income people to “stretch out” their doses by halving them or skipping every other day—or to stop using insulin completely. Some, she reports, are returning to an older type of insulin, NPH (isophane insulin), which is less expensive but also less effective.

Into this sea of bad news wades the National Institutes of Health (NIH), with some alarming statistics about a phenomenon that is already alarming enough: that young people, teens, and even children are developing type 2 (noninsulin-dependent) diabetes at an increasing-rate. According to the NIH, young people with type 2 seem to be developing complications more often than their peers with type 1 diabetes. According to an NIH- and CDC-funded study:

• For youth with type 2 diabetes, nearly 20 percent developed a sign of kidney disease by the end of the study, compared to about six percent of youth with type 1 diabetes.

• For youth with type 2, about 18 percent developed nerve disease, versus about nine percent with type 1.

• For youth with type 2, about nine percent developed eye disease, compared to about six percent of youth with type 1.

• Measures for two risk factors for heart disease (hypertension and arterial stiffness) were greater for youth with type 2 but close to equal for a third risk factor (cardiovascular autonomic neuropathy).

• By age 21, about one-third of study participants with type 1 diabetes and about three-fourths of participants with type 2 had at least one complication from diabetes or were at high risk for a complication.

The role of the clinical lab is clear in this gathering storm: screening, diagnostics, and clinical monitoring of diabetes are key to controlling and eventually reversing the epidemic. More than ever, the lab will be at the forefront in giving clinicians the information they need to manage their patients with diabetes and prediabetes. Point-of-care diagnostics also are likely to play an increasingly important role.

The lab can also play a role in educating the public.

How can you, working with your larger institutions, help to make your community more aware of the dangers of diabetes, the relevant screenings, and the lifestyle and diet changes that can help people to avoid or delay diabetes, or to manage it?

Alan Lenhoff
FAST FACTS

Colorectal cancer is the third most common cancer diagnosis (excluding skin cancer) in the U.S. Additional statistics include:

- 50 years is the recommended age to start colon cancer screening.
- 95,520 is the number of newly diagnosed cases of colon cancer each year.
- 39,910 is the number of newly diagnosed cases of rectal cancer each year.
- 1 in 21 (4.7%) is the lifetime risk of developing colorectal cancer for men.
- 1 in 23 (4.4%) is the lifetime risk of developing colorectal cancer for women.

Colorectal cancer is the 2nd leading cause of cancer-related deaths in U.S. men.

Colorectal cancer is the 3rd leading cause of cancer-related deaths in U.S. women.

50,260 is the number of colorectal cancer deaths expected in 2017.


sequence analysis of the samples at the NVSL. All eight gene segments of the virus are North American wild bird lineage. This is not the same as the China H7N9 virus that has impacted poultry and infected humans in Asia. While the subtype is the same as the China H7N9 lineage that emerged in 2013, this is a different virus and is genetically distinct from the China H7N9 lineage.

Avian influenza viruses are classified by a combination of two groups of proteins: hemagglutinin or “H” proteins, of which there are 16 (H1–H16), and neuraminidase or “N” proteins, of which there are 9 (N1–N9). Many different combinations of “H” and “N” proteins are possible. Each combination is considered a different subtype, and subtypes are further broken down into different strains. Genetically related strains within a subtype are referred to as lineage.

The USDA continues to work with the Tennessee Department of Agriculture on the joint incident response. Birds on the affected premises have been depopulated, and burial is in progress. An epidemiological investigation is underway to determine the source of the infection.

Federal and state partners continue to conduct surveillance and testing of poultry within an expanded 10-mile radius around the affected premises to ensure all commercial operations in the area are disease-free. In addition, strict movement controls are in place within an established control zone to prevent the disease from spreading. As of March 6, all commercial premises within the surveillance area had been tested, and all of the tests from the surrounding facilities were negative for disease. Officials were continuing to observe commercial and backyard poultry for signs of influenza, and all flocks in the surveillance zone will be tested again.

Infectious Diseases

WHO publishes list of bacteria for which new antibiotics are urgently needed. The World Health Organization (WHO) has published its first-ever list of antibiotic-resistant “priority pathogens”—a catalogue of 12 families of bacteria that pose the greatest threat to human health. The list was drawn up in a bid to guide and promote research and development (R&D) of new antibiotics, as part of the WHO’s efforts to address growing global resistance to antimicrobial medications.

The list highlights in particular the threat of gram-negative bacteria that are resistant to multiple antibiotics. These bacteria have inherent abilities to find new ways to resist treatment and can pass along genetic material that allows other bacteria to become drug-resistant as well. The WHO list is divided into three categories according to the urgency of need for new antibiotics: critical, high, and medium priority.

The most critical group of all includes multidrug resistant bacteria that pose a particular threat in hospitals and nursing homes and among patients whose care requires devices such as ventilators and blood catheters. They include Acinetobacter, Pseudomonas, and various Enterobacteriaceae (including Klebsiella, E. coli, Serratia, and Proteus). They can cause severe and often deadly infections such as bloodstream infections and pneumonia.

These bacteria have become resistant to a large number of antibiotics, including carbapenems and third-generation cephalosporins—the best available antibiotics for treating multidrug-resistant bacteria.

The second and third tiers in the WHO’s list—that is, the high and medium priority categories—contain other increasingly drug-resistant bacteria that cause more common diseases such as gonorrhea and food poisoning caused by salmonella.

The list is intended to spur governments to put in place policies that incentivize basic science and advanced R&D by both public agencies and the private sector investing in new antibiotic discovery. It will provide guidance to new R&D initiatives such as the WHO/Drugs for Neglected Diseases initiative (DNDI) Global Antibiotic R&D Partnership, which is engaging in not-for-profit development of new antibiotics.

Genetics/Genomics

Gene variant linked to breast cancer risk in premenopausal African American women. Scientists at The Wistar Institute, in collaboration with Roswell Park Cancer Institute, have found a significant association between a rare genetic variant of the p53 gene present in African American women and their risk of developing breast cancer in premenopausal age. The study was published online by the journal NPJ Breast Cancer.

TP53 is the most frequently mutated gene in human cancer. The p53 protein is a critical tumor suppressor in the cell, and genetic mutations that occur in cancer cause a loss of its function in regulating proliferation arrest and cell death. In addition to these changes, there are several minor, naturally occurring genetic variants of the p53 gene, known as polymorphisms, and some are associated with an increased risk of cancer.
The rare p53 polymorphism analyzed in this study is found almost exclusively in populations of African descent. Wistar scientists have previously shown that this polymorphism impairs the ability of p53 to induce cell death in vitro and significantly increases cancer risk when recreated in a mouse model. The new study analyzed the statistical association of this variant with the risk of developing breast cancer in African American women.

Researchers conducted statistical studies on a cohort of more than 14,000 women of African descent and didn’t find any association of the polymorphism with increased breast cancer risk overall. However, as previously observed with other genetic variants of p53, a significant association was present in women in premenopausal age.

Elucidating the effects of p53 polymorphisms on cancer risk is a challenging task, especially due to the limited availability of sample cohorts from specific populations. This study provides a strong suggestion that the genetic variant considered might be associated with a significant increase in breast cancer risk, although this association will need to be confirmed in a larger sample set.

**Cancer**

**New blood test could help detect and locate cancer early on.** Bioengineers at the University of California San Diego have developed a new blood test that could detect cancer—and locate where in the body the tumor is growing. The study could provide a way to diagnose cancer early on without having to do invasive surgical procedures like biopsies. Researchers published their findings last month in *Nature Genetics*.

Cancer blood tests work by screening for DNA released by dying tumor cells. These tests are showing promise for detecting traces of tumor DNA in the blood of cancer patients. However, the results don’t indicate where the tumor resides.

“Knowing the tumor’s location is critical for effective early detection,” says Kun Zhang, senior author of the study.

In this study, Zhang and his team discovered a new clue in blood that could both detect tumor cells and identify where they are. When a tumor starts to take over a part of the body, it competes with normal cells for nutrients and space, killing them off in the process. As normal cells die, they release their DNA into the bloodstream—and that DNA could identify the affected tissue.

The method screens for a particular DNA signature called CpG methylation haplotypes, which are the addition of methyl groups to multiple adjacent CG sequences in a DNA molecule. Each tissue in the body can be identified by its unique signature of methylation haplotypes.

To develop their new method, the researchers put together a database of the complete CpG methylation patterns of 10 different normal tissues (liver, intestine, colon, lung, brain, kidney, pancreas, spleen, stomach, and blood). They also analyzed tumor samples and blood samples from cancer patients to compile a database of cancer-specific genetic markers.

The team then screened blood samples from individuals with and without tumors. They looked for signals of the cancer markers and the tissue-specific methylation patterns. The test works like a dual authentication process: the combination of both signals, above a statistical cutoff, is required to assign a positive match.

**Study finds biomarker for lung cancer detection in the nasal passages of smokers.** A new nasal test may allow patients suspected of having lung cancer to undergo a simple swab of their nose to determine if they have the disease. Researchers at Boston University School of Medicine have found that a genomic biomarker in the nasal passage can accurately determine the likelihood of a lung lesion being malignant.

The findings, which appear online in the *Journal of the National Cancer Institute*, will allow physicians to identify patients at low probability for having lung cancer, sparing them costly and risky procedures.

The diagnostic evaluation of lung cancer among high-risk current and former smokers with lesions found on chest imaging (computed tomography or CT) represents a growing clinical challenge given the current clinical recommendations for routine CT screening of high-risk smokers. While there are guidelines for the management of pulmonary nodules, unnecessary, invasive follow-up procedures (including surgical lung biopsies) are frequently performed on patients who are ultimately diagnosed with benign disease.

After examining nasal epithelial brushings from current and former smokers undergoing diagnostic evaluation for pulmonary lesions suspicious for lung cancer, the researchers determined that the nasal airway epithelial field of lung cancer-associated injury in smokers extends to the nose and has the potential of being a non-invasive biomarker for lung cancer detection.

**Autism**

Cerebrospinal fluid shows promise as autism biomarker. Researchers from the UC Davis MIND Institute, the University of North Carolina (UNC), and other institutions have found that altered distribution of cerebrospinal fluid (CSF) in high-risk infants can predict whether they will develop autism spectrum disorder (ASD). The study appears in the journal *Biological Psychiatry*.

Produced by the brain, CSF was once cast as a neural shock absorber, keeping the brain from bumping up against the skull. More recent findings have shown that CSF can influence neuronal migration and other mechanisms associated with brain development, as well as removing dangerous molecules.

This study confirms earlier research that showed infants with increased CSF in the subarachnoid space (near the brain’s perimeter) have increased risk of developing autism. The current study sought to validate the previous results in a larger sample of infants in the Infant Brain Imaging Study (IBIS), a national research network of institutions.

To test whether CSF might indicate increased risk of developing ASD, the researchers examined MRIs from 343 infants at six months, 12, and 24 months. In this group, 221 babies had older siblings with ASD and were therefore at higher risk for autism. The other 122 subjects had no family history.

Infants who later developed ASD had significantly more subarachnoid CSF at six months than those who did not develop the condition. Among high-risk infants, those who were ultimately diagnosed with ASD had 18 percent more. These measurements predicted ASD in the high-risk group with roughly 70 percent accuracy.

Finding biomarkers for autism, or any disorder, can be tricky. Quite often, early successes are never replicated. That this larger, more robust, follow-up study confirms the earlier finding is a significant step forward, the researchers say.

Still, this is early work, and there are many unanswered questions. The researchers do not know whether the CSF accumulation contributes to autism or is simply an effect from another, more subtle, cause. In addition, the biomarker is not sensitive enough to say with certainty that a child will develop ASD. However, the apparent link between increased CSF and autism could have significant clinical impact.
Bedside blood glucose testing in critically ill patients

Addressing discrepancies and confusion in the use of handheld meters

By T. Scott Isbell, PhD, DABCC, FACB

Studies have demonstrated that the practice of hospital bedside blood glucose testing is a necessary and effective means of managing and monitoring glycemic control. Protocols vary by institution, but there is general consensus among providers that this process is an essential component of patient care. However, the use of handheld blood glucose meters within some critically ill patient populations has resulted in varying degrees of confusion about off-label use and potential discrepancies in results.

As the most widely used option for measuring blood glucose at the point-of-care (POC), handheld meters offer the benefits of portability, ease of use, and procurement of quick results (less than 10 seconds) using small samples of capillary blood that can be obtained for frequent measurements. Testing can be performed by nurses, medical assistants, and technicians, and entails low risks of blood loss and arterial line infection. In comparison, core lab testing using arterial or venous blood involves a higher degree of complexity, along with the requirement that testing be performed by appropriately trained, qualified personnel.

Under most circumstances and conditions, handheld blood glucose testing meters can provide reliable readings with a high degree of accuracy. In a hospital setting, there are certain factors, including user errors in preparation and testing, that can contribute to inconsistent results: low hemocrit levels; the presence of vasopressors, ascorbic acid and other drugs; and the use of capillary blood specimens as opposed to arterial or venous blood samples. These factors can potentially lead to incorrect insulin administration or other treatments among specific populations of patients—namely, those who may be considered critically ill. In turn, this has created confusion among hospital staff and laboratory professionals across the country about the appropriate use of handheld blood glucose meters for critically ill patients.

Defining “critically ill”

The first step in providing clarification is to define what critically ill means for the purpose of blood glucose monitoring. Generally speaking, critically ill status can be determined by two considerations—the patient’s location (usually within an ICU or other acute-care department) and the patient’s health condition—or a combination of these criteria. In either category, critically ill should be defined in such a way as to identify patients in which POC glucose testing using a handheld meter is likely to yield erroneous results.

It’s important to note that the U.S. Food and Drug Administration (FDA) has not cleared any commercially available handheld blood glucose meter for use in testing capillary whole blood specimens collected from critically ill patients, meaning this practice would be considered off-label regardless of the meter. The probability for testing errors is highest when capillary blood samples are collected from patients who have impaired peripheral perfusion, which can occur when the conditions of dehydration, shock or hypotension, or hyperosmolar hyperglycemic shock are present. These conditions most commonly occur in critical care or acute care settings.

The definition of exactly what constitutes “critically ill” can vary by institution. For instance, some hospitals may define “critically ill” as any patient who has a mean arterial pressure of less than 60 mmHg; other institutions may consider any patient who is in the ICU and has an arterial line or a central venous catheter as “critically ill.” In any event, the definition should easily allow any provider to quickly identify patients who have impaired peripheral perfusion secondary to hypotension/shock.

Within this critically ill patient population, capillary blood specimens for glucose testing via handheld meter may not yield accurate measurements, and providers should default to the use of arterial or venous blood specimens to achieve the most reliable results. It is impossible to predict exactly which patient with impaired peripheral perfusion is going to have erroneous capillary POC results, and of what magnitude, if any, the error will be. For example, you could have two patients in shock, both with a mean arterial pressure of less than 60 mmHg. One patient’s capillary blood glucose result could be completely in agreement with a central laboratory measurement of glucose, while the other’s could be discordant to the point of clinical concern. There is no indisputable way to anticipate the probability of error, or to quantify it in definitive terms. Therefore, restricting use of capillary blood in patients with impaired peripheral perfusion is a reasonable thing to do to mitigate the risk of erroneous POC glucose values.

Off-label use

This all leads to the big question that is causing so much confusion among providers: Is using a handheld blood glucose meter in critically ill patients considered off-label, and if so, continued on page 10...
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Studies highlight the limitations of capillary blood

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<td>“Glucose meters using arterial/venous whole blood may be utilized in the MICU; however, due to the increased variability of results we do not recommend the routine use of capillary blood sampling for monitoring glucose levels in the MICU setting.”</td>
<td>Petersen JR, et al. Comparison of POCT and central laboratory blood glucose results using arterial, capillary, and venous samples from MICU patients on a tight glycemic protocol. <em>Clin Chim Acta.</em> 2008;396(1-2):10-13.</td>
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<td>“With capillary samples there were high numbers of errors as compared to the reference instrument. Measurement of blood glucose with arterial samples demonstrates a higher degree of accuracy.”</td>
<td>Slater-MacLean L, et al. Accuracy of glycemic measurements in the critically ill. <em>Diabetes Technol Ther.</em> 2008;10(3):169-177.</td>
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CMS interpretation

The original language in the Code of Federal Regulations as outlined in CLIA 88 speaks to modification of a testing device and indicates that changes must be validated to demonstrate that they still provide a robust, clinically appropriate measurement. By this guideline, the Centers for Medicare and Medicaid Services (CMS) could interpret modification to mean use of a device in a population of patients not specified in the package insert. CMS maintains its position that any deviation from the manufacturer’s package labeling may constitute off-label use of the device, which means it automatically defaults to the high complexity category. But there is no hard-and-fast rule across the board. Each of the major handheld blood glucose meters currently on the market today has its own unique package insert language, leaving each open to some degree of interpretation. This creates confusion about exactly what off-label use involves.

Glucose meters are generally labeled for the quantitative measurement of glucose in whole blood. Most indicate that the meter is not to be used for the diagnosis of diabetes, but rather as a tool to monitor the effectiveness of diabetes control programs. This language stems from the original intent of the devices to be used at home in the self-management of blood glucose concentrations in patients previously diagnosed with diabetes.

Hospital glucose meters are arguably used on almost all patients in the facility, not strictly for diabetes control, but rather for the management of dysequilibrium. Some meter package inserts include a clause that states the device has not been evaluated for use in critically ill patients. Only one glucose meter manufacturer has secured approval from the FDA for use throughout the hospital, including critically ill patient populations, when using arterial and venous blood specimens. No glucose meter manufacturer has secured approval from the FDA for use of capillary blood samples from patients who are considered critically ill.

From the current CMS perspective, if providers use a waived handheld blood glucose meter with labeling restrictions or limitations in patients defined as critically ill, it’s considered off-label use and immediately defaults to high complexity, which entails lab compliance with CLIA requirements for high complexity testing. At this point, only qualified personnel who have been trained as medical technologists, or individuals who...
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how a bachelor’s degree with an appropriate amount of science course work, can operate the meter in a population defined as critically ill. Additionally, the off-label use must then require full validation via method evaluation studies including but not limited to accuracy studies, precision studies, and analytical sensitivity and specificity studies. These studies are typically performed by the manufacturer and submitted to the FDA as part of the device review and labeling process.

**How to stay compliant**

Under CLIA protections, labs have the ability to go off-label at their own discretion, but they also must then adhere to all of the appropriate standards and rules as outlined by CLIA and CAP with respect to validations, personnel, training, competency, and periodic method evaluations of the device. Choosing to ignore these rules can result in severe consequences that may include citations and threats to accreditation. Habitual disregard of these standards can lead to the downstream effects of discredited lab reputation, CLIA license default, and even federal intervention.

Overcoming resistance to change is another wrinkle in the debate about the use of handheld blood glucose meters. Providers are always striving to find a balance between remaining compliant and ensuring optimal patient care. If clinicians aren’t properly convinced about—or even aware of—the limitations regarding capillary blood use for handheld glucose meter testing in critically ill patients, they may continue to perform these tests as they’ve always done in the past under the premise of interest in patient care. And, providers may struggle to understand why capillary blood is suddenly no longer permissible, when in their own personal experience, they’ve never had a problem using it before.

Achieving the best solution for the institution may require laboratory management to educate clinical and administrative staff about the limitations involved in using capillary blood specimens of critically ill patients for handheld blood glucose meter testing. Critical care doctors also have a valuable opportunity to play a role in drafting the definition of “critically ill” for purposes of blood glucose meter testing. Obtaining consensus on that definition within individual institutions is a strong first step toward eliminating a great deal of confusion about this ongoing issue.

The bottom line? Experience proves that blood glucose testing performed bedside using a handheld meter offers great value within the hospital setting. But care should be taken in determining whether capillary blood glucose measurements are the best choice among critically ill patient populations with impaired peripheral perfusion. In these cases, using an arterial or venous blood sample instead of a capillary blood specimen may be well advised. Institutions that decide to use a handheld blood glucose meter for any purpose possibly considered off-label should then follow the appropriate measures to remain compliant without compromising patient care.
Once-a-day QC works just fine, until it doesn’t.

How much of a risk is your lab taking?

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Understanding diabetes testing: Where are we, and where are we going?

By Jack Zakowski, PhD, FACB

Diabetes is a prevalent and pressing health concern, affecting 29.1 million people in the United States alone—8.1 million of whom are as-of-yet undiagnosed.1 While people with diabetes make up more than nine percent of the entire U.S. population, the Centers for Disease Control and Prevention (CDC) estimates that 86 million more people have some level of prediabetes,2 meaning they have blood glucose or hemoglobin A1c levels that are elevated but not to the point that they demonstrate frank type 2 diabetes. Prediabetes is an increased likelihood of developing diabetes.

Worldwide, in 2015, there were 415 million people with diabetes. That number is expected to jump to 642 million by the year 2040. North America, the Caribbean, and Europe will experience incremental growth in diabetes cases during that time, but other regions of the world will see numbers of patients with diabetes more than double (Table 1). A total of $673 billion—12 percent of global health expenditure—is allocated to diabetes.3

Type 1 and type 2
Not everyone with prediabetes will develop diabetes; however, an estimated 15 to 30 percent will develop non-insulin-dependent type 2 diabetes within five years.4 Non-insulin-dependent diabetes was formulated as a category after the discovery, in 1959, that some people with diabetes still produce insulin.5 Insulin-dependent diabetes, originally called “juvenile” diabetes, is categorized as type 1 and manifests with symptoms that are sudden and dramatic.

This distinction between type 1 and type 2 should not be seen as minimizing the health risks associated with type 2 diabetes, once also termed adult onset diabetes. Although the pancreas may produce insulin, the cells may not respond and, over time, the body may, in fact, stop producing insulin altogether. Alarmingly, too, an increasing number of people under 20 are being diagnosed with type 2 diabetes.

Both type 1 and type 2 diabetes carry the risk of significant complications, including heart disease and stroke, retinopathies and blindness, and chronic kidney disease. The poor peripheral circulation often seen in diabetes makes it the leading cause of amputations in many patient populations. Adults with diabetes have a 50 percent higher risk of death than those without diabetes.6 In 2012, $245 billion dollars were spent in the U.S. on both the direct (medical) and indirect (job loss, disability, and premature death) costs related to diabetes. Additionally, people with diabetes spend an average of 2.3 times more on medical care than those without diabetes.7

Successful diabetes management relies on early diagnosis and accurate monitoring. The human and economic toll of this fast-growing, often-undiagnosed health concern has led the medical community to seek testing that offers fast, cost-effective and reliable diagnosis and monitoring for better patient outcomes. The laboratory’s role in the diagnosis of diabetes, as well as evaluation of the type and severity, has become vitally important to the management of the disease, prevention or delay of onset, and prevention of complications. Defining diabetes has shifted to the laboratory, as symptoms alone (excessive thirst, frequent urination) are often not adequate for evaluating the presence or the progression of the disease.

Testing: glycemic control and risk prediction
Predominantly, two testing methods are used to diagnose and monitor diabetes: fasting plasma glucose (FPG or “glucose”) and hemoglobin A1c (HbA1c) testing. Both testing methods have their strengths and weaknesses, and proper understanding of the pros and cons of each enables appropriate application of the right test at the right time for better overall diabetes patient management.

<table>
<thead>
<tr>
<th>Range</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 mg/dL</td>
<td>Normal</td>
</tr>
<tr>
<td>100 - 125 mg/dL</td>
<td>Prediabetes</td>
</tr>
<tr>
<td>&gt;126 mg/dL</td>
<td>Diabetes</td>
</tr>
</tbody>
</table>

Table 2. Fasting plasma glucose (FPG or “glucose”) test ranges and results.7

FPG testing measures short-term glucose metabolism, indicating blood glucose levels at a given time. To get an accurate baseline glucose measurement, patients are required to fast at least eight hours prior to the test. Not all patients are compliant. Patients may think if they skip breakfast and only have some orange juice and a little toast, they are still “fasting.” This compromises the reliability of test results. Other factors that can affect results include acute illness, stress, and exercise. An FPG of less than 100 mg/dL is considered normal, while a reading above 126 mg/dL puts a patient in the range for diagnosis of diabetes (Table 2).7

While not ideal for diabetes diagnosis and management, there is a place for non-fasting glucose testing in giving physicians and patients quick results regarding the current

continued on page 16
## Diabetes Calibration Verification/Linearity and Daily QC

<table>
<thead>
<tr>
<th>Linearity Drop LQ Blood Glucose</th>
<th>Linearity FD Glycohemoglobin A1c</th>
<th>Control Drop LQ Blood Glucose</th>
<th>Control LQ Glycohemoglobin A1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order Number: K736M-5</td>
<td>Order Number: K703M-5</td>
<td>Order Number: K078M-8</td>
<td>Order Number: K067M-8</td>
</tr>
<tr>
<td>Levels: Five</td>
<td>Levels: Five</td>
<td>Levels: Two</td>
<td>Levels: Two</td>
</tr>
<tr>
<td>Format: Liquid</td>
<td>Format: Freeze Dried</td>
<td>Format: Liquid</td>
<td>Format: Liquid</td>
</tr>
<tr>
<td>Open Vial:</td>
<td>Open Vial:</td>
<td>Open Vial:</td>
<td>Open Vial:</td>
</tr>
<tr>
<td>7 days when stored at 2-8°C</td>
<td>7 days when stored at 2-8°C</td>
<td>7 days when stored at 2-8°C</td>
<td>50 days when stored at 2-8°C</td>
</tr>
<tr>
<td>Analytes: Glucose</td>
<td>Analytes: Glycohemoglobin A1c</td>
<td>Analytes: Glucose</td>
<td>Analytes: Glycohemoglobin A1c</td>
</tr>
</tbody>
</table>

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Hemoglobinopathies are genetic variants that affect the amount of glucose in the circulation. This glycated hemoglobin, measured as percentage of total hemoglobin, thus serves as an indicator of how much glucose is in the blood. A test result >6.5 percent HbA1c indicates diabetes (Table 3). Despite its widespread acceptance and use, HbA1c is not a replacement for FPG testing in managing diabetes. FPG is a measure of short-term glucose levels, while HbA1c is a measure of average long-term glucose levels. Thus, neither is a replacement for the other. Understanding each test, and their potential interferences, ensures proper use and interpretation, which results in more effective patient care (Table 4).

While there are some factors that interfere with FPG testing, interference related to HbA1c testing is more complex. Hemoglobin variants and analytical variables can interfere with HbA1c measurements, as well as the interpretation of results, leading to serious implications for both patients and the clinicians caring for them.

**HbA1c: hemoglobin variables**

Hemoglobinopathies are genetic variants that affect the structure of a patient’s hemoglobin, which, in turn, can impact an HbA1c test. There are hundreds of types and subtypes of hemoglobinopathies; most of them do not seem to have any physiological consequences nor an effect on HbA1c testing. Others are clinically significant. These include HbS (sickle cell), HbC, HbD, HbE and HbF (elevated fetal hemoglobin). Because HbA1c reference intervals and result interpretation are predicated on the assumption of a 90-day RBC average lifespan, any conditions that shorten (such as anemia) or lengthen the red cells’ average lifespans affect the concentration of HbA1c. Assays will accurately measure the concentration of HbA1c, but they cannot compensate for unknown changes to RBC lifespan. Laboratory personnel should work with physicians to understand patients’ underlying conditions and inform them that results must be interpreted with these factors in mind. Advances in laboratory testing capabilities have led many physicians to rely more heavily on the assistance of laboratory professionals in the clinical interpretation of test results. Offering a report that includes a statement that warns that anemia and thalassemia may affect interpretation, for example, may assist busy physicians in identifying patients who need more careful consideration.

Hemoglobin variants can cause some HbA1c tests to give false high or low results, leading to treatment that is inadequate or too aggressive. The National Glycohemoglobin Standardization Program (NGSP) offers a listing of tests from various manufacturers and their interactions with the most common hemoglobinopathies. Additionally, lab personnel should be familiar with the patient populations served by their laboratory and the potential genetic variants that may be prevalent in those populations.

**HbA1c: analytical variants**

Analytical variables relate to factors that interfere with the testing process itself. A test is only as accurate as the sample at the time it was assayed. Some errors are introduced during the handling of the sample, so it is vital for personnel to ensure samples are managed in a way that yields accurate results. An area of particular consideration is sample pre-treatment. Manual and automated sample pre-treatment options both offer benefits; however, each also presents conditions that must be taken into consideration.

While manual pre-treatment of samples often increases testing time, labor and cost, it enables personnel to maintain tighter control of the sample. At the same time, because it is a manual process, there is greater opportunity for human error during the pre-treatment step. Automated sample pre-treatment streamlines the pre-treatment process, reducing time, labor and costs; however, a sample can only stand upright for so long before a separation begins to occur, as the heavier red blood cells settle to the bottom of the tube. HbA1c test systems need to accommodate this behavior.

**Testing frequency**

The American Diabetes Association (ADA), the Endocrine Society, and the World Health Organization (WHO) have all endorsed the use of HbA1c for diabetes screening, diagnosis, and management. Recommendations for testing frequency are dependent upon a patient’s condition, compliance level, and risk factors (Table 5, pg. 18).
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<table>
<thead>
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<th>NAME:</th>
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<td>FACILITY NAME:</td>
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<td>CITY:</td>
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<td>PHONE:</td>
<td>EMAIL:</td>
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Table 6. HbA1c testing frequency. 

<table>
<thead>
<tr>
<th>Patients/Factors</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Diabetic patients who are stable and meeting treatment goals</td>
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<tr>
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<td>Quarterly</td>
</tr>
<tr>
<td>Testing or risk assessment of future diabetes in asymptomatic patients</td>
<td>Every 3 years, if prior HbA1C test is normal</td>
</tr>
</tbody>
</table>

The future of diabetes testing
Diabetes and its complications have become a growing concern for patients, physicians, laboratory personnel, and society as a whole. Present and future testing methods offer information that covers the spectrum of care. Laboratory professionals are often called upon to take a more active role in helping clinicians understand tests and interpret results; therefore, proper understanding of the strengths and weaknesses of today’s testing methods is imperative for proper disease diagnosis, monitoring and management. As future advancements in testing fill the gaps left by today’s technology, clinicians will continue to gain a better view of a patient’s condition, leading to more effective treatment and improved health outcomes.

REFERENCES

Table 5. HbA1c testing frequency. 

<table>
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</tbody>
</table>

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1. The benefit(s) of using handheld bedside glucose meters include:
   - a. portability and ease of use.
   - b. the fact that small samples of blood are required.
   - c. quick turnaround time of results.
   - d. all of the above

2. Factors that contribute to potentially erroneous bedside glucose results in the critically ill include:
   - a. low hematocrit level, vasopressor presence, ascorbic acid, capillary blood specimen dilution.
   - b. high hematocrit level, vasopressor presence, vitamins, capillary blood specimen dilution.
   - c. low WBC count, low hematocrit level, high blood pressure, blood specimen dilution.
   - d. low hematocrit level, high blood pressure, vitamins, capillary blood specimen dilution.

3. What consideration(s) is/are used to define a critically ill status?
   - a. the patient's location in a healthcare institution.
   - b. the patient's health condition.
   - c. a combination of the patient's location in a healthcare institution and the patient's health condition.
   - d. none of the above

4. Currently, the FDA has cleared one commercially available handheld glucose meter for capillary measurement in the critically ill population of patients.
   - a. True
   - b. False

5. The use of handheld blood glucose meters in critically ill patients is a practice that is
   - a. endorsed.
   - b. validated.
   - c. off-label.
   - d. accredited.

6. According to CMS rules, off-label use of devices should result in:
   - a. a change to high complexity testing.
   - b. only RNs performing the test.
   - c. a higher frequency of running QC within a 24-hour period.
   - d. all of the above

7. The use of an off-label device requires appropriate measures to be taken that
   - a. require validations, personnel training, competency, and periodic method evaluations of the device.
   - b. True
   - c. False

8. Disregard for the standards set in place for off-label use can lead to potential
   - a. discredited lab reputation.
   - b. CLIA license default.
   - c. federal intervention.
   - d. all of the above

9. The CDC states that, in addition to the diabetic population, the number of Americans with prediabetes is estimated to be more than:
   - a. 45 million people.
   - b. 66 million people.
   - c. 75 million people.
   - d. 88 million people.

10. According to the article by Dr. Zakowski, what percent of the total worldwide healthcare expenditure is allocated to diabetes?
    - a. 4 percent
    - b. 9 percent
    - c. 12 percent
    - d. 16 percent

11. It is estimated that most people with prediabetes will develop type 2 diabetes within ________ years.
    - a. 2
    - b. 5
    - c. 7
    - d. 10

12. Significant complications experienced by people with diabetes include heart disease, stroke, retinopathies, blindness, and kidney disease.
    - a. True
    - b. False

13. Which are the most common testing methods used to diagnose and monitor diabetes?
    - a. fasting plasma glucose and hemoglobin A1c
    - b. fasting plasma glucose and plasma insulin levels
    - c. hemoglobin A1c and plasma insulin levels
    - d. none of the above

14. Factors that interfere with fasting plasma glucose (FPG) testing include all but the following:
    - a. fasting noncompliance
    - b. exercise
    - c. thalassemia
    - d. acute illness/stress

15. Non-fasting glucose values are most appropriately used to manage which condition(s)?
    - a. average long-term glucose levels
    - b. acute hyperglycemia
    - c. hypoglycemia
    - d. b and c

16. Any condition that shortens or lengthens red cells’ average lifespan has the potential to give false-high or false-low hemoglobin A1c levels.
    - a. True
    - b. False

17. The analytical variable(s) of concern that may affect hemoglobin A1c results is/are
    - a. manual dilution errors
    - b. interfering substances in the specimen
    - c. manual pretreatment of specimen before testing
    - d. all of the above

18. Which organization(s) has/have endorsed the use of hemoglobin A1c for diabetes screening and diagnosis?
    - a. ADA
    - b. Endocrine Society
    - c. WHO
    - d. all of the above
Travis Air Force Base, located in the San Francisco Bay area, near the town of Fairfield, California in Solano County, is an integral part of the American military. The host unit at Travis AFB is the 60th Air Mobility Wing, which is the largest wing in the Air Force’s Air Mobility Command. Travis AFB has a fleet of C-5 Galaxies, KC-10 Extenders, and C-17 Globemaster III aircraft. It is home to the 60th Air Mobility Wing, the 349th Air Mobility Wing, and the 621st Contingency Response Wing.

It is also home to the David Grant USAF Medical Center, and the David Grant Medical Center (DGMC) Laboratory, which is the largest clinical laboratory in the Air Force Medical Services (AFMS). The editors of Medical Laboratory Observer are proud to salute the David Grant Medical Center Laboratory as the 2017 Lab of the Year. We congratulate all of the labs who submitted nominations, as we celebrate with our readers Medical Laboratory Professionals Week, April 23 through April 29, 2017.

As the largest clinical laboratory in the AFMS, the DGMC Laboratory, with 91 military and civilian full-time equivalents, provides a full spectrum of testing for 465 healthcare providers, who in turn serve a patient population of 368,000 active duty/reserve/veteran/retiree military, military family member, and Department of Defense (DoD) civilian staff. The DGMC lab supports 325,000 annual patient visits and 6,000 admissions. It is the largest point-of-care testing program in the Air Force, managing 23 sites. David Grant Medical Center is a 116-bed medical treatment facility, and the lab performs 1.2 million tests annually in Chemistry, Special Chemistry, Hematology, Coagulation, Immunology, Microbiology, Point-of-Care Testing, Histology, Cytology, and Transfusion Services.

MLO asked those submitting nominations for the 2017 Lab of the Year award to discuss their lab in terms of these six criteria: Customer Service, Productivity, Teamwork, Education and Training, Strategic Outlook, and Lab Inspections.

In the nominating form and in a subsequent interview with lab leaders, the DGMC Lab gave MLO much more information than we have space to present here, but, to organize this article, we will use those categories as sub-sections to review some highlights.

Customer Service
In discussing service provided to both internal and external customers, DGMC lab leaders stress the importance of access and communication. They have facilitated better patient care by implementing the MiCare secure messaging service, which allows patients to access health information online. Patients can choose to receive notifications when their lab results are reported, view and print lab results, and look up pending tests from their MiCare online profile. MiCare can be accessed from phone, tablet, or computer. The patient community, including veterans, is being encouraged to use this valuable service.

Healthcare providers are also able to access test results via four IT platforms: CHCS, ALTA, CoPath and Essentris. Outside providers that order lab tests for patients receive results via secure fax line, enhancing continuity of care from the DGMC to their organizations.

During 2016, the DGMC Lab initiated an auto-validation process improvement. This process, used in many of the core laboratory testing platforms including chemistry, hematology, and coagulation, has reduced “lab to provider” result times by more than 30 percent. The lab also has an extensive, proactive outreach program that joins with all hospital departments that use lab services to ensure that it has the appropriate test menu, that physicians are using resources responsibly, and that an interactive format is in place to address safety-related or operational incidents.

Productivity
The military as a whole focuses on productivity in utilizing resources effectively to meet mission needs, and the DGMC Lab fosters and reflects that focus in a variety of measurable ways.

In 2016, the lab formed a 10-person team tasked with creating an upgrade plan for eight core laboratory analyzers and initiated new contracts worth $8 million. This 400-hour undertaking enabled the lab to obtain (from Siemens) a fully automated robotic testing line, which is projected to recoup five FTEs/$1,500,000. Leveraging this new technology will allow the lab to run more tests, more efficiently, with less staff.

At the same time, process improvements related to how the lab manages cardiac panels led to expedited processing, outdoing the national turnaround time average by 41 percent. In addition, process improvements to tuberculosis management procedures led to a reduction from 72 to
24 hours, reducing costs and decreasing isolation times for patients. The histology department improved its tissue staining procedures, reducing staining time by half. The lab also revamped its records management procedures last year, allowing it to recoup 33 percent of storage space while still upholding HIPAA requirements.

In Microbiology, the launch of a new analyzer cut processing time from 15 minutes to five, and increased accuracy by 20 percent. The implementation of five new rapid tests, including Shiga Toxin, Stat Campylobacter, and Bacterial Motility, cut manual testing time by 25 percent and led to a five percent reduction in errors. By creating and implementing a new cross-training generalist program, the Micro lab saved two FTEs via efficient human resources allocation. It also began a new construction redesign project that improved workflow by 11 percent. In Transfusion Services, an effective new blood utilization project reduced waste of blood products by more than 50 percent.

**Teamwork**

DGMC holds trainings for staff members on how to work together to provide cost-effective, efficient care in the safest manner possible. Individual lab departments hold “safety huddles” daily, followed by a comprehensive, hospital-level safety huddle to which the lab contributes its input. Lab leaders stress that these daily interactive meetings are valuable vehicles for sharing lessons learned, innovative ideas, and patient and staff safety concerns. Says Lt. Col. Patrick Kennedy, Clinical Laboratory & Pathology Flight Commander, “These meetings allow us to come together as a unit and create a synergy that helps our staff to be more efficient, patient-centered, and productive.”

The lab also teams with other organizations in various capacities. It partners with the Department of Veterans Affairs, which has a clinic in the hospital, to perform lab testing for veterans. It teams with the Air Force and Armed Services Blood Program to ensure the safety, purity, and potency of blood products and to provide input for planning for next-generation IT and blood processes and procedures. The lab also partners with the hospital’s Clinical Investigation Facility, providing manpower and lab work to support research efforts, and joins with the Armed Services Whole Blood Processing Laboratory (West) to support its mission to provide blood products for military treatment facilities throughout the Pacific region.

DGMC pathologists also provide medical director oversight for seven other military medical facilities, traveling around the country to ensure that uniform standards are observed. The Anatomic Pathology department is a West Coast hub for DoD consultations, receiving samples from 39 other DoD and 10 VA/civilian facilities. These include DoD hospitals in Japan and the Republic of South Korea.

Internally, lab personnel are key members of hospital disaster management teams. Regular training is held at the hospital or in other designated areas to simulate a natural or human-made disaster. Those drills continuously improve coordination between the lab and other departments, as well as between the hospital, the military base, and civilian authorities, responders and healthcare facilities.

In addition, in 2016 more than 30 lab staff and students collaborated with base and community agencies to volunteer 387 hours for 12 community service projects. Examples of staff volunteer work include the Boy Scouts, Habitat for Humanity, Airmen Against Drunk Driving, Foster a Dream, the USO, and youth sports. In the military culture, volunteer activities are closely tied to team-building.

Teamwork is also promoted by professional development courses offered to the staff. The lab facilitated three Four Lenses Personality Test classes to foster communication and understanding. A total of 46 personnel completed the six-hour class.

The Air Force brings together men and women from various backgrounds and cultures and instills in them common ideals and a common purpose. Furthermore, in the lab, there...
is a significant turnover. “Turnover is a special challenge that our military laboratory faces,” says Lt. Col. Jimmy Labit, Laboratory Services Chief. “Because our military members transfer from base to base every two to three years, we can experience anywhere from a 33 percent to a 50 percent turnover annually. A focus on leadership and a strong training program are key to meeting this challenge.”

“One special quality about our laboratory as a military organization is our focus on leadership,” adds Maj. Edward Griffin, Central Operations and POCT Chief. “Managers organize; leaders inspire. We do not focus only on the organizational aspect of our mission. We also seek to provide leadership by example—to inspire our staff to be the best they can through teamwork and inner dedication to the cause of protecting our country.”

Education and Training
In that context, the lab has a thorough and standardized new employee orientation and training program, including an overview of DGMC’s healthcare service and support mission and operating structure. It has an extensive and standardized competency program and process, and it focuses on exceeding training standards as set forth by CAP, The Joint Commission, and AABB. Of special note is the implementation of a computerized CAP competency program. Courses are built for each lab task/procedure and include such items as checklists that can be referenced by staff, educational materials, and a post-course exam. The program tracks initial, six-month, and annual assessments and automatically assigns and notifies staff members when they are due for their next assessment.

As part of the strategy to train and incorporate junior laboratorians, the DGMC lab has implemented an “All Hands on Deck” program, daily from 10 AM to 2 PM. During that time, senior leadership and technical supervisors are on the bench working side-by-side with airmen (junior techs) to ensure that they receive the mentorship required to master necessary skills. Mentors engage the junior staff in critical thinking exercises to promote ownership of duty and ensure focus on patient welfare.

In addition, military staff members receive extra training on the military aspects of their work with a special focus on skills and competencies needed for missions and agencies that they may deploy to such areas as Iraq, Afghanistan, Qatar, Jordan, Kuwait, and other areas to support the nation’s strategic goals. Staff members provide laboratory services, blood support, and other general military services as needed. These additional levels of training and responsibility are not found in the civilian world and are a unique aspect of the DGMC lab’s utilization, education, and training programs.

With regard to education and career advancement, the lab also has a dual military and laboratory professional support system. Base facilities include an educational center and several local and national college representatives to assist staff members and their families. Military staff can receive tuition assistance to help pay for college costs, and the Air Force has a program to reimburse staff members who pay for and pass professional laboratory certifications. Military staff members also receive the Post 9/11 GI Bill, which pays for up to three years of full-time college tuition.

All staff members have access to free online CMEs at the lab’s expense to assist them in staying current in their field and with their professional certification renewals. Military staff members new to the field are given free career development courses on every aspect of laboratory testing and procedures spanning, on average, one year’s worth of coursework. Military staff are also offered free College Level Examination Programs on base, and the lab also has instituted a volunteer study program to assist medical laboratory students in passing their ASCP MLT exams.

The lab has also led with a comprehensive Individualized Quality Control Plan (IQCP) Program that meets the requirements for an alternate quality control option as allowed by 42CFR493.1250. Implementing its IQCP program, which includes 12 IQCPs, has allowed the lab to customize its quality control plan based on its testing use and methodology, personnel competency, and clinical environment.

At the 2016 Clinical Laboratory Management Association/Society of American Federal Medical Laboratory Scientists (CLMA/SAFMLS) annual meeting, the staff presented on management and team building, and the DCMG lab was selected to make four presentations at the 2017 meeting, continued on page 26
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Sources:
Strategic Outlook

The DGMC lab’s strategic outlook includes its mission, its vision, and its strategic plan:

- Laboratory Mission: “To optimize patient care 24/7 through accurate, timely, laboratory support and state-of-the-art technology, and to train tomorrow’s leaders in the science of laboratory medicine.”
- Laboratory Vision: “To lead the way in laboratory innovation, readiness, service, and training.”
- Strategic Plan: The lab’s plan focuses on three areas:
  - “Improving efficiencies through better training innovation, standardization, and communication by utilizing the right personnel while optimizing the resources to complete the job.”
  - “Developing staff members through professional development and empowerment.”
  - “Leaning forward to better serve patients by increasing customer focus areas both internally and externally, and maintaining an effective continuous quality improvement program [while] implementing as many ‘best lab practices’ as possible.”

“What binds us together in the Air Force is our Core Values: Integrity First, Service Before Self, and Excellence in All We Do,” says Lt. Col. Kennedy. “We have a very diverse staff from different backgrounds. Our Core Values are our guiding principles that enable us to work as a team to provide quality healthcare service support.”

Lab Inspections

DGMC is The Joint Commission-accredited, and the laboratory has a record of outstanding regulatory inspection results. The lab is CAP-accredited. Its Transfusion Service laboratory technician clinical training program in the United States.

The Quality Assurance Team includes staff members from all departments. Team members have diverse backgrounds and many decades of laboratory experience and include specialty-focused members such as Certified Quality Auditor (ASQ), Specialist in Blood Banking (ASCP), MBA in Finance, MA in Organizational Leadership, MS in Business, California licensed Clinical Laboratory Scientists, and many others. Several members are also active CAP inspectors and AABB assessors. Members ensure that the lab is current with CAP, AABB, TJC, FDA, Department of Defense Clinical Laboratory Improvement Program (the military form of CLIA), and ISO standards and requirements.

The laboratory has a strong quality program. Members of the Quality Assurance Team perform audits and process improvement initiatives on a continual basis. In the area of management responsibility, managers provide a vision, are customer-centered and committed, and keep staff members informed. In resource management, the focus of the lab is having the right person do the right job while creating and maintaining a positive work environment. In its quality management system, the lab ensures proper oversight and documentation of processes to ensure quality work in meeting patient needs. In the area of product realization, the lab ensures that final testing results and blood products issued are top quality, meet regulatory requirements, and are delivered to patients and healthcare providers in a timely and proper manner.

“Our laboratory’s continuous quality improvement committee has facilitated improved processes and attained excellent reviews from accreditation agencies,” says Laboratory QA Manager Maria Langeslay, MT (ASCP), CLS. “This committee tracks more than 35 quality monitors including all areas of the lab and POCT to evaluate trends in all process components (preanalytical, analytical and post-analytical). As part of our High Reliability Organization initiative, which is David Grant Medical Center’s goal, we use any findings as an opportunity to learn and improve lab practices and processes to provide better care and ensure patient safety.”

Celebrating Lab Week

And, the DGMC Lab has big plans for Lab Week, both in terms of acknowledging its internal customers and reaching out to its external customers, the public. The Wing Commander will formally declare Lab Week, and then the celebration will begin. Among scheduled activities are a 5K run and multiple games; a blood drive; sponsored meals; an Open House so that community members, including patients, can see how the lab operates—how the profession of clinical laboratory medicine unites with the profession of arms to create excellence. In addition, a series of articles about different sections in the lab will appear in the base publication, as a build-up to what will surely be a memorable Lab Week for the David Grant Medical Center Laboratory.

The editors of MLO wish all of our readers the very same!
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Also last year, the CSMC Microbiology division expanded the use of existing molecular platforms using syndromic pathogen identification panels to diagnose sepsis, respiratory, HSV, diarrheal and parasitic infections. Organism identifications that used to take two to three days via culture are now available the same day.

The lab also saw significant advancements in 2016 with regard to turnaround time more generally:

- CSMC added a new STAT PTH assay to their Roche Cobas e411 in the Cancer Center has reduced TAT by 60 percent.
- Fluid Cell Count (FCT) specimens from the Emergency Department (ED) are now sent to the Core Laboratory instead of the ED, resulting in 80 percent of testing completed within a 60-minute goal (vs. 26 percent, previously).
- The lab implemented a workflow analysis for its Kidney Transplant Services, which reduced lab TAT by 15 percent. It also worked with laboratory support services to ensure that is was getting samples in a timely manner, which reduced TAT by 50 percent.

CSMC has also been successful with adding an automated coagulation testing process, improving a process that frequently had issues where the specimen was not delivered either in a timely manner or at all. The programming of the automated line was modified such that when testing at the first location was complete, all coagulation specimens would be put back on the line and aliquoted for the secondary location if there was additional testing. In this manner, the process was automated and no specimens are missed for secondary tests.

In 2015, the Molecular Pathology division was selected as the sole Roche Ampliprep testing site for Bio-Rad’s Value Assignment Program. Molecular pathology establishes the reference range for Bio-Rad QC materials manufactured for HBV, HIV, and HCV quantitative viral load tests.

In 2016 Cedars-Sinai was selected by the U.S. Department of Health and Human Services to serve as a regional treatment center. Cedars-Sinai and the California Department of Public Health will share the grant from the federal agency through fiscal year 2019 to strengthen the delivery of specialized emergency medical care. The federal grant is part of the $339.5 million in emergency funding appropriated by Congress in 2014 to ensure that the nation’s healthcare system is prepared to treat future patients with Ebola or other highly infectious pathogens. Their national network will serve patients from California, Arizona, Nevada, Hawaii, and United States territories in the Pacific.

Improving the patient’s experience has been a major initiative over the past year. CSMC lab leaders have identified the following four “Vital Behaviors:”

1) Treat patients, family members, and co-workers with courtesy and respect.
2) Explain things in a way that patients, family members, and co-workers will understand.
3) Listen carefully in order to understand patients, family members, and co-workers.
4) Anticipate and respond to patient, family member, and co-worker requests and concerns in a timely manner.

In partnership with the Antimicrobial Stewardship committee at Cedars-Sinai, the Microbiology division collaborated with Pharmacy to expand rapid diagnostic testing (RDT) to support timely decision making for a patient with bacteremia, with the goal of optimizing antimicrobial therapy. This has resulted in a 10 percent decrease in Antibiotic Days of Therapy house-wide. An even more significant decrease (32 percent) was also seen in days of therapy using anti-pseudomonal antibiotics without substitution.

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Headquartered in Lexington, KY, University of Kentucky Healthcare Enterprise Laboratories (UKHC) performs laboratory services to clinical and anatomic labs at UK Chandler and UK Good Samaritan Hospitals.

UKHC has grown dramatically in recent years. Between 2004 and 2015, hospital discharges increased 88 percent while the complexity of the cases they treated moved them from the 25th percentile of academic medical centers to the 75th. At the same time, overall improvements in the quality of care and patient safety led to UK HealthCare receiving the UHC Rising Star Award in 2013 and becoming a national leader in patient safety in 2015. It has received Magnet status, the highest recognition available in the nursing field.

The UKHC lab bills approximately 3.4 million tests per year. Its disciplines include Core Chemistry, Microbiology, Special Chemistry, Blood Bank, Immunomolecular Pathology, Genomics, Cytogenetics, Cytology, Surgical Pathology, Histology, Immunohistochemistry, Cell therapy and Autopsy.

Both patient and employee safety are of utmost importance for UKHC. As one example of the lab’s dedication to safety and comfort of both internal and external customers, lab leaders recently identified noise pollution caused by nitrogen generators in Toxicology and are installing a centralized nitrogen generation system to supply nitrogen to the four LCMSMSs in the lab and reduce the noise level.

Also, several technologists and leaders have created a focused customer service training module for the Central Processing and Core lab staff to ensure that a consistent and positive message is being delivered to customers.

In addition to investing in and upgrading the lab’s state-of-the-art technology during the past few years, lab leaders also undertook a department “face-lift” both to raise morale and increase output, while a reshuffled floor plan allows for easier maintenance of processors and recycling management. Revised policies and procedures have been implemented, nearly eliminating redundancy, which ultimately reduces errors that could jeopardize patient care.

Implementing teamwork within other departments, such as collaborating with nursing to enhance education, has also been part of UKHC’s strategy. The lab staff recognizes that without teamwork within the lab and between the lab and other departments of the hospitals, it would not be able to sustain high quality in light of the organization’s growth over the last several years. Input from all staff is part of continuing improvement, as the best ideas often come from the staff performing the work.

In submitting their nomination form to MLO, UKHC representatives noted, “A critical component of employee engagement is personal acknowledgement.” Education and training are stressed as opportunities for employees to advance their care. Three career development tiers have been established to provide recognition of a high level of performance: bronze, silver, and gold. Advancement is predicated on achieving a set of performance standards and personal development initiatives and does not carry over from year to year.

In 2016 UKHC took on the conversion of staff titles from MT to MLS; a big undertaking, but the lab had reached a point where it was necessary to separate the staff titles in the esoteric labs from the traditional Medical Technology disciplines. The lab now has Laboratory Scientists, certified and uncertified, and MLS, certified.

In line with replacing and embracing new and emerging technologies to provide more accurate, timely results, the lab has acquired a high end LC/MS/MS to develop in-house testing (LDTs). It also continuously evaluates and improves point-of-care testing (POCT) practices at ambulatory clinics. Other strategies include investing in Microbiology automation (Wasp and WaspLab) and Core Lab (Roche automation and Sysmex), and the lab has pioneered interfacing with Copan Italy and Beckman Coulter to develop the Sunquest interface for WaspLab. Lab leaders are currently working with Lumixen to validate/develop the Sunquest interface for the Verigene system.

UKHC is accredited by CAP, AABB, FDA, TJC, FACT (Foundation for the Accreditation of Cellular Therapy), and OIG (Office of Inspector General). Many UKHC staffers are seasoned inspectors for CAP, AABB, and the Forensic Urine Drug Testing CAP program. The lab also has recently acquired a Quality Manager at Chandler Hospital and a Quality Coordinator at Good Samaritan, which allows lab leaders to keep abreast of changes in regulatory management and manage quality, compliance, and safety on a daily basis. UKHC’s lab inspections have been consistently successful.

Second runner-up: UKHC Enterprise Laboratories
Using strategic marketing approaches in lab outreach

By Peter Francis

According to more than one survey, hospital labs have dedicated more resources to outreach in recent years than they did in the past. The same surveys, however, indicate that many labs do not have sales representation. There may be valid reasons why a hospital claiming to have a lab outreach program prefers not to employ staff to compete for additional business. However, it stands to reason that if a business enterprise wants to grow, it must have a well-qualified field person. The situation compounds itself in this preordained zero-sum game. “Bang on doors” in an attempt to steal lab work from anyone in this limited fashion (e.g., referring only STAT testing). Given some service equivalence, however, it’s possible for an effective field rep to transform the hospital lab into the primary reference source.

Commercial competitors work diligently to pinch routine lab work that could just as easily go to a local hospital. Using the hospital’s services helps to support its well-being, help the local economy, and contribute toward the employment base. Yes, there are some financial investments that must be made in order to compete; however, the return on investment can be worth the expense as long as there is focused management oversight, someone to make sales and service calls, and C-suite advocacy.

Outreach strategies

Medical centers should investigate the following approaches. Some of them may seem obvious, but there are hospital labs across the U.S. that have not implemented even some of the most conventional ideas:

- Provide in-office phlebotomy services in high-volume offices/clinics (state law dependent).
- Create a professional-looking four-color capabilities brochure with the help of your internal Marketing Department— or seek outside consultative help.
- Ensure the hospital’s website has easy-to-find, dedicated lab client services and billing, test menu, specimen requirements, and professional staff listing/contact information).
- If the hospital owns a medical building and a competitor rents space for a draw center, either cancel the lease or do not renew it. Install a hospital phlebotomy center in its place.
- Hire a dedicated representative to service existing accounts and market potential accounts. Pay him/her a competitive salary, with incentives for maintaining and adding new business.
- Properly train the field rep with regard to:
  - In-house test menu
  - IT connectivity (EMR, lab portal, fax)
  - Your lab’s reference lab and high volume send-outs
  - Upselling strategies
  - Billing intricacies
  - Sales compliance
  - Unique competitive differences
  - Sales strategies
  - Tactical sales methodologies
  - Required weekly/monthly sales reports
  - Clinical decision support tools to aid physicians.

This knowledge establishes credibility and trust with the customer—the foundation of sales and service.

Marketing motives

Consider how much a lab outreach program can evolve beyond the bullet-points mentioned above. A portion of this transformation requires someone with proficient marketing skills to visit prospects, build rapport, ask focused questions, discuss positive attributes, overcome objections, and eventually show them why it is in their interest to support the organization he or she represents. The potential client may be inclined to use the lab in a limited fashion (e.g., referring only STAT testing). Given some service equivalence, however, it’s possible for an effective field rep to transform the hospital lab into the primary reference source.

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A practical checklist for creating lab value with your physicians

By Linda Newman, MT(ASCP), MBA

Historically the lab’s focus has been on the quality of analytical performance, volume of activity, and cost of delivery. If results were accurate and delivered in a timely and cost-effective manner, the lab had fulfilled its function. But it is more complicated than that in the current—and future—healthcare environment.

Laboratories must use new approaches to demonstrate value. Those approaches include collaboration with administrative, medical, and information technology leaders to help physicians quickly and accurately diagnose patients, improve patient outcomes, and reduce the cost of care.

Changing times for physician reimbursement

In October 2016, the Centers for Medicare and Medicaid Services (CMS) released the final rule for the Medicare Access and CHIP Reauthorization Act (MACRA), a landmark law that replaces the sustainable growth rate formula in determining physician payments under Medicare Part B. In 2017, physicians begin reporting under a Quality Payment Program. This program is focused on moving the payment system to reward high-value, patient-centered care. There are two pathways for provider participation in MACRA’s Quality Payment Program: the Merit-Based Incentive Payment System, or MIPS, and the Advanced Alternative Payment Model, or Advanced APM.

The Merit-based Incentive Payment System (MIPS) is a new program for Medicare-participating clinicians that will make payment adjustments based on performance on quality, cost, and other measures, and will consolidate components of three existing programs—the Physician Quality Reporting System (PQRS), the Physician Value-based Payment Modifier (VM), and the Medicare Electronic Health Record (EHR) Incentive. The results of physicians’ reporting in 2017 will affect their reimbursement in 2019.1,2 The Advanced Alternative Payment Models (APMs) are a set of risk-sharing programs, some similar to Accountable Care Organizations (ACOs), created by CMS. APMs are also measured on quality of care, patient outcomes, and cost of care.

The laboratory’s role in general

The ultimate role of the laboratory has always been to deliver results that enable clinicians to improve their diagnostic and therapeutic decisions and thus improve patients’ outcomes. In the current environment, however, labs must go beyond simply enabling clinicians. Somewhere within the healthcare organization, there should be a group or an IT system that does the analyses so that clinicians can easily, quickly, and visually identify patients who require therapeutic changes or are not following a prescribed treatment plan.

You may be thinking “but that isn’t the lab’s job.” But in healthcare today, that is everyone’s job.

A good example is chronic disease management. According to the U.S. Centers for Disease Control and Prevention (CDC), chronic diseases are responsible for seven of 10 deaths each year, and treating people with chronic diseases accounts for 56 percent of our nation’s healthcare costs.3 More than 20 percent of healthcare spending is for people with diagnosed diabetes.4

Laboratories can contribute to chronic disease management by identifying laboratory data that indicates care gaps, and monitor risk factors by analyzing and tracking laboratory results.

Under MIPS, one of the quality measures that physicians report for diabetes is “Hemoglobin A1c Poor Control.” This measurement is defined as the percentage of patients from 18 to 75 years of age with diabetes who had hemoglobin A1c > 9.0 percent during the measurement period. In a clinical setting, this measure (> 9.0 percent) would normally indicate that the patient is not adhering to the recommended therapy or needs therapy revisions.5

There are many other quality measures that rely on laboratory results. These can be found at: https://ecqi.healthit.gov/ep/ecqms-2016-reporting-period.

The lab’s role regarding information technology

Since the introduction of Meaningful Use Incentives in 2012, most physicians have acquired some type of EHR system. Unfortunately, not all EHR systems are created equal. Some are very full-functioned and provide tools to automatically identify (staying with diabetes as an example) patients that have A1cs that require attention or flag patients who have not followed treatment plans, such as having blood drawn. Some EHRs do not have these features, however, and it can be a very laborious process for a physician practice to get this information.

If data is pulled from a data base at the end of a reporting period only for the purpose of reporting QA measures to CMS, it has no effect on patient outcomes. Physicians need information in real time, or at least weekly reports.

Given that 70 percent of the data stored in the EHR is laboratory data, laboratories are well positioned to provide innovative solutions to connectivity and interoperability. If real-time reports are not possible within the physician’s existing infrastructure, the lab can generate them.

How? Start with a small pilot project of physicians who have a large number of diabetic patients, and develop an action plan.

Elements of a plan

What will such a plan consist of? Here’s a possible template for how you might proceed:

Gather data. Meet with a representative sample of your physicians to understand their level of access to information—what they currently have, and what they need. Be sure to include physicians on different EHR platforms.

If there is an unmet provider need, move on to meeting with your organization. Find out what is being done, future plans, and what is possible. Meet with IT management to make sure the needs are well understood and represented during budget cycles. Make sure they understand why you need it. Help with preparing the presentation, or, better yet, get invited to the meeting if possible.

Other allies and mentors within your organization could be the Chief Medical Officer, Care Coordinators, ACO Coordinators, wellness programs, community outreach initiatives, etc.

Create a management proposal. After your meetings you will have a better understanding of what is important to your clients, both internal and external, and what gaps they are experiencing.

Deliver clear, succinct, fact-driven ideas for solutions to the problems you have identified. Focus on how those ideas can save healthcare dollars or improve patient outcomes.

Monitor and report monthly. Monitor the solutions you have in place and update results routinely. Conduct informal satisfaction surveys so you can make improvements.

continued on page 34
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SPECIAL FEATURE

OUTREACH

continued from page 30

- Implement a client relationship management (CRM) computer tool for management’s and field rep’s use.
- Create a net revenue outreach profitability report.
- Create a monthly net dollar amount for new sales expectation.
- Have a dedicated lab IT team to create internal/external reports and provide LIS-to-EMR connectivity support.
- Provide coaching for the field representative (in-house or an outside consultant).

Customer service is marketing

A wise person once said, “If you’re not serving the client, you’d better be serving someone who is.” For labs that want to build test volume, this motto should become their mantra. Customer service can be the difference between gaining and losing business. Obviously, front-line employees such as couriers, phlebotomists, and those receiving incoming calls (including billing) become critical to imparting a high degree of customer service. These staff members are the points of contact for “moments of truth” that occur any time the client/patient comes in contact with the lab. In turn, the client or the patient uses that opportunity to judge service quality.

Unless the culture of the hospital lab supports—and rewards—attention to patient and client needs, service will get no more than lip service over the long run. Every lab employee must understand that his or her job exists because of and for the patient and the customer. If the lab’s culture does not demonstrate that service and quality are the most important things the lab offers, then they aren’t.

Hospital lab outreach can provide welcome profits to the bottom line that not only support the lab with state-of-the-art instrumentation and additional employees, but also help other areas of the hospital. Providing basic services such as phlebotomy for outpatients translates to what one might consider a “first tier” approach. Employing and properly training field reps stands as a fundamental component of successful lab outreach. Having lab-dedicated information technology specialists becomes equally important. Easy access to the professional staff (including their visits to clients) will support a “we’re here for you, support your local hospital, we’re-all-in-this-together” philosophy. Most people welcome this kind of appeal to community solidarity.

Commercial laboratories have always been fearful of the potency and control of local hospitals. Why should commercial enterprises embezzle routine lab business away from hospitals? Part of the reason lies in the fact they are assertive and strategic. But there currently exist a number of successful hospital lab outreach programs that compete very well with—and win the perception battle against—national and strategic. But there currently exist a number of success-

continued from page 32

the physicians and your management what you are doing to help with chronic patient management and what results you have experienced to date. Throughout this process you will probably uncover opportunities for Outreach business. Outreach is a good way to add revenue and use excess capacity in the lab.

Assist with therapy compliance. If your lab has received a lab order, or the patient has a standing order but hasn’t been in for the draw, send an e-mail to remind him or her. The patient and the physician will see this as a service. If the patient utilizes a family member or caregiver, the e-mails should go to that person. (Collect this information on their first draw.) If possible, let patients make appointments for draws and send reminders one or two days prior. They are much more likely to come in if they have an appointment and have received a reminder.

Engage the patients. Laboratories can help engage patients by sharing test results directly with them. Test results should be accompanied by historical trending graphs and information that helps patients understand the implications of the results. This information can be valuable for patients as they discuss test results with treating physicians and determine if action needs to be taken.

This method of distributing lab test results is routine for national reference laboratories, but often lab results from health systems and community laboratories reside only in physician EHR patient portals. High-risk patients often have multiple physicians and therefore multiple locations for their laboratory results. This approach complicates patients’ access to their lab results and often leads to duplicate testing.

Healthcare reimbursement has been in a state of flux for many years and will continue to be for many more. Remember this quotation from Charles Darwin: “It is not the strongest or the most intelligent who will survive but those who can best manage change.”

Become part of the solution—and build value for your laboratory.

REFERENCES


Peter Francis is president of Clinical Laboratory Sales Training, LLC, a training and development company dedicated to helping laboratories increase their revenues and reputation through prepared, professional, and productive representatives. He has published more than 45 articles and regularly speaks at national industry conferences.

Linda Newman is the Director of Marketing and Strategic Projects for CareRevolve. Linda’s prior experience includes senior management positions in both start-ups and Fortune 100 corporations specializing in market assessment, product development, launch and support of technology products and services in the healthcare marketplace. She has also managed the chemistry laboratory of a 1200-bed hospital. She holds a BS in Medical Technology and is ASCP certified.
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Assessing the suitability of NGS panels for clinical sequencing

By Kristina Giorda, PhD

Next generation sequencing (NGS) is beginning to live up to its promise in clinical diagnostics, but obtaining data that influences diagnostic decisions and patient outcomes requires products that deliver consistent, high-quality results. GMP (Good Manufacturing Practices)-compliant manufacturing is an indicator of such quality and consistency; however, clinical lab scientists still need to assess each new tool and product for clinical utility before integrating it into the workflow.

To determine the underlying genetics of disease states, various commercial NGS panels are available and increasingly prevalent in the clinical laboratory. Whole genome sequencing has limited utility in clinical diagnostics due to its cost and time drain, but targeted panels make variant calling cheaper, faster, and more accessible. Panels range from those that cover the human exome to those specifically targeting a particular disease or range of conditions, such as cancers, and inherited and rare diseases. Where there is an even smaller subset of genes of interest or a need to target a specific combination of genes, various vendors offer customized target enrichment panels, further improving cost-efficiency.

Regardless of panel choice, for clinical utility, a panel must provide the level of quality and accuracy required for clinical samples. As each vendor employs differing technologies and manufacturing methods, quality and accuracy can vary to a surprising degree.

A study of NGS panels

To determine the suitability of an NGS panel for the production of clinical data, lab leaders need to assess several key performance factors. Common factors that influence targeted NGS include:

- Accurate and sufficient enrichment of targets
- Sufficient depth and uniformity of coverage
- Reliability of reads through GC-rich regions

Data from a recent study conducted by a large independent genome center illustrate the relevance of meeting these challenges in diagnostics. The study evaluated several key metrics of four commercially available clinical exome panels. While exome panels themselves are not commonplace for routine diagnostics, their data, generated in clinical research, feed into content on smaller targeted panels. Given that exome panels contain a vast amount of data, analyzed in clinical research, feed into content on smaller targeted panels. Given that exome panels contain a vast amount of data, analyzed in clinical research, feed into content on smaller targeted panels. Genomic studies using NGS have expanded the diagnostic scope of laboratories, with exome sequencing being the most popular method.

The study selected hybridization-based panels from different vendors with comparable target spaces covering the human exome. The metrics compared were on-target performance, depth and uniformity of coverage, and guanine-cytosine (GC) content bias. The results demonstrate the variability between similar panels, highlighting the importance of thorough assessment before integrating with workflows.

Key NGS performance metrics

Probe design and enrichment protocols influence on-target performance, measured as the ratio of bases within a target region to total bases output by the sequencer. A higher on-target percentage indicates that more probes successfully bind to the intended target under the given hybridization conditions. This improves accuracy and reduces off-target noise, simplifying analysis. Taking a similar number of sequencing reads, 34 million reads per library, the study calculated the percentage of probes on-target across a 250 bp flanking region covered by all panels, enabling a comparison (Figure 1).

The study also assessed the coverage depth and uniformity across intended target regions. Reliable variant calling depends on sufficient depth of coverage, generally accepted to be ≥20x or more; to minimize the risk of false positives and missing variants due to insufficient data. Each panel’s BED files provided target and probe locations, allowing for a bioinformatics comparison of coverage (Table 1). A further comparison to the human reference sequence database, RefSeq, normalizes these data to the annotated human exome (Figure 2). This provides an indication of how well the panels cover the exome, and therefore potential clinical relevance of any diagnostic panels based on the same technology.

A common challenge in diagnostics is generating sufficient reads through the first exons of genes, where GC content tends to be higher than average. Methods to compensate for GC bias in sequencing do exist, however, it continues to pose a challenge for efficient probe binding for target enrichment. Unreliable first exon data reduces confidence in analysis, and potentially leads to missed variants. The study compared the percentage of bases with >10x, >20x, and >30x coverage for each panel in first exon locations taken from RefSeq with the database as a whole (Figure 3a). Any GC bias in the panels shows as a reduction in first exon coverage relative to the whole database.

Exploring the data

The data from these comparisons indicate that the key performance metrics vary noticeably among panels.
In these tests, Panel 1 performed more consistently than the others. It demonstrated an on-target percentage slightly higher than that of Panel 4, and provided more uniform coverage of the exome. At 20x depth, suitable for variant calling, Panel 1 covered 93 percent of target bases versus 72 percent by the next closest panel. These profiles remained consistent when normalizing to RefSeq gene locations. Panel 1 also remained more consistent with increasing coverage depth for first exon enrichment, as demonstrated by the example from the gene RB1 (Figure 3b).

Several distinctions that may account for the difference in performance between Panel 1 and the other panels include probe length, probe composition (DNA vs. RNA), and the manufacturing method. Panel 1 contained column-based individually synthesized DNA probes, affording individual re-synthesis should quality control checks identify any stochastic failures. The resulting 120mer full-length probes, pooled at equimolar concentrations in the panel, display reduced GC content bias.

Some of the other panels consisted of array-synthesized probes, which also suffer stochastic synthesis failures, but do not afford individual probe re-synthesis. As a result, those panels are likely to contain probes of heterogeneous lengths and greater variation among batches, potentially requiring multiple sequencing runs to confirm the presence of a clinically significant variant. One of the panels uses RNA probes, which are known to have an inherent GC bias.

The performance differences among individual probes resulting from the two manufacturing approaches are probably minor, but are likely to be compounded across multiple probes, targets, and whole panels.

**Takeaways for decision makers**

Accurate and reliable data are critical in diagnostics, requiring clinical lab scientists to carefully evaluate the NGS tools they select for use. The independent study identified and tested several key metrics and demonstrated the performance variability between NGS panels with similar target spaces.

The results indicated that the panel built with individually synthesized, 120mer DNA probes provided the most consistent performance. Given the need for high quality data, the ability to enrich GC-rich regions is of particular significance in diagnostics where the successful identification of a disease-relevant variant may rely on accurate first exon sequencing.
Long-read sequencing
An alternative to Sanger-based instruments

By Kathryn Keho

Sanger sequencing has been a mainstay in clinical labs for years, where it is used to detect genetic variants for a wide variety of diseases and other phenotypes. This high-quality technology has been essential for accurate diagnoses of patients.

Today, though, the use of Sanger sequencing as a clinical standard is increasingly hard to justify. Technology development efforts have focused on other sequencing tools, with the result that Sanger instruments are often far more expensive and lower-throughput than newer options. However, they continue to be the primary sequencers in many labs because of their accuracy, read lengths, and familiarity. In some labs, next generation sequencing (NGS) platforms have been adopted as an alternative, but even in those cases Sanger remains an important tool for validating clinically relevant findings.

Another approach is now gaining traction in clinical labs: the use of long-read sequencing, such as single molecule, real-time (SMRT) sequencing, to replace Sanger technology for applications such as amplicon sequencing and validation of variants detected with NGS tools. Like Sanger, SMRT sequencing has very high consensus accuracy rates. Unlike other platforms, though, this kind of sequencing produces extremely long reads. Average read lengths are about 10,000 bases, which can easily span amplicon lengths used in traditional Sanger sequencing panels.

By contrast, short-read NGS technologies typically produce reads in the 200 bp to 300 bp range, necessitating algorithmic processes that stitch shorter amplicon sequences together to generate clinically useful information. Unfortunately, those processes can introduce errors, cause mismapping, and miss important genomic elements such as haplotype phase.

In the clinical lab setting, long-read sequencing has the potential to be used on its own to analyze important regions such as the HLA locus or the CYP2D6 gene; it can also be used as a complement to NGS-based testing, serving as an orthogonal tool for validation of medically actionable findings. For either workflow, long-read sequencing can deliver lower project costs and higher throughput than Sanger sequencing. The technology also affords new opportunities to deliver clinically useful information for repeat expansion disorders and other diseases marked by significant amounts of structural variation.

Amplicon sequencing

Many clinical and translational research labs have developed protocols for amplicon analysis based on long-read sequencing. With this approach, scientists capture the genomic region of interest to generate sequence data that outperforms Sanger results in quality and accuracy.

The CYP2D6 gene, which encodes an enzyme responsible for metabolizing 25 percent of commonly used drugs, was an early target for scientists interested in amplicon-based, long-read sequencing. Variants within the gene correspond to how a person will tolerate or metabolize many therapeutics, so analyzing CYP2D6 is a common task in clinical labs. The gene is highly polymorphic, with more than 100 known allelic variations, and has a nearby pseudogene with very high-sequence homology. Together, these features have made sequencing CYP2D6 a challenge, while genotyping-based tools only test for the most common alleles.

Scientists at the Icahn School of Medicine at Mount Sinai turned to SMRT sequencing as an alternative, finding that they could produce amplicons covering the gene and its copies as well as the pseudogene. A pilot project and follow-up studies showed that the long-read technology could not only sequence through the whole amplicon repeatedly, but also allowed for allele phasing to provide clinically meaningful information. Long-read sequencing was able to resolve discrepancies in samples that had produced inconclusive results with other sequencing or genotyping techniques. The scientists also discovered novel CYP2D6 alleles and structural variants during this evaluation study, even in samples previously examined with other analysis methods where those features were missed.

Long-read sequencing has also been evaluated for use in HLA typing labs. Like CYP2D6, the HLA genes are complex and extensive; there are more than 13,000 alleles catalogued for the six HLA genes. At the Anthony Nolan Research Institute, scientists conducted a feasibility study to determine whether long-read sequencing could more successfully represent this group of genes, which are essential for matching donors and recipients for successful organ transplantation. In the project, they pooled full-length HLA class I genes from seven samples, sequencing each to at least 150x-fold coverage, producing a mean quality value of 70 or better, and fully phasing alleles. Results were concordant with previous analyses of the samples, but the SMRT sequencing data also identified novel alleles. The process took three working days, less time than existing HLA typing methods.

Structural variation

Long-read sequencing has been proven to detect far more structural variation than NGS tools because its reads can span even large genomic elements. That makes it a good fit for use in repeat expansion disorders such as fragile X syndrome, Huntington’s disease, and many ataxias.

At the University of California, Davis, School of Medicine, scientists have demonstrated that long-read sequencing can be used to get through the FMR1 gene, which harbors the repeat expansion responsible for fragile X syndrome. Prior to this work, no sequencing technology had ever been able to completely characterize this region, which is marked by repeating CGG sequences—as many as 750 repeats in individuals with the disorder. Scientists not only produced the first full sequence of this region, but they have also been able to show that an accurate count of repeats is important for diagnosing an individual with fragile X or with other disorders that have fewer CGG repeats, typically between 55 and 200 copies.

Research has proven that being able to identify two AGG interruptions among the CGG repeats is important for determining a woman’s likelihood of having children with fragile X syndrome. With long-read sequencing, it is now possible to fully sequence this region with accuracy high enough to pinpoint the two A changes in a sea of CGGs, generating information with tremendous clinical value.

Looking ahead

These studies suggest that long-read sequencing technology will serve as an effective, affordable replacement of Sanger sequencing for NGS variant validation, amplicon sequencing, structural variant detection, and more. The findings also indicate that SMRT sequencing will reveal more information about clinically important genes, genetic elements, and other regions than can be detected with existing lab tools, improving the accuracy and comprehensiveness of data reported back to physicians.

References available online.

Kathryn Keho is a senior director at PacBio, provider of the Sequel System for long-read single molecule sequencing.
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In recent months, the U.S. Food and Drug Administration (FDA) has communicated more frequently with the laboratory community than it had in the previous 25 years. Specifically, we have seen a modification of prior approaches to federal regulation of laboratory-developed tests (LDTs). The changes may indicate a better understanding on the part of the agency of the way in-house tests are developed and qualified under the current regulations in 42 CFR 493.

**Background and issues**

Both FDA and the Centers for Medicare and Medicaid Services (CMS) seem to have authority to ensure performance of LDTs. The first Citizen’s Petition (CP) against FDA authority was submitted in 1992 after the publication of an RUO/ICO Guideline that asserted FDA authority indirectly. This CP requested FDA to state unambiguously that FDA did not regulate LDTs. Two other petitions did the same in later years. The following reasons were given, and they represent most of the legal arguments for no FDA involvement in LDTs:

- Labs were already regulated by CLIA. If there is a problem, CMS (then HCFA) should take action, not FDA.
- CMS gives CMS authority to require performance specifications for LDTs.
- Labs are not manufacturers, but service providers.
- No article was shipped in interstate commerce, a requirement for FDA’s authority.
- A change like this would be costly and detrimental to public health, by limiting availability of needed tests.
- Such a change would be substantial and require rulemaking, not simply guidance.
- HHS is the Agency that is responsible for both CMS and FDA, and FDA cannot assume authority over LDTs unless HHS allows it, which they have not.
- FDA has yet to provide scientific evidence of a public health concern that leads them to insist on changing the current system for ensuring test quality.

Answers to these arguments have come from FDA and from a number of interested parties. Genentech published a petition in 2006 asking FDA to stop “enforcement discretion,” develop a regulation, and enforce it for LDTs. The position agreeing with FDA to state unambiguously that FDA did not regulate LDTs. Two other petitions did the same in later years. The following reasons were given, and they represent most of the legal arguments for no FDA involvement in LDTs:

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FDA’s two attempts to develop guidance

The IVD Multivariate Index Assays (IVDMIA) draft guidance was published in 2006. These assays, corresponding roughly to tests in the High Complexity category, must be subject to FDA review pre-market. The reaction of the lab community was negative, and instead of taking their concerns to FDA, they went to Congress. Congress responded by including LDTs in the FDA Safety and Innovation Act (FDASIA) in 2012. They required FDA to discard the IVDMIA guidance, and to start over with a new approach.

FDA published two drafts in late 2014, one addressing the general regulatory approach and the other addressing reporting and notification/registration. The framework guidance re-defined LDT, and continued to require either pre-market clearance or approval in high and very high risk categories. The draft developed the concept that the test developer was also responsible for demonstrating the clinical validity of the test—that is, the effect of test result on the health of patients. The draft received more than 1,400 comments, and FDA continued to claim that it would produce a final guidance last year. FDA continued to assure the lab community that a final draft was in progress, but in November, FDA stated that it was not going to finalize the guidance. The reasons given were the irreconcilable differences among many comments, such that it was impossible to reach consensus. With such disagreement, the preferred route would be through Congress.

FDA’s discussion paper

On January 13, 2017, FDA signaled that, although its second draft guidance was as dead as the IVDMIA draft, the agency still had something to say about LDTs. The discussion paper repeats some of the discarded draft guidance but adds some new possibilities:

- Grandfathering: LDTs currently being offered would not be required to do pre-submissions. They would be expected to maintain complaint files and comply with post marketing reporting. FDA would not demand public availability of performance data for these products, but would “suggest.” (This change alone would reduce FDA workload significantly)
- Explicit description of performance data—it can include both bench and clinical data.
- A discussion of difference between current LDT QA and FDA QSR. CMS/FDA QA joint taskforce was referenced.

By Anna Longwell, JD, MBA, MS
ACUSERA 24/7
Stress free QC analysis

smarter, faster & more powerful
than ever before

Advanced statistical analysis
Automatically calculate performance metrics including Sigma, UM, TE & %Bias.

Peer group statistics
updated live in real-time
Instantly discover how you compare to your peers, reducing time and money spent troubleshooting.

Unique dashboard
Immediately identify QC tails from the last 7 days allowing time spent reviewing reports.

Interactive charts
Add events and multiple data sets to a single chart for quick and easy performance monitoring.

World leading QC
Benefits from unrivalled commutability, consistency, stability and comparability.

Connectivity
Eliminate manual data entry or file import with bi-directional connection to LIMS.

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Speed up your review process with access to on-demand reports.

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In this month’s installment of The Primer, we’re going to cover something which applies equally well to non-molecular and molecular diagnostic assays: the use and meaning of some common metrics for assay accuracy. While this is likely a review of something all readers will have encountered at some time in the past, it’s a crucial enough concept to warrant attention for any of us who perhaps don’t recall quite what these metrics mean, and how they differ from each other. Such an understanding can prove useful in the minority of cases where a laboratory result seems at odds with other indications for a particular diagnosis.

Sensitivity and specificity

The first two metrics we’ll consider are sensitivity and specificity. These are perhaps the simplest of the metrics, as they are direct measurements of assay performance attributes which should in theory remain constant across all users (assuming identical instrumentation, reagents, and protocols). To address these terms, we’ll first need to embrace the concept of “true positives” and “true negatives”. These apply in the context of specific question with a Boolean (yes/no) answer, such as “Is Pathogen X present in Sample Y?” True positives are those cases where the answer is “yes,” and true negatives are those cases where the answer is “no,” from the context of some “omniscient” observer.

Readers who are of a more critical bent may immediately wish to point out there is no such omniscient data source that we can query in this situation. Such an argument is correct, and in reality, we shall have to settle for use of some “gold standard,” or accepted best accuracy reference method, as our surrogate for absolute yes/no truth in such matters. (The implications of this are something we’ll come back to later.) Other readers may also note that there is no room for “indeterminate” answers in our concept here, which is another divergence between theory and reality, at least in the case of those assays with defined “grey zones” which are not to be interpreted as evidence of either positivity or negativity. Pragmatists that we are, we will proceed regardless of these issues.

Sensitivity of an assay is then defined as the fraction (or percentage, if you prefer) of true positives which are detected as positive by the assay under a defined performance and interpretation method. On the surface, this is a readily grasped concept: if, for instance, we test 50 true positive samples and our assay calls positive on 49 of these, we would have a 98 percent sensitivity. One might even be forgiven for thinking that this is all one needs to know to establish one’s degree of trust in an assay result; however, as we’ll demonstrate later this is not the case. Nor is a claim of 100 percent sensitivity always reassuring.

Specificity is rather the inverse concept of this; it is defined as the fraction (or percentage) of true negatives which are detected as negative by the assay—again, under a defined set of performance and interpretation conditions. If we consider an example similar to the above, and run our assay on 50 true negative samples with results calling 48 of the 50 negative, we have a specificity of 96 percent. Again, this seems on the surface to be a simple concept.

One important point that needs to be made is that we must be simultaneously aware of both the sensitivity and specificity of an assay, with the values determined via the same protocol and interpretation, for the values to be meaningful. Either value alone can be wildly misleading, as will be demonstrated below.

(Note that there are also the terms False Positive Rate, which is 1-[Specificity], and False Negative Rate, which is 1-[Sensitivity]; strictly speaking, then, the FPR [false positive rate] could stand in for specificity, and the FNR [false negative rate] for sensitivity in our ability to fully appreciate the performance reliability of an assay).

PPV and NPV

Other commonly encountered but more complex metrics for assay performance are the Positive Predictive Value (PPV) and Negative Predictive Value (NPV). The PPV can be thought of as the likelihood that a positive test result is positive if the sample examined is a true positive, or the fraction of true positives over assay positive calls in a set. Similarly, the NPV is the likelihood that a negative test result is obtained on a true negative sample. A complexity of PPV and NPV is that unlike sensitivity and specificity, these are not hard and fast values that one can assume to be invariant between assay sites with identical assays and processes; in fact, they can’t even be assumed invariant over time at a single site with absolute uniformity in its assay method. That is because each naturally incorporates the target prevalence rate at the time the assay was performed.

In other words, and at extreme cases for simplicity of consideration, in cases of low prevalence the PPV will trend low due to the (fixed) probability of a false positive result becoming large relative to the actual probability of a sample being positive. NPV shows an equivalent relationship to prevalence. Thus, while PPV and NPV values are highly valuable snapshots of a time and place, an appreciation for whether the intrinsic target prevalence is similar between when the value was generated and the present is needed to evaluate their applicability.

The Magic Box

A useful exercise in putting all of these concepts together, and in a way which shows how they can be misleading if they are not understood, is by consideration of the Magic Box assay. This amazing assay—not available from any manufacturer, but within the “homebrew” capabilities of any lab manager—has a remarkable set of properties. It costs less than fifty cents in equipment and infrastructure; it requires no consumables; it requires only a few moments of operator training for expert operation; it has a turnaround time of less than 30 seconds; it is non-destructive of specimen material; although a simplex (single target) assay, it can be instantly reconfigured to test for any target desired; and it’s 100 percent sensitive.

Before you decide this is clearly the next must-have assay for your lab, let’s consider how the Magic Box Assay works, and how all of the above statements are absolutely true. To build the assay device, simply take a small cardboard box of your choice, remove the lid, and use a marker to draw a large “+” on the outside box bottom. Using the assay is also easy: place your specimen to test (still in its container) on the lab bench; place the Magic Box upside down over the sample; consider what target you want to assay for; and then look down at the box. If you see a “+”, the sample is positive, and you’re done and ready to go onto the next sample (or test for another target in the same sample).

Now let’s fill in some more details. Let’s say, for the sake of argument, that the actual prevalence of the target you “tested”
for, in the sample stream under examination, is 70 percent. This is not an unreasonable value, either through the target currently being one that’s undergoing an outbreak in your patient population, or through the target being one with a highly characteristic presentation such that the requesting physician already had a strong suggestion of likely positivity, and is merely submitting the sample for confirmatory testing. Of course, both of these can occur simultaneously, and during known outbreaks for a pathogen with characteristic presentation, the prevalence in submitted sample stream can be very high.

How does our Magic Box assay perform under these real-life conditions? Well, recall first that by definition of sensitivity—that true positives are detected as positive—the advertising hype of “100 percent sensitive” is true; every time you put a positive sample under the box and looked down, you saw “+” The PPV would be a little less reassuring, at only 70 percent, and should raise the first red flags indicating that results are likely to be wrong some 30 percent of the time. This is hardly the sort of confidence one would want out of a clinical diagnostic. Consideration of NPV and specificity are truly disturbing, as each would be zero percent; the Magic Box, after all, never reports a sample as negative.

There’s no real magic

In many ways, the above discussion is another reflection on a concept generally well understood by laboratorians: that sensitivity and specificity are something of a trade-off, with improvements to one causing losses in the other. Selection of assay cutoff criteria to find an acceptable “maximum utility” compromise between these metrics is frequently done through application of methods such as analysis of Receiver Operating Characteristic (ROC) curves. While these are a fascinating topic in their own right (and one which delightfully demonstrates how disparate branches of science can benefit one another; in this case, how rules for use of primitive Chain Home radar installations from the Second World War led to better medical tests), we are constrained by space from further consideration of the topic for now.

The take-home message from this month’s topic is thus that laboratorians should never accept just a sensitivity value on its own, as providing any real insight into the true utility of a test. The same of course goes for specificity; one could after all make a Magic Box with a minus sign on it, which could now in all truth claim 100 percent specificity; all true negatives would be reported as negative. If this message is one some readers think too obvious to need mention, or overheard conversations at their next conference for evidence that not all people understand the crucial requirement for reporting all relevant assay performance metrics, rather than just a select few. Finally, recall our earlier reference to “absolute” positives and negatives; in reality, while gold standard assays can be 100 percent correct; our values for sensitivity, specificity, PPV, and NPV are thus all probably not exactly correct. This variance from exactitude is, however, likely of such small magnitude as to be of no practical concern, and is thus generally ignored.

Differences found in design control and vendor qualification, many similarities. Possibility of non-FDA inspection to continue was noted.

d. Novel approach to significant changes in product post-marketing. FDA only reviews the protocol for validating changes.

e. Third party review of LDT 510(k)s should be considered.

f. Public availability of performance data required.

g. Comparison between FDA Clinical Validity and CMS Clinical Utility: intended use of the data: CMS Economic Effect, FDA Health Care effect. (A distinction without a difference?)

So, what next?

FDA, like any agency in our new administration, will not be encouraged to issue new regulations or guidances unless clearly required by Congress. The anticipation is that FDA will not continue to issue untitled letters to laboratories offering LDTs unless there appears to be a real public health issue. Additionally, the 21st Century Cures Act urges the Agency to be very serious about facilitating new medical device development, especially in oncology. The new law gives the Office of Device Evaluation (ODE) and Office of In Vitro Diagnostics and Radiological Health many tasks that will require development of guidance or regulation in the coming months. It is unlikely that FDA will continue to pursue laboratories, but it is possible that CMS and FDA would agree to cooperate in certain laboratory QA activities.

Notes

1. The issue of the necessity for change was also explored. In 2015, FDA published 20 cases which illustrated its concern with LDTs. The report was descriptive only, and was not scientific proof or even a rationale for FDA concern. Some of the cases were not easily related to a testing error. No one considered these to be convincing evidence that the current CMS system needed revision. (But a number of the respondents to the 2014 draft guidance indicated that there were elements of FDA oversight that would be an improvement for labs.)


3. For example, the 2008 Genentech CP pointed out that they had developed and tested Herceptin using companion diagnostics for HER2 in tumor tissue. These tests had been subject to extensive FDA scrutiny, and had published test performance. However, laboratories were offering LDTs for HER2 without such extensive scrutiny pre-marketing, and Genentech had no assurance that these tests would in fact indicate use of Herceptin in treatment.

4. The absence of FDA representatives at a September 2016 hearing of the Senate Committee on Health, Education Labor and Pension “Laboratory Testing in the Era of Precision Medicine” may have been a signal of this withdrawal.

5. For example, risk-based test categorization, and exemptions for some LDTs.

6. Twentieth Century Cures Act, Title III, Subtitle F, Section 305ff.

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Summer’s coming! What’s new with Zika?
By MLO staff

On November 18, 2016, the World Health Organization (WHO) declared that an “international emergency” no longer existed with regard to the Zika virus (ZIKV). At the same time, however, the global health agency and other health-care entities urged researchers to continue to increase efforts to better understand Zika and its effects on pregnant women and their babies, to improve diagnostics, to develop vaccines and therapeutics, and to refine epidemiological surveillance techniques that would help in controlling Zika and other vector-borne diseases. The mosquito season was coming to an end in the Northern Hemisphere, but the battle against the Zika virus was just beginning.

Indeed, efforts in all of those areas and more have ramped up in the months since the WHO’s declaration. Here are some updates on recent studies and ongoing research.

Twenty-fold increase in birth defects due to ZIKV
The proportion of Zika-affected pregnancies with birth defects is approximately 20-fold higher compared with the proportion of pregnancies seen in 2013-2014, before Zika was introduced into the Americas, according to an article recently published in the Center for Disease Control and Prevention’s (CDC) Morbidity and Mortality Weekly Report. The types of birth defects—including brain abnormalities and/or microcephaly, neural tube defects and other early brain malformations, eye defects, and other central nervous system problems—were seen in about three of every 1,000 births in 2013-2014. In 2016, the proportion of infants with these same types of birth defects born to women with ZIKV infection during pregnancy was about six percent, or nearly 60 of every 1,000 completed pregnancies with Zika.

The researchers analyzed 2013-2014 data from three birth defects surveillance programs in the United States, in Massachusetts, North Carolina, and Georgia, to provide the baseline frequency for Zika-related birth defects. To assess the effect of ZIKV infection during pregnancy, the scientists compared that 2013-2014 baseline number with previously published numbers among pregnancies with ZIKV infection from the US Zika Pregnancy Registry (USZPR) from 2016.

They identified 747 infants and fetuses with one or more of these defects from the programs in MA, NC, and GA, from 2013-2014. Brain abnormalities and/or microcephaly were the most frequent conditions reported. Data from the USZPR identified 26 infants and fetuses with these same birth defects among the 442 completed pregnancies of women with possible Zika infection from January through September 2016. These findings demonstrate the importance of having monitoring systems that collect data on birth defects.

Additional mosquito species may transmit ZIKV
So far, the Zika virus is known to have been spread primarily by Aedes aegypti or Aedes albopictus. But Zika may be transmitted by more mosquito species, according to a new predictive model created by ecologists at the University of Georgia and the Cary Institute of Ecosystem Studies. Their findings, published last month in *eLife*, offer a list of potential candidate species.

Targeting Zika’s potential vectors—species that can transmit the virus from one host to another—is time-consuming and expensive, requiring collection of mosquitoes in affected areas, testing them to see which ones are carrying the virus, and conducting laboratory studies. The new model could streamline the initial step of pinpointing Zika vectors.

“What we’ve done is to draw up a list of potential vector candidates based on the associations with viruses that they’ve had in the past as well as other traits that are specific to that species,” says paper co-author Courtney C. Murdock. “That allows us to have a predictive framework to effectively get a list of candidate species to pursue further.”

Data used in the model consisted of information about the traits of flaviviruses—the family that includes Zika and dengue—and all the mosquito species that have been associated with them. For mosquito species, these included general traits such as subgenus and geographic distribution as well as traits relevant to the ability of each species to transmit disease, such as proximity to human populations, whether they typically bite humans, and how many different viruses they are known to transmit. For viruses, traits included how many different mosquito species they infect, whether they have ever infected humans, and the severity of the diseases they cause.

Analyzing known mosquito-virus pairs, the researchers found that certain traits were strong predictors of whether a linkage would form. The most important of these for mosquitoes were the subgenus, the continents it occurred on, and the number of viruses it was able to transmit. For viruses, the most important trait was the number of mosquito species able to act as a vector.

Researchers used the model to test the combination of ZIKV with all the mosquito species known to transmit at least one flavivirus. The model found 35 predicted Zika vectors, including 26 previously unsuspected possibilities. Seven of those occur in the continental U.S.

New device could rapidly detect ZIKV
About the size of a tablet, a portable device that could be used in a host of environments such as airports or remote locations (e.g., in South America) may hold the key to detecting the Zika virus accurately, rapidly, and inexpensively using a saliva sample. Researchers from Florida Atlantic University are working to develop a diagnostic tool to reduce the impact of the outbreak until a vaccine is identified.

“Most of the Zika cases in the United States and especially in Florida are travel-related,” says Waseem Asghar, PhD. “We are working to develop a tool that can be used without expensive laboratory equipment and skilled technicians in various settings like an airport or a community health center to provide reassurance to expectant families and those concerned because of recent travel. For about two dollars and within 15 minutes, we hope to accurately determine whether or not an individual has an active infection.”

Currently, patients are diagnosed by testing whether they have antibodies against the ZIKV in their bloodstream. However, the antibody test cannot discriminate accurately between the Zika virus and other flaviviruses such as dengue, West Nile virus, and chikungunya. The more accurate method for detecting the virus is by looking for pieces of the viral genome in a patient’s blood sample using a test known as polymerase chain reaction (PCR).
This new device is based on technology that Asghar and colleagues developed to detect human immunodeficiency virus (HIV). It uses inexpensive paper- or plastic-based materials, a cassette-sized container holding up to 12 samples at a time, and a receptacle about the size of a tablet. These materials are easy to make, easy to use, and can easily and safely be disposed of by burning, providing an appealing strategy for developing an affordable tool for diagnosing ZIKV in developing countries as well as low- and middle-income countries where there is limited laboratory infrastructure.

The researchers are working to adapt their device to diagnose the Zika virus, and they recently received a grant from the Florida Department of Health to establish proof-of-principle and then further test and commercialize this device.

**Scientists uncover how ZIKV causes microcephaly**

A multidisciplinary team from The University of Texas Medical Branch (UTMB) at Galveston has uncovered the mechanisms that ZIKV uses to alter brain development. These findings are detailed in *Stem Cell Reports*.

Since a normal brain develops from simple cells called stem cells that are able to develop into any one of various kinds of cells, the UTMB team deduced that microcephaly is most likely linked with abnormal function of these cells.

There are two main lineages of the virus, African and Asian. Recently, the UTMB team found that only the Asian lineage has been linked with microcephaly. So, what is it about this particular form of the virus that inflicts such damage?

The researchers established a method of investigating how Zika alters the production, survival, and maturation of brain stem cells using cells donated from three human fetal brains. They focused on the impact of the Asian lineage ZIKV that was involved in the first outbreak in North America in late 2015.

“We discovered that the Asian lineage Zika virus halted the proliferation of brain stem cells and hindered their ability to develop into brain nerve cells,” says Ping Wu, senior author on the study. “However, the effect that the Zika virus had on the ability of stem cells to develop into specialized cells differed between donors. This difference seems to be linked with a Zika-induced change in global gene expression pattern. It remains to be seen which genes are responsible. The unique system containing stem cells from three donors will allow us to dissect molecular mechanisms underlying Zika virus-induced brain malformation.”

**Promising investigational ZIKV mRNA vaccine**

A novel, gene-based investigational vaccine protected mice and monkeys against Zika virus infection after a single dose, according to a study appearing online in *Nature*. The research was conducted by investigators funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), NIAID scientists, and other partners.

The candidate vaccine, called ZIKV prM-E mRNA-LNP, uses messenger RNA (mRNA), with which the body produces Zika virus proteins designed to elicit infection-neutralizing antibodies. Scientists at the University of Pennsylvania in Philadelphia and at the company BioNTech in Mainz, Germany, developed the vaccine.

Similar to DNA vaccines, mRNA vaccines do not contain live or inactivated virus and therefore cannot cause Zika infection. The mRNA vaccine platform can be quickly adapted to express most viral proteins and can be manufactured efficiently. NIAID and the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services, are developing additional mRNA vaccines against Zika.

For this study, investigators vaccinated 19 mice with a single shot of ZIKV prM-E mRNA-LNP, and they gave a placebo vaccine to a control group consisting of 14 mice. They then exposed 18 mice (nine control and nine vaccinated) to Zika virus two weeks after vaccination and exposed the remaining mice (five control and 10 vaccinated) to Zika virus 20 weeks after vaccination. Nearly all control mice had Zika virus in the blood by day three, while all of the immunized mice showed no detectable virus. Investigators also gave various doses of the vaccine to five monkeys and gave a placebo vaccine to a control group of six monkeys. All monkeys were injected with Zika virus five weeks after vaccination. All monkeys in the control group had Zika virus in their blood, while four out of the five monkeys in the vaccinated group, including those that received the lowest dose, were protected from infection with no detectable virus.

The authors note that additional research is required to explore adding a boost to the vaccine regimen to see if that would increase its immunogenicity and to determine whether the investigational vaccine can prevent Zika infection and disease in humans.

**NIH begins study of vaccine to protect against mosquito-borne diseases**

The NIH's National Institute of Allergy and Infectious Diseases (NIAID) has also launched a Phase 1 clinical trial to test an investigational vaccine intended to provide broad protection against a range of mosquito-transmitted diseases, such as Zika, malaria, West Nile fever and dengue fever, and to hinder the ability of mosquitoes to transmit such infections. The study, which is being conducted at the NIH Clinical Center in Bethesda, MD, will examine the experimental vaccine’s safety and ability to generate an immune response.

The investigational vaccine, called AGS-v, was developed by the London-based pharmaceutical company SEEK, which has since formed a joint venture with hVIVO in London.

Unlike other vaccines targeting specific mosquito-borne diseases, the AGS-v candidate is designed to trigger an immune response to mosquito saliva rather than to a specific virus or parasite carried by mosquitoes. The test vaccine contains four synthetic proteins from mosquito salivary glands. The proteins are designed to induce antibodies in a vaccinated individual and to cause a modified allergic response that can prevent infection when a person is bitten by a disease-carrying mosquito.

The clinical trial is expected to enroll up to 60 healthy adults ages 18 to 50. Participants will be randomly assigned to receive one of three vaccine regimens. The first group will receive two injections of the AGS-v vaccine, 21 days apart. The second group will receive two injections of AGS-v combined with an adjuvant, 21 days apart. The adjuvant is an oil and water mixture commonly added to vaccines to enhance immune responses. The third group will receive two placebo injections of sterile water 21 days apart. Neither the study investigators nor the participants will know who is assigned to each group.

Participants will return to the clinic twice between vaccinations and twice after the second vaccination to undergo a physical exam and to provide blood samples. Study investigators will examine the blood samples to measure levels of antibodies triggered by vaccination.

Each participant also will return to the Clinical Center approximately 21 days after completing the vaccination schedule to undergo a controlled exposure to biting mosquitoes. The mosquitoes will not be carrying viruses or parasites, so the participants are not at risk of becoming infected with a mosquito-borne disease. Five to 10 female *Aedes aegypti* mosquitoes from the insectary in NIAID's Laboratory of Malaria and Vector Research will be put in a feeding device that will be placed on each participant’s arm for 20 minutes. The mosquitoes will bite the participants’ arms through the netting on the feeding devices.

Afterward, investigators will take blood samples from each participant at various time points to see if participants experience a modified response to the mosquito bites as a result of AGS-v vaccination. The study is expected to be completed by summer 2018.
A system-wide movement to improve patient care and reduce unnecessary laboratory testing

By Pracha Eamranond, MD, MPH, Megha Joshi, MD, Insha Haque, DO, Alison Scarry, MS, H, BB(ASCP), Stephan Geary, MLS(ASCP)SH, and Brian Collins, BS

A grassroots movement initiated by phlebotomists began a revolution at Lawrence General Hospital (LGH) in Lawrence, Massachusetts. These healthcare team members championed the cause of patients and staff who had reported unnecessary lab testing. Their dedication to patient care led to a hospital-wide procedural change. This article identifies a common problem affecting many hospitals adversely, our process of change management at LGH, and the subsequent improvement in both laboratory utilization and cost-reduction outcomes.

Relevant background and context

In July 2014, LGH’s Lab Utilization Committee (LUC) formed the Duplicate Order Task Force to address a concern that had been raised by members of the phlebotomy team. Phlebotomists had observed that there were many duplicate lab order requests, resulting in excessive blood draws and numerous patient complaints.

LGH staff knew that excessive blood draws and adverse patient outcomes were problems that were far from unique to their institution. One published survey of 17,676 patients in 57 United States hospitals from 2000 to 2008 showed that 20 percent of patients who didn’t have anemia when admitted for heart attacks developed moderate to severe cases of the red blood-cell deficiency by the time they left. The average volume of blood drawn from patients who developed anemia was 174 milliliters (more than double the 83.5 milliliters from patients who didn’t develop anemia). For every 50 milliliters of blood drawn, risk of moderate to severe hospital-acquired anemia increased by 18 percent. The average blood loss across hospitals ranged from 119 to 246 milliliters, indicating that some blood loss could be prevented by eliminating routine testing. Moderate to severe hospital-acquired anemia is independently associated with higher in-hospital mortality in patients with myocardial infarction.

Risk Management at LGH received 512 formal incident reports in a three-month span. This observation surfaced during a crucial period in LGH history. Six months prior, the labs’ ordering practice had changed from laboratory information system (LIS) to hospital information system (HIS). The LIS had built-in logic to prevent duplicate order placement. When the HIS launched live, no internal system existed to alert duplicate orders. Hospitalists, primary care providers, and specialists were ordering the same labs, as there were no alerts in the computerized physician order entry system (CPOE). Daily repeat labs were ordered, such as international normalized ratio (INR) for patients on warfarin and basic metabolic panels (BMP) to follow creatine for patients with acute kidney injury. Patients were subject to multiple draws of the same tests on the same day.

As the multidisciplinary team gathered support for prevention of duplicate and daily blood testing, there was a strong contingent of physicians who opposed this project. The previous physician culture was reluctant to implement systemic changes to prevent duplicate testing. However, after several meetings with the
Utilization Review Committee and the Medical Executive Committee, it became clear that removal of duplicate orders was the appropriate action for patients.

CPOE has many proven benefits, such as reduction of illegible hand written orders, optimization of clinical time, and streamlining of communication between clinicians and other departments. However, there was an obvious disconnect in the quality of patient care. This problem led to utilization of Clinical Decision Support (CDS) alerts and an alert system embedded in CPOE (Figure 1). Studies demonstrate that CDS alerts led to reduction of medical errors and quality of care improvement. It is important to note that overuse of diagnostic laboratory tests is in fact identified as medical error. The reduction of medical error can have significant impacts on cost reduction. The Triple Aim—better care for lower costs and better patient experiences—is certainly a goal at LGH, and the introduction of CDS is one example of a strategy designed to meet that goal.

**Process and outcomes of change**

A multidisciplinary team assembled to move toward the goal of reduced duplicate orders. Figure 1 highlights the top duplicate order tests. The associated fiscal savings are shown in Figure 2. The peak of lab ordering occurred in December 2013, which coincided with the launching of CPOE. Data was collected over a four-year period from January 2012 to June 2016. A three percent decrease was demonstrated for the following orders: basic metabolic panel (Figure 3), comprehensive metabolic panel, complete blood count, prothrombin time, phosphorous, magnesium, international normalized ratio, lipids, and troponin. This reduction of ordering was achieved by CDS alerts. The projected savings from this intervention is $37,542. Furthermore, CPOE was modified with removal of daily esoteric testing and a three-day consecutive test max for the top six assays. The savings, fiscal year to date, amounted to $83,500.

The Duplicate Order Task Force utilized CDS to promote key tenets of population health: improved patient experience, quality of care with fewer adverse events, and significant cost reduction. CDS has been studied to show improvement of clinician performance in lab ordering via the following measures: display of cost of the lab order, display of previous test results, use of reminders, and display of recommendations. LGH saw a gradual shift in culture from reactive to proactive measures to foster patient health and wellness. Reduction of waste led to a gain in efficiency and increased patient satisfaction. Financial performance grew stronger as the process of care delivery trimmed unnecessary measures. The endpoint for LGH and our project is the delivery of evidence-based care and adherence to best practice, which helped our institution achieve the Triple Aim.

The reduction in unnecessary utilization of lab resources is an enabling factor to the lab bottom line as an outpatient revenue center. The lab is meeting increased outpatient demand without matching increases in cost. Fewer inpatient orders and better utilization has increased our capacity to do more outpatient lab tests, which is fee-for-service. CDS embedded into CPOE frees lab personnel to complete other value-added tasks rather than manually sifting through duplicate order sets, thus furthering the opportunity for better utilization of lab staff time.

**Better safety and satisfaction**

In summary, CDS implementation in CPOE reduced unnecessary lab utilization without a single reported adverse event. Sustainable healthcare systems are founded in quality of care and reduction of cost and medical error. As such, proper resource utilization is essential to move forward in the climate of healthcare reform. The success of this project is a testament to the value of coordinated team care and a multidisciplinary approach. A multidisciplinary support for the Lab Utilization Committee enabled the Duplicate Order Task Force to reach out to other hospital committees and departments to facilitate a transferrable workflow change. In the case of duplicate orders, less proved to be more and change moved forward as a collaborative effort. The ripple effects of this project led to multi-department changes at LGH in MRI services, CT Scans, and Pharmacy.

**REFERENCES**


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One of the first lessons I learned in business was that “pigs get fat; hogs get slaughtered,” with the idea being that too much greed can be a bad thing. In that context, I believe that the business strategy employed by the nation’s largest commercial laboratories to aggressively negotiate steep discounts on their clinical laboratory fee schedules to gain market share will result in driving the most disruptive change to Medicare’s Clinical Laboratory Fee Schedule (CLFS) in more than 20 years. Beginning in January 2018, Medicare’s payment rates (under the CLFS) will use private payer rates to set CLFS rates, which are projected to be 20 percent to 30 percent less than the current CLFS rates.

In 1984, the Centers for Medicare and Medicaid Services (CMS) established the CLFS, which was based on cost data at the time. Since then, lab test rates have been adjusted annually for inflation and, for the most part, market changes and innovation in the laboratory (technology, private payer rates, etc.) were ignored—until a study in 2013 showed that CMS was paying 20 percent more than private payers. This data led to legislation under the Protecting Access to Medicare Act (PAMA) of 2014, which requires, among other things, applicable laboratories to report private payer reimbursement rates for individual tests. Private payer data will subsequently be used to set future Medicare payment rates, which is expected to result in a reduction in Medicare lab payments by $3.9 billion over the next 10 years. The decline in payments for clinical lab tests will have an impact on all laboratories, including hospital, commercial, and physician office-based laboratories.

Drivers of PAMA
Since its introduction, there have been many questions as to what drove PAMA legislation and how to accurately anticipate and proactively mitigate the potential impact. The origin of PAMA dates back to Office of Inspector General (OIG) studies conducted in 2010 and 2013, which showed that Medicare paid between 18 percent and 30 percent more than private payers for 25 high-volume and/or high-expenditure laboratory tests. These 25 highest-volume, highly-automated tests make up 59 percent, or approximately $4.1 billion dollars, that Medicare paid out of the total $7 billion in 2015 alone. The payments break down as shown in Table 1.

Two key factors affected private payer rates being less than the existing Medicare reimbursement rate:

- Aggressive discounting of rates by commercial laboratories with private payers in an effort to grow market share.
- The ability of health plans to negotiate lower payment rates for new commercial laboratories entering the space, all of whom lacked leverage to aggressively negotiate more favorable rates.

Key payment, reporting, and fee schedule changes
Under Medicare payment reform, updated rates will be determined based on new reporting requirements. “Applicable laboratories” as defined by CLIA will need to report data on private payer rates if they have a unique national provider identifier (NPI), receive greater than 50 percent of all Medicare revenue from the CLFS, and received at least $12,500 in Medicare revenues from laboratory services on the CLFS. These applicable laboratories will need to report the test volume that corresponds to each private payer rate for specific CPT codes associated with each test for the six-month period of January 2016 through June 2016. Out-of-network, non-contracted work for private insurers as well as patient deductibles and coinsurance will be included in the private payer rate. Exclusions that will not require reporting fall into four key categories: capititated payments, partial payments, denied claims, and claim-level payments.

Moving forward, migration to one national fee schedule is planned. CMS will calculate the weighted median private payer rate for each test and set rates accordingly. Most hospital-based labs will be excluded unless they maintain a separate NPI for the laboratory and meet the revenue-based thresholds. Estimates from CMS indicate that 56 percent of independent laboratories, 95 percent of physician laboratories, and the majority of hospital-based laboratories will not meet the definition. The omission of hospital private payer rates from the reporting group has a negative impact on the market data as hospitals are typically paid 20 percent to 30 percent more than independent laboratories. As such, the exclusion of the majority of hospital-based labs skews the data in favor of a lower private payer weighted median and, therefore, a lower rate per the CLFS. New rates will include the weighted median of private payer rates/test volume and be updated on a three-year rotation. Beginning in 2018, a phase-in approach for reductions will be implemented, with limits on reductions for each test by a maximum of 10 percent through 2020 and 15 percent from 2021 to 2023.

The impact of PAMA legislation
What is the estimated impact that PAMA will have on providers in the clinical laboratory segment? Using the total spend of $7.0 billion in Table 1, hospital-based laboratory reimbursement is expected to decline by approximately $0.9 billion over the next five years, while independent and physician office laboratory reimbursement is expected to decline $2.7 billion over the same time period.

Perhaps the only good news is that rates are likely to stabilize once all initial reductions have been implemented.

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<tr>
<th>Laboratory Type</th>
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<td>Independent Labs</td>
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<td>Hospitals</td>
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<td>Physician Office Labs</td>
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<tr>
<td>Total</td>
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Table 1. Medicare payments for clinical diagnostic tests in 2015.
Proactively mitigating pending cuts
Assessing the impact of pending reimbursement cuts on your organization is critical. In addition to PAMA, price transparency, value-based care, test utilization, and population health are expected to put additional revenue pressures on clinical laboratory service providers. The best long-term solution is a global laboratory strategy that encompasses cost reductions, outreach growth, test utilization, quality and service improvements, and improvements to information technology.

Important strategies to consider to offset reimbursement reductions include standardization of equipment and reagents, maximizing synergies from consolidation, growing the laboratory outreach program, managing reference lab and blood costs, and applying lean practices as necessary. Moving from a passive to a proactive response will require hospitals and health systems to look beyond common reactions to change when it comes to their outreach programs.

The most successful approaches include strategic price transparency, development of tools to manage the business (such as distinct accounting and financial reporting for the laboratory), strategic alignment with clients, development of sales with professional staff, outsourcing billing, aggressive cost-reduction initiatives, and a “for-profit” approach that includes the structure and autonomy to run as a serious business. Those are just a few options to explore. To achieve best-in-class performance, there is no magic formula. It simply requires doing a lot of things right. Keep in mind that 20 percent of the things that you do right will impact 80 percent of the opportunity for improvement and better performance.

REFERENCES

Jeffrey H. Myers, CPA, serves as Vice President of Consulting for Accumen Inc., and its subsidiary Chi Solutions, Inc., providers of clinical laboratory consulting, outreach, comprehensive patient blood management (cPBM), and laboratory excellence solutions for hospitals and health systems.
Fecal specimen handling

Many labs perform molecular testing for enteric pathogens, especially for viruses where culture methods are labor-intensive and time-consuming. Fecal samples in traditional containers can represent a challenge because too much sample can result in interference. FecalSwab provides an optimal ratio of sample to media to support molecular platforms. FecalSwab converts solid or semi-solid fecal specimens into liquid phase, using a flocked swab and 2mL Cary-Blair media. In addition to FDA clearance for bacterial culture, FecalSwab is widely used with molecular tests for viruses causing gastrointestinal infections.

Visit COPAN, www.rsleads.com/704ml-150

Hepatitis C assay

Hologic announces FDA approval for the Aptima HCV Quant Dx assay for the detection and quantitation of hepatitis C virus on the fully automated Panther system. The assay has ultrasensitive, highly precise performance in confirmation of active infection and sustained virologic response.

There is high viral load result agreement between Aptima HCV Quant Dx assay and comparators for confidence in switching assays without disrupting patient care. This assay is the latest in the growing virology portfolio from Hologic, following the recent launch and FDA approval of the Aptima HIV-1 Quant assay.

Visit Hologic, www.rsleads.com/704ml-151

Herpes simplex virus assay

The ARIES HSV 1 & 2 Assay is a real-time polymerase chain reaction (rt-PCR)-based qualitative in vitro diagnostic test for the direct detection and typing of herpes simplex virus (HSV 1 & 2) DNA in cutaneous or mucocutaneous lesion specimens from symptomatic patients, or in cerebrospinal fluid (CSF) from patients suspected of HSV infections of the central nervous system. The test is indicated for use with symptomatic individuals to aid in the diagnosis of HSV infections. The assay is not intended to be used for prenatal screening. The ARIES HSV 1 & 2 Assay is indicated for use on the Luminex ARIES System.

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STD assays

Puritan’s UniTranz-RT Universal Transport Systems with PurFlock Ultra flocked swabs can be used to conclusively collect and test viruses, chlamydia, mycoplasma, and ureaplasma specimens. Features include: (a) safe, effective, and easy-to-use transport system; (b) available in 1mL or 3mL fill configurations, with or without swabs; (c) fully compatible with automation systems, EIA, PCR, DFA, and molecular assays; (d) a shelf life of 18 months at room temperature (25°C maximum); and (e) helps prevent unnecessary delays and costs. Product is in stock and ready to ship now. Made in the USA.


HSV 1+2/VZV assays

Solana HSV 1+2/VZV, a multiplex in vitro diagnostic test, detects and differentiates herpes simplex virus type 1, type 2, and varicella-zoster virus in 60 minutes. Solana HSV 1+2/VZV offers a scalable and flexible molecular solution that delivers highly accurate results in an actionable timeframe. Solana’s workflow is easy and flexible, capable of testing a single specimen or batching up to 12 tests at a time. Solana HSV 1+2/VZV is used with Solana, a small bench-top instrument that combines Quidel’s proprietary helicase-dependent amplification with fluorescence detection to deliver molecular results.

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Dual-target HIV-1 PCR test

Built upon the unique dual-target assay design from Roche, the cobas HIV-1 viral load test simultaneously amplifies and detects two separate regions of the HIV-1 genome, which are not subject to selective drug pressure. This allows for more reliable results and supports physicians in making informed treatment decisions for HIV-1 patients undergoing antiretroviral therapy. The test is performed on the fully automated cobas 6800 and 8800 systems, which also run the FDA-approved cobas HBV and cobas HCV viral load tests from Roche. The systems offer fast time to results, high throughput and long walk-away time.

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continued on page 53
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Sources:
4. Three scientific studies to be presented at ASM Microbe 2017.
Transforming the microbiology laboratory to address the Triple Aim in healthcare
By Irene K. Dusich, MT(ASCP)SM

For several years, hospitals across the country have been striving to deliver the Institute for Healthcare Improvement’s “Triple Aim” by improving patient outcomes, improving the patient experience, and delivering care at a lower cost. However, successfully delivering on the goals of the Triple Aim must be achieved in a challenging environment resulting from a number of factors, including some provisions of The Patient Protection and Affordable Care Act, labor shortages, increasing rates of antimicrobial resistance, declining budgets, demands to increase quality measures, and an increasing number of patients with access to health insurance. All of these are occurring as the Centers for Medicare and Medicaid Services (CMS) has introduced the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) in an effort to gain an objective comparison of hospitals on topics important to consumers, provide public reporting of survey results to create new incentives for hospitals to improve quality of care, and enhance accountability by increasing transparency in the quality of hospital care provided.

Identifying the challenges
In the midst of our journey to achieve the Triple Aim, our microbiology laboratory here at NorthShore University HealthSystem, Evanston Hospital collaborated with senior management and other departments to determine how we could contribute as a solutions provider to address the challenges being faced in our hospital. We recognized that we had challenges within our own department that we needed to solve in order to support the hospital more broadly. We opted for an ambitious plan to implement an innovative new technology in our microbiology laboratory that would allow us to address an impending labor shortage at a time when our volume of microbiology testing was increasing. We also recognized a need to improve the turnaround time we provided for our bacteriology results and increase the quality by minimizing the variability that exists in our current process of inoculating, streaking, and incubating plates. For our needs, we decided to introduce a microbiology laboratory automation system that utilizes magnetic rolling bead technology to accomplish these tasks. During our implementation process, we noticed more colonies with greater isolation using the magnetic rolling bead compared to traditional streaking with a loop. This is important because it contributes to our organizational desire to provide the right patient with the right treatment at the right time. In addition, we needed to increase our productivity. We discovered from discussions with microbiology leaders in Europe that they were able to double their Laboratory Productivity Index (LPI), the number of samples processed per technologist per day, from 37.4 to 75.9. This level of productivity increase was exactly what we required in an era of anticipated reductions in staffing due to retirement and increasing volumes.

As we grew comfortable with the productivity gains and the high quality of the streaking of the magnetic rolling bead, we turned our attention to improvements in turnaround time for our bacteriology results. Improving the turnaround time is a function of earlier isolate availability and the selection of an identification technology. In our laboratory, we use matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry for rapid identification of isolates. The microbiology automation system has provided earlier isolate availability due to more consistent incubation times and temperatures, imaging capabilities, and a reduction of subcultures. In a study we conducted, the MALDI-TOF technology and the microbiology laboratory automation system significantly improved turnaround time for identification and susceptibility compared to MALDI-TOF and traditional processing of urine cultures. This is in alignment with the Triple Aim because it allows us to inform clinicians and pharmacy up to a day earlier regarding the appropriate therapy for the patient.

The context of the literature
Earlier results have documented that automated systems have a positive impact clinically, operationally, and economically. As reported by Lodise et al., delayed antibiotic treatment in patients with hospital-acquired Staphylococcus aureus bacteremia was found to be an independent predictor of infection-related mortality and was associated with a length of stay increase of 41.2 percent. Huang et al. found that rapid organism identification, combined with an antimicrobial stewardship team intervention, improved time to effective antibiotic therapy and optimal antibiotic therapy by 9.7 hours and 43 hours, respectively. In addition, mortality, length of ICU stay and recurrent bacteremia all declined. Finally, Perez et al. found a reduction in length of stay by 2.6 days and a reduction in hospital costs of $19,583 per patient. This combination of improvements is exactly the desired impact of the Triple Aim.

Responding to new imperatives
Hospitals across the country are working in an environment of increased transparency relative to quality and patient experience metrics that have a financial impact tied to HCAHPS. As a result, this pay for performance allows for payment or potential penalties based on clinical data and the perception of the patient. In this era of increasing challenges in healthcare, the microbiology laboratory has an opportunity to play a significant role as a solution provider by collaborating with administrative staff, medical staff, and partners in pharmacy and infection control to drive successful antimicrobial stewardship programs, reduce healthcare-associated infections, reduce length of stay on the wards, increase bed capacity to meet patient demand, and ultimately reduce costs in the healthcare system. An effective microbiology laboratory automation system is allowing my organization to successfully pursue our organizational desires to deliver on the Triple Aim.

REFERENCES

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Bacterial vaginitis assay

Bacterial vaginitis (BV) is the most common cause of infectious vaginitis that affects millions of women worldwide. The goal of a BV diagnostic test is to accurately and rapidly detect infection by the organisms causing BV, and thereby enable initiation of appropriate treatment as soon as possible. The OSOM BVBlue by Sekisui Diagnostics, is a rapid test that detects sialidase activity in a vaginal sample from the following bacterial pathogens: Gardnerella, Bacteroides, Prevotella, and Mobiluncus. OSOM BVBlue is an easy-to-use, cost-efficient, point-of-care diagnostic test that provides rapid results, allowing a test-and-treat approach to the management of patients with BV. Visit Sekisui Diagnostics, www.rsleads.com/704ml-156

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AUDT MicroControls, Inc............... www.auditmicro.com ........................................3 IFC
BD Diagnostics ........................................... http://labautomationsolutions.bd.com ................25
Becton Couter Inc ............................. www.beckmancouter.com/contact .........................3
Binding Site ................................................... www.bindingsite.com ...............................10 IBC
Bio-Rad Laboratories ....................... www.qcnet.com/mc-mlo ..................................13
BioFire Diagnostics ............................ biofiredx.com ..................................................4 BC
CompGroup Medical ......................... www.cgm.com/us ...........................................31
Copan Diagnostics ............................... www.copanusa.com ......................................51
DiaSorin Molecular (formerly Focus Diagnostic) ........................................... www.focusdx.com ...................................12
Hologic - HIV ............................................. USAPtimaVirology.com ............................... 19-20
Kamiya Biomedical Co .................... www.k-assay.com/MLO.php ............................... 5
KRONUS ...................................................... www.kronus.com .......................................11
LGP Consulting ........................................... www.lgconsulting.com ................................27
NovaBiomedical ......................................... novabiomedical.com ..................................39
Orchard Software ............................... www.orchardsoft.com ....................................33
Owen Mumford Inc ........................... owenmumford.com ......................................17
Randox Laboratories ...................... randoxgp.com ..................................................41
Streck ...................................................... streck.com/miniicube ....................................9
Sysmex America Inc ......................... www.sysmex.com/beyond_mlo .........................1
Verbatim Americas LLC .................. www.pathfast.com ...........................................18

INDEX OF ADVERTISERS

Laboratory Network Quality & Standardization Coordinator

The Laboratory Network Quality & Standardization Coordinator is the central organization point for the laboratory quality, compliance, and operational standardization for the Guthrie system laboratories. This position works closely with all laboratory and Guthrie system administration to help facilitate system operational and reporting standardization and provide consistent standardized monitoring for both consolidated laboratory operations and site specific data. The position is viewed as the system lab expert for regulatory compliance and risk management. This person will assist in the identification of trends and proposal of strategies.

The position requires a person with strategic and forward thinking ideas. The individual should have a high degree of initiative and energy, along with excellent interpersonal and communication skills. Three plus years of clinical laboratory experience spanning most laboratory sections is highly desired. Requires the ability to analyze data, problem solve and identify issues and trends, then assist in prioritizing and moving solutions forward.

Bachelor’s degree in biology, chemistry or medical technology, certification as a medical technologist by the ASCP Board of Registry or equivalent preferred. Master’s degree in health care plus Lean or Six Sigma background or significant experience a plus.

Guthrie is a member of the Mayo Clinic Care Network, and is the first health system based in Pennsylvania and New York to join this network. Guthrie is comprised of a research institute, home care/hospice, four hospitals as well as a multi-specialty group practice of more than 290 physicians and 175 mid-level.

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Fostering a culture of innovation in laboratory diagnostics

If you were explaining Sysmex America, Inc., to someone who is not familiar with the organization, how would you characterize its primary areas of expertise? Sysmex is known around the globe for its leading-edge innovation in laboratory diagnostics. In particular, we are known for hematology instrumentation. Here in the United States, our success flows from our products, service, and customer support.

What are the major categories of solutions that the company provides for the clinical lab?

Sysmex is a manufacturer and marketer of advanced instrumentation, automation, and IT in the fields of hematology, hemostasis, urinalysis, flow cytometry, immunossay, and other areas of the life sciences.

Your website says that Sysmex has created “a holistic, intuitive ecosystem that helps improve lab operations and promote better healthcare and patient management practices” for customers. Can you expand on that? Sysmex reshaped hematology diagnostics with our innovative analyzers. But these advanced tools and technologies were only the beginning. Our next generation diagnosticians include our expanded CBC to give the clinician more information about various disease states such as infection. We offer process optimization for the lab to help balance work flow. In addition, we have our “BeyondCare Team” of associates who offer harmonized support to our customers. We call this entire experience that we offer to the clinical lab, “Beyond a Better Box.”

Sysmex recently announced the launch of the XN-L Series hematology analyzers in Canada. How do these analyzers represent advancements for the hematology lab? Sysmex Canada launched the XN-L Series hematology analyzers late last year, and the Series has already launched in many other parts of the world. The new, smaller XN-L brings Sysmex XN-Series automated hematology systems’ clinical and operational value to lower-volume hematology laboratories. This enables small hospitals and clinics to offer the same leading-edge technology in their labs as larger hospital and reference labs. In February the XN-L Series instruments were cleared for sale in the United States and should be launched before the end of the first half of 2017.

Last year, Sysmex also introduced the CyFlow monoclonal antibodies, for RUO in the U.S. and Canada. How do these reagents complement Sysmex’s existing flow cytometry product line? Our new line of flow cytometry products is for use in pharmaceutical, industrial, and clinical research. We introduced our CyFlow monoclonal antibodies last summer to complement our existing line of CyFlow Cube and Space flow cytometers and reagents. All our flow cytometry products are for research use only.

Sysmex is also much associated with urinalysis. What is new under the sun with regard to the oldest laboratory test? Urinalysis is a traditionally labor-intensive area of the laboratory. Sysmex is continually developing new products for urinalysis and intends to deliver a degree of automation that will bring efficiencies and improve turnaround time. Sysmex believes it is time for urinalysis to catch up with the rest of the innovation occurring in the lab environment.

Your company’s user base has expanded much in recent years. With success comes greater responsibility; how has Sysmex responded to the challenge and opportunity? Sysmex’s mission is to shape the advancement of healthcare. This is the basis of The Sysmex Way, our corporate philosophy, which is practiced by everyone in the lab, around the world. We take our mission seriously and spend our energy, resources, and R&D dollars to continue delivering new innovations to laboratories around the globe. In hematology, we will continue to automate and drive precise results, such as with our expanded CBC including immature granulocyte (IG) analysis, immature platelet fraction (IPF), and reticulocyte hemoglobin (RET-He). All of these innovations and more are designed with patients and our customers in mind.

You joined Sysmex in 1989 and have been with Sysmex America since 2000. How does this longevity with the company serve you in your current role? Over my time with Sysmex, I have been fortunate to meet and learn from many of the finest laboratory hematologists and other pathologists around the world. My roles have been varied, from sales and marketing, from R&D to IT, and from training to operations. All of these collective learnings have helped me establish a breadth and depth of knowledge which I can use today to help Sysmex America continue to deliver leading-edge instruments and assays to our customers, helping them to increase their efficiencies and face financial, logistical, and operational challenges, all while maintaining clinical excellence. Even though we have seen amazing growth in our business, we have always maintained that the patient and the customer come first.

From my time in the lab, I also learned about the human aspect of the patients who are on the receiving end of lab testing, when I used to meet and work with them directly. I never forget that feeling of responsibility, nor do my colleagues at Sysmex. I firmly believe if we continue to innovate and do the right thing for the patients of our customers, then we will continue to bring value and achieve success as a member of the healthcare community.
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