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MEDICAL LABORATORY OBSERVER

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CE:

The challenge of antimicrobial resistance:

The role of the antibiogram

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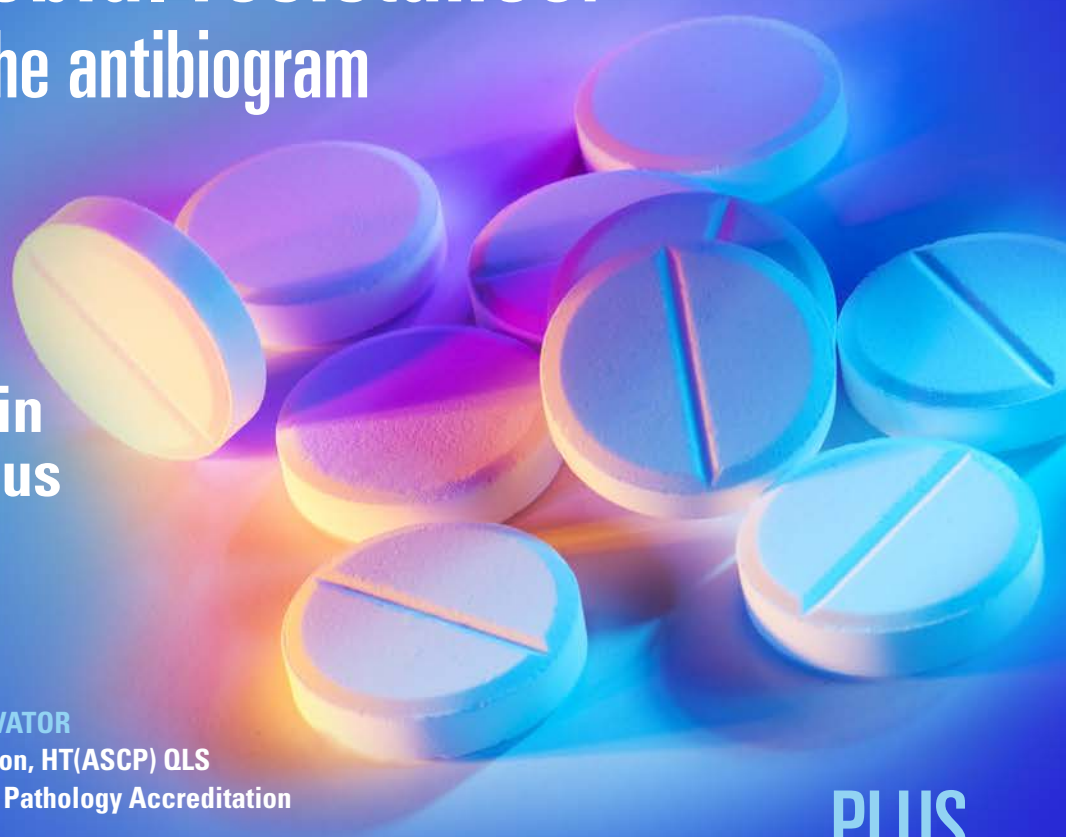

What's new in viral infectious diseases

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LAB INNOVATOR

Kathy Wilson, HT(ASCP) QLS

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- CT/NG
- *Mycoplasma genitalium*
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- HSV 1 & 2
- HPV
- HPV 16 18/45
- Zika Virus*

INFECTIOUS DISEASE

- HIV-1 Quant Dx
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- CMV Quant
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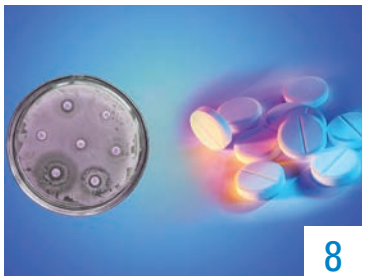

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Polio's reemergence

By Christina Wichmann
Senior Editor

While editing this month's Clinical Issues article, *"Plague take it! What's new in viral infectious diseases?"* the Centers for Disease Control and Prevention (CDC) announced that it will be expanding efforts to test wastewater in the Philadelphia and Detroit areas, and that preliminary discussions with other selected state and local health departments are underway for testing. This follows confirmation of a case of paralytic polio in Rockland County, New York this past summer in an unvaccinated young adult. Wastewater samples, which were originally collected for SARS-CoV-2 surveillance, were linked to the type 2 vaccine-derived poliovirus. Before this summer, polio was not on the top of many people's minds. This patient was only the second identification of community transmission of poliovirus in the United States since 1979; the previous instance, in 2005, was an Amish infant that was hospitalized with type 1 vaccine-derived poliovirus in Minnesota.

The CDC stated, "Even a single case of paralytic polio represents a public health emergency in the United States."[1] The reasons being that polio has potentially severe consequences and low vaccination coverage in the patient's county of residence indicates that the community is at risk for additional cases of paralytic polio. As of December 5th, sequencing analysis by the CDC confirmed the presence of poliovirus in a total of 94 positive samples of concern taken from Rockland and surrounding counties. Of the 94 positive samples of concern, 87 samples were found to be genetically linked to the individual case of paralytic polio in the Rockland County patient.[2]

There are two types of polio vaccines. The inactivated polio vaccine creates antibodies that enter the central nervous system and must be administered through injection by a trained health worker. The oral polio vaccine, which contains a weakened form of the virus, triggers the immune system to create antibodies to fight off the disease. The oral vaccine is effective but in rare cases can mutate and cause vaccine-derived poliovirus. The oral polio vaccine has not been used in the United States since 2000 because of that risk.

Most Americans are vaccinated for polio as children. However, there are pockets of the population that have not been vaccinated. Those who are unvaccinated or incompletely vaccinated are at risk of contracting and spreading polio. According to the CDC press release, poliovirus wastewater testing is not routinely or broadly recommended, and there are strict laboratory safety requirements. However, the strategic use of wastewater testing in a limited number of at-risk communities can help determine if poliovirus is present in other parts of the United States outside the areas tested following the New York case and can be used to target vaccination efforts to rapidly improve local polio vaccination coverage if needed. Over the next few months, the CDC-led wastewater testing will inform vulnerable communities whether there are positive wastewater detections and hopefully improve vaccination rates in these communities.

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

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Ionized Magnesium (iMg) Hypomagnesemia is a frequent finding in critically ill patients.[1] Magnesium therapy guided by real time ionized magnesium monitoring has been shown to improve outcome in these patients.[2]

Estimated Plasma Volume (ePV) The plasma volume status of a patient is one of the top priorities in evaluating and treating critical illness including CHF, ARDS, AKI, Surgery, and Sepsis.[3-5]

Urea, Creatinine and eGFR Over 50% of patients admitted to the ICU develop some degree of acute kidney injury.[6] Creatinine, eGFR, and Urea point-of-care monitoring provides early indication of changes in kidney function and helps guide therapy to prevent AKI.

MCHC Mean corpuscular hemoglobin concentration (MCHC) provides insight into certain causes of anemia, such as iron deficiency or inability of the body to absorb iron, chronic low grade blood loss over time, and autoimmune hemolysis.

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Fast Facts

Reducing the burden of death due to infection is an urgent global public health priority. Previous studies have estimated the number of deaths associated with drug-resistant infections and sepsis and found that infections remain a leading cause of death globally. Understanding the global burden of common bacterial pathogens (both susceptible and resistant to antimicrobials) is essential to identify the greatest threats to public health. A study published in the *Lancet* presented global comprehensive estimates of deaths associated with 33 bacterial pathogens across 11 major infectious syndromes:

13.7 million (95% UI 10.9–17.1)

infection-related deaths in 2019 were estimated.

7.7 million deaths (5.7–10.2)

were associated with the 33 bacterial pathogens (both resistant and susceptible to antimicrobials).

13.6% (10.2–18.1)

of all global deaths were associated with the 33 bacterial pathogens and

56.2% (52.1–60.1)

of all sepsis-related deaths in 2019.

54.9% (52.9–56.9)

of deaths among the investigated bacteria were caused by five leading pathogens—Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Klebsiella pneumoniae, and Pseudomonas aeruginosa.

230 deaths (185–285)

per 100,000 population was the age-standardized mortality rate associated with these bacterial pathogens in the sub-Saharan Africa super-region where the rates were the highest. The deadliest infectious syndromes and pathogens varied by location and age.

Source: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02185-7/fulltext

New blood test can detect 'toxic' protein years before Alzheimer's symptoms emerge, study shows

A team led by researchers at the University of Washington has developed a laboratory test that can measure levels of amyloid beta oligomers in blood samples. Their test — known by the acronym SOBA — could detect oligomers in the blood of patients with Alzheimer's disease.

However, SOBA did detect oligomers in the blood of 11 individuals from the control group. Follow-up examination records were available for 10 of these individuals, and all were diagnosed years later with mild cognitive impairment or brain pathology consistent with Alzheimer's disease. Essentially, for these 10 individuals, SOBA had detected the toxic oligomers before symptoms surfaced.

SOBA, which stands for soluble oligomer binding assay, exploits a unique property of the toxic oligomers. When misfolded amyloid beta proteins begin to clump into oligomers, they form a structure known as an alpha sheet. Alpha sheets are not ordinarily found in nature, and past research by Daggett's team showed that alpha sheets tend to bind to other alpha sheets. At the heart of SOBA is a synthetic alpha sheet designed by her team that can bind to oligomers in samples of either cerebrospinal fluid or blood. The test then uses standard methods to confirm that the oligomers attached to the test surface are made up of amyloid beta proteins.

The team tested SOBA on blood samples from 310 research subjects who had previously made their blood samples and some of their medical records available for Alzheimer's research. At the time the blood samples had been taken, the subjects were recorded as having no signs of cognitive impairment, mild cognitive impairment, Alzheimer's disease, or another form of dementia.

SOBA detected oligomers in the blood of individuals with mild cognitive impairment and moderate to severe Alzheimer's. In 53 cases, the research subject's diagnosis of Alzheimer's was verified after death by autopsy — and the blood samples of 52 of them, which had been taken years before their deaths, contained toxic oligomers.

SOBA also detected oligomers in those members of the control group who, records show, later developed mild cognitive impairment. Blood samples from other individuals in the control group who remained unimpaired lacked toxic oligomers.

FDA approves drug that can delay onset of type 1 diabetes

The U.S. Food and Drug Administration approved Tzield (teplizumab-mzwv) injection to delay the onset of stage 3 type 1 diabetes in adults and pediatric patients 8 years and older who currently have stage 2 type 1 diabetes.

Tzield binds to certain immune system cells and delays progression to stage 3 type 1 diabetes. Tzield may deactivate the immune cells that attack insulin-producing cells, while increasing the proportion of cells that help moderate the immune response. Tzield is administered by intravenous infusion once daily for 14 consecutive days.

Tzield's safety and efficacy were evaluated in a randomized, double-blind, event-driven, placebo-controlled trial with 76 patients with stage 2 type 1 diabetes.

The most common side effects of Tzield include decreased levels of certain white blood cells, rash and headache. The use of Tzield comes with warnings and precautions, including premedicating and monitoring for symptoms of Cytokine Release Syndrome; risk of serious infections; decreased levels of a type of white blood cell called lymphocytes; risk of hypersensitivity reactions; the need to administer all age-appropriate vaccinations prior to starting Tzield; as well as avoiding concurrent use of live, inactivated and mRNA vaccines with Tzield.

New research shows indoor tanning can increase melanoma risk

A new article published in the *Journal of the American Academy of Dermatology* suggests that indoor tanning is the most frequent cause of multiple primary melanomas, which is when a patient develops additional melanomas after their first one.

In fact, the research showed that melanoma patients with who use tanning beds more than 10 times have nearly double the risk of having a second or multiple melanomas.

This research adds to the growing body of research on the dangers of indoor tanning, including:

- Indoor tanning equipment emits harmful UVA and UVB radiation. The amount of radiation produced during indoor tanning is similar to that of the sun, and in some cases might be stronger.
- Using tanning beds before age 20 can increase your chances of developing melanoma by 47%, and the risk increases with each use.

Observatory continued on page 33

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

Readers' questions answered

Many laboratories offer PCR testing panels for various diseases, such as urinary tract infection, gastrointestinal, etc. It's obvious that PCR testing is a major breakthrough in clinical medicine, providing fast turnaround time with definitive organism results. However, where does susceptibility testing come into play? Do providers just know that if a specific organism is identified that they know which specific antibiotic is best to use?

Amplified polymerase chain reaction (PCR) tests can detect microbial genetic sequences of infectious pathogens with high sensitivity and specificity and with rapid turnaround time. These tests can often be multiplexed to simultaneously test for the most common potential pathogens for a particular clinical syndrome. In some cases, PCR can even provide information regarding a pathogen's susceptibility to antimicrobial therapies. For example, there are PCR tests which can detect mecA, which is the most common gene mediating oxacillin resistance in staphylococci. There are also PCR tests that can be used for positive blood cultures to detect common antimicrobial resistance genes for gram-positive organisms such as vanA/B as well as detect multiple specific gram-negative carbapenemases at once, including K. pneumoniae carbapenemases, specific metallo-beta-lactamases, and OXA-type carbapenemases.

Despite these advances in the detection of antimicrobial resistance, such testing often does not eliminate the need for traditional growth-based methods for the determination of antimicrobial susceptibility or resistance. Antibiotic therapy selection is also often informed by a patient's history (such as known colonization with resistant organisms) or by knowledge of the prevalence of antimicrobial resistance in the facility or community (such as with the use of antibiograms). Since this information does not require a lab test result, it is often useful to inform initial "empiric" antimicrobial therapy selection, which can later be adjusted when lab test rests are returned. Ultimately, some combination of a number of different pieces of information (such as prevalence of resistance, patient risk factors, likely organism, PCR results, growth-based microbiology results) combine to inform antibiotic selection.

We refer positive hepatitis C (HCV) patients with increased liver enzymes to a gastroenterologist. Besides other tests, they often will request an INR to access the cirrhosis. We perform a waived INR. Since the INR is only valid for patients on Coumadin (Warfarin), is the INR the appropriate test, or should we have a pro-time performed instead?

It's common for patients with advanced liver disease to have abnormal routine laboratory tests of coagulation (PT, PTT, INR). However, because these patients have defects in both the synthesis of anticoagulant and procoagulant factors, these laboratory abnormalities are not an accurate predictor of a patient's risk for bleeding. For this reason, laboratory coagulation tests such as INR are not typically used to manage coagulation abnormalities that often exist in patients with liver disease. Despite this, the measurements of these labs can still provide useful information. For example, INR is still very important in patients with liver disease, particularly since it is needed to perform a MELD/MELD-Na score. This score uses INR as well as bilirubin, creatine, sodium, and dialysis history to estimate three-month survival. In patients with cirrhosis, an increased MELD score is associated with increased liver disease severity and increased three-month mortality. The results of this score are often used to inform transplant decision making such as transplant list prioritization. The other scenario when laboratory tests of coagulation may be informative is when there is a large, rapid change in the results. This typically leads to an evaluation to identify the cause, which could involve worsening of the liver disease among other possible causes.

The challenge of antimicrobial resistance for the clinical laboratory: The role of the antibiogram

By Fred C. Tenover, Ph.D., D(ABMM), FIDSA, FAAM, FISAC

Simply stated, antimicrobial agents, which include antibacterial, antifungal, antiviral, and antiparasitic agents, are life-saving medicines that are losing their effectiveness globally. A combination of over prescribing and indiscriminate use in human, veterinary, agriculture and other sectors, coupled with the continuing evolution of novel resistance mechanisms, has led to a pandemic of resistant organisms globally. Unlike COVID-19, this pandemic has been escalating for several decades, causing some to refer to it as "the hidden threat."[1] For many patients with life threatening infections that resist even our newest antimicrobial agents, it is all too real. Multidrug-resistant bacteria have emerged not only in healthcare settings, but also in our food supply, and even in our pets. Among humans living in the United States, data from the Centers for Disease Control and Prevention show that a new antimicrobial resistant infection develops every 11 seconds and every 15 minutes someone dies of an antimicrobial resistant infection. That translates into 2.8 million new resistant infections in the United States every year and >35,000 deaths.[2] Globally, the data are much starker with deaths associated with antimicrobial-resistant organisms approaching 5 million annually.[3] Infections caused by antimicrobial-resistant organisms lead to longer hospital stays, more serious complications, and increased mortality rates because effective treatment is delayed or simply not available. Everyone, not just immune compromised patients, is at risk.

How did we get to this point? For many years, there was a sense among physicians that antimicrobial agents, even if they were not really needed, caused no harm. In other words, many antibiotics were prescribed for patients "just to be on the safe side." Thus, the barrier to prescribing antimicrobial agents, especially for respiratory illnesses in both children and adults, was low. We now know better. The adverse drug events that can occur can send people to emergency rooms with nausea, vomiting, skin rashes, and in some instances anaphylaxis. Yet, a more insidious side effect is infection with an anaerobic toxin-producing gram-positive bacillus known as *Clostridioides* (formerly *Clostridium*) *difficile*, or more simply "C. diff." When antimicrobial agents disrupt the bowel flora, many of the resident microorganisms that form a natural barrier to infection with pathogenic microbes are killed. This allows colonization of the gut with C. diff that leads to infection. Infection with C. diff is associated with elaboration of one or more toxins, resulting in gastrointestinal disease that can range from mild diarrhea to pseudomembranous colitis and even death.[4] More than 225,000 *C. difficile* cases are observed in the US annually according to the CDC.2 In fact, we are still learning about the long term-side effects of antimicrobial use including effects on immune function and metabolism.[5] Thus, taking an antimicrobial agent is not without risk and should be reserved for treating infections, where the benefits of the taking the drug clearly outweigh the risk of adverse events. Even so, a World Health Organization (WHO) study in 2020 among 2000 COVID-19 cases from multiple countries, reported that 72% of patients received antimicrobial agents even though only 8% had a documented bacterial or fungal infection.[6] Granted, early on in the

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LEARNING OBJECTIVES

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

1. List the reasons that have led to antimicrobial resistance.
2. Discuss healthcare statistics and outcomes of multidrug-resistant bacteria.
3. Describe how proper antibiotic treatment is selected for individual patients.
4. Discuss how antibiograms are generated, used, and developed.

XYZ Institution
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1 January - 31 December 2021 Cumulative Antimicrobial Susceptibility Test Data - Antibiogram

	PERCENTAGE (%) SUSCEPTIBLE*															
		Aminoglycosides			β-Lactams						Quinolones		Others			
	# Isolates Tested	Amikacin	Gentamicin	Tobramycin	Oxacillin	Ampicillin	Piperacillin/ Tazobactam	Ceftazidime	Ceftriaxone	Meropenem	Ciprofloxacin	Levofloxacin	Clindamycin	Nitrofurantoin§	Chloramphenicol	Trimethoprim sulfamethoxazole
GRAM NEGATIVE																
Escherichia coli	**670**	99	53	92	-	50	97	92	93	99	28	-	-	90	-	72
Klebsiella sp.	**300**	99	72	94	-	R	52	60	61	68	50	-	-	50	-	54
Proteus mirabilis	**75**	100	70	93	-	53	58	61	63	95	55	-	-	R	-	79
Salmonella enterica ser. Typhi (blood isolates only)	**50**	-	-	-	-	50	-	-	69	-	90	-	-	-	22	86
Pseudomonas aeruginosa	**187**	97	70	83	-	R	45	53	R	76	60	-	-	-	-	R
GRAM POSITIVE																
Staphylococcus aureus **ALL**	**850**	-	-	-	66	-	-	-	-	-	-	-	81	-	-	97
Staphylococcus aureus **MRSA**	**289**	-	-	-	0	-	-	-	-	-	-	-	32	100#	-	96
Staphylococcus aureus **MSSA**	**561**	-	-	-	100	-	-	-	-	-	-	-	82	100	-	97

* %S for each organism/antimicrobial combination generated by including first isolate of organism encountered in a given patient
§ Nitrofurantoin data for urine isolates only R = intrinsic resistance (-) drug not routinely tested or indicated for this organism

Figure 1. Example data from an antibiogram.

COVID-19 pandemic, we didn't know what the risk of secondary bacterial infections was so antimicrobial agents flowed freely to patients. But, even as our understanding of COVID-19 infections expanded and secondary bacterial infections were noted to occur in <10% of cases, antimicrobial agents still flowed freely. This is but one example of how the overuse of antimicrobial agents can fuel the development of resistant microorganisms.

Before the onset of COVID-19, the combined efforts of public health organizations, physicians, laboratorians, and professional societies in the United States were making progress in lowering the numbers of healthcare-associated infections, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and drug-resistant *Pseudomonas aeruginosa*.[7] However, that progress was reversed with resurgences of these organisms in hospitals during COVID-19 when our concern for transmission of COVID-19 among patients took priority over transmission of traditional healthcare–associated pathogens, including MRSA and VRE. There was one notable exception to the successful reduction of healthcare-associated infections in the United States prior to COVID-19: the rates of infections with carbapenem-resistant gram-negative organisms remained stable. Carbapenems are often referred to as the antibiotics of last resort and the development and spread of organisms that are resistant to this class of agents has been cited as a global menace.[8] Outside of the hospital, two other antimicrobial resistance problems were gaining momentum. In 2020, rates of infections caused by *Mycobacterium tuberculosis* (the bacterial species that causes tuberculosis) increased for the first time in over a decade. Years of progress in fighting tuberculosis were reversed in a single year due to COVID-19's impact on tuberculosis control programs, which were often halted to deal with the COVID-19 pandemic. Not only M. tuberculosis strains but multidrug-resistant M. tuberculosis strains were on the increase, which was a major blow to public health programs globally. Besides tuberculosis control programs, the other public health efforts that were extremely compromised by COVID-19 were those focused on preventing sexually transmitted infections. Multidrug-resistant strains of the sexually transmitted bacterial pathogen *Neisseria gonorrhoeae* emerged.[9] The challenges of resistance are growing both inside and outside of hospitals worldwide.

The laboratory perspective

What is often overlooked when considering all the journal articles and news stories on antimicrobial resistance are the Herculean efforts of the clinical laboratory, and the microbiology laboratory in particular, to generate all of the data on the emergence of resistant microorganisms in both hospital and community settings. The microbiology laboratory remains the unsung hero in the fight to control the spread of resistance globally. Without the antimicrobial susceptibility data that flows from the microbiology laboratory, physicians would not know how to select the most effective therapy for patients with infections, infection preventionists would not know which patients with resistant organisms needed to be placed in contact precautions to prevent spread in hospitals, and public health officials would not know where outbreaks of multidrug-resistant infections were occurring.

Guiding treatment for the individual patient

Physicians, pharmacists, and antimicrobial stewardship committees look to the microbiology laboratory to guide the selection of antimicrobial agents via antimicrobial susceptibility test results to treat patients with infections. To perform this function, the laboratory first isolates the microbial pathogen from clinical specimens (e.g., blood, urine, sputum, or wounds), identifies the bacterial species, and generates the antimicrobial susceptibility pattern of the isolate to a variety of antimicrobial agents via some form of broth microdilution or disk diffusion testing. This traditional approach may take up to 72 hours to complete, which for critically ill patients may be too long to impact care. Thus, rapid molecular diagnostic methods can be employed to detect organisms directly in clinical specimens (such as sputum or wounds) or from positive blood culture specimens, reducing the turnaround time of identification

sometimes to as little as one hour. Some commercial panels also have a limited selection of antimicrobial resistance genes that can be used to predict resistance to some classes of antimicrobial agents for bacterial pathogens earlier in the course of infection. A meta-analysis of the impact of molecular methods shows that using these rapid laboratory tests significantly improves patient outcomes, especially when the results were shared with an antimicrobial stewardship committee.[10]

Generating antibiograms

Traditional susceptibility test results guide the treatment of the individual patient, but when the results from all patient specimens over the course of a year are pooled, the cumulative percent susceptibility data for the most commonly used antimicrobial agents for the key bacterial pathogens enables physicians to formulate anti-infective strategies before the data from the standardized susceptibility tests are known. This is known as "empiric therapy" and the cumulative susceptibility tests results are known collectively as the hospital's "antibiogram."These results are critical for the management of patients in the early stages of infection. For septic shock, every hour a patient is on ineffective therapy, the chance of death increases by 7.6%.[11]Thus, the antibiogram is relied upon to narrow therapeutic choices to those most likely to be effective. When additional data become available through standard susceptibility testing or molecular test methods, the therapy is adjusted appropriately.

Antibiograms are typically assembled at least annually, often in collaboration with the hospital's pharmacy and the antimicrobial stewardship team. The report typically includes data for both gram-positive and gram-negative organisms **(See Figure 1)**. Laboratories often customize their antibiograms to provide more detailed information on specific patient populations or hospital units. For example, a separate antibiogram may be generated for outpatients, for pediatric patients, or for hematology/oncology patients. Further stratification may be done for blood and urine isolates depending on the hospital's needs. The Clinical and Laboratory Standards Institute has produced document M39, which focuses on guiding laboratories in the preparation of their antibiograms.[12]

The utility of antibiograms

Antibiograms not only help guide physicians and pharmacists in selecting the best empiric antimicrobial treatment while culture and susceptibility results are pending, antibiograms also impact the broader healthcare ecosystem by providing data that can guide infection prevention programs designed to contain the spread of antimicrobial-resistant infections in the hospital. Following the annual incidences of MRSA, VRE, and carbapenemase-producing organisms (CPO) through antibiograms is one indicator of the effectiveness of infection prevention programs in a hospital. However, the data, if getting worse, may be signaling the emergence of new multidrug-resistant strains or organisms with novel resistance mechanisms. In some cases, it may be of public health value to share resistance data more broadly, thus, the aggregated susceptibility data from a region can be exported to external surveillance systems and used to understand the epidemiologic spread of resistant organisms. Tracking CPOs has become a major public health priority. This is because serine-based carbapenemases, like KPC, can often be treated with one of the newer beta-lactam/beta-lactamase inhibitor combinations (ceftazidime/avibactam, meropenem/vaborbactam, or imipenem/relebactam) while organisms with

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metallo-carbapenemases, like NDM, IMP, and VIM, typically do not respond to these new agents. This is very important information especially for those committees developing empiric therapy guidelines.

Among the many challenges for the microbiology laboratory when populating antibiograms with data is making sure that they are using the most current interpretive criteria, i.e., susceptible, intermediate, and resistant interpretations (also known as breakpoints). Laboratories in the United States adhere to the standards produced by the Clinical and Laboratory Standards Institute. The definitions of susceptibility and resistance are fluid and change over time with the accumulation of clinical use and outcomes data and the emergence of new resistant strains. Both minimal inhibitory concentration (MIC) and disk diffusion criteria may change. Significant changes include, but are not limited to, the interpretations of cephalosporins, carbapenems, and fluoroquinolones. It often takes a few years for the automated susceptibility testing systems to incorporate the new interpretive criteria in the instrument's software once the updated criteria are approved by the U.S. Food and Drug Administration. When released, the laboratory needs to verify the updated criteria in-house. A recent review showed that many laboratories in the United States have yet to incorporate new breakpoints especially for cephalosporins and carbapenems and this may lead to misidentifying resistant organisms as drug susceptible.[13] That in turn may lead to treatment failures and poor patient outcomes. If the outdated criteria are incorporated into antibiograms, the impact is compounded. Thus, it is incumbent on the microbiology lab to make sure it is using the most up-to-date criteria to ensure that positive patient outcomes are realized. In fact, using updated breakpoints is now a requirement of the College of American Pathologists.[14]

Aids for developing antibiograms

There are multiple sources of information to aid laboratories in preparing their antibiograms. In addition to CLSI document M39 (which must be purchased), a free software program called WHONET (http://www.who.int/drugresistance/whonetsoftware/en/) is available that can download data from automated susceptibility testing methods or import disk diffusion data from spread sheets. Data can be displayed in a variety of ways for the laboratory, the antimicrobial stewardship committee, and for infection control practitioners. The program also facilitates exporting data to surveillance systems, such as the World Health Organization GLASS program.

Summary

Antimicrobial resistance is a global problem. When antibacterial agents are used inappropriately, resistance develops in bacterial strains and patients' therapies fail. The laboratory plays a central role in providing the antimicrobial susceptibility test results that guide treatment of individual patients and, when assembled in an annual antibiogram, guides empiric therapy, infection prevention, and antimicrobial stewardship activities. It is important to ensure that the susceptibility data generated are reported with the latest interpretive criteria. Antibiograms are an important tool to inform infection prevention activities and monitor resistance trends over time. Thus, antibiograms are a critical factor in our efforts to bring antimicrobial resistance under control.

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The challenge of antimicrobial resistance for the clinical laboratory: The role of the antibiogram

JANUARY 2023 *[This form may be photocopied. It is no longer valid for CEUs after JUNE 30, 2025.]*

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TEST QUESTIONS

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

1. **Which of the following has led to the pandemic of resistant organisms globally?**
   - a. Nonselective use of antibiotics in human, veterinary, agriculture and other sectors
   - b. Ongoing evolution of novel resistance mechanisms
   - c. Over prescribing antibiotics
   - d. All of the above

2. **How many C. difficile cases are observed annually in the United States?**
   - a. 25,000
   - b. 125,000
   - c. 200,000
   - d. 225,000

3. **According to a study of 2,000 COVID-19 patients from different countries done in 2020 by the World Health Organization (WHO), what percentage of the patients received antimicrobial agents even though only 8% had a documented bacterial or fungal infection?**
   - a. 70
   - b. 72
   - c. 74
   - d. 78

4. **When antibacterial agents disrupt the normal flora of the gut, what anaerobic gram-positive bacillus organism can colonize in the gut and cause an infection?**
   - a. Methicillin-resistant Staphylococcus aureus (MRSA)
   - b. Mycobacterium tuberculosis
   - c. Clostridium difficile
   - d. Neisseria gonorrhea

5. **Which organism is known to cause a healthcare-associated infection?**
   - a. Methicillin-resistant Staphylococcus aureus (MRSA)
   - b. Mycobacterium tuberculosis
   - c. Neisseria gonorrhoeae
   - d. A Salmonella species

6. **Before the onset of COVID-19, progress was being made in lowering the number of infections caused by MRSA, VRE, and drug-resistant Pseudomonas aeruginosa.**
   - a. True
   - b. False

7. **What class of antibiotics are referred to as the antibiotics of last resort?**
   - a. Penicillins
   - b. Carbepenems
   - c. Fluoruquinolones
   - d. Tetracylines

8. **Which organism have we seen the rate of infections increase for the first time in ten years?**
   - a. Pseudomonas aeruginosa
   - b. E. coli
   - c. Mycobacterium tuberculosis
   - d. Mycobacterium smegmatis

9. **Data from the Centers for Disease Control and Prevention (CDC) show that a new antimicrobial resistant infection develops**
   - a. Every 5 seconds
   - b. Every 11 seconds
   - c. Every 17 seconds
   - d. Every 21 seconds

10. **Rapid molecular diagnostic methods can be used to reduce the turn-around time of organism identification to as little as one hour.**
    - a. True
    - b. False

11. **Which Clinical and Laboratory Standards Institute (CLSI) document focuses on guiding laboratories in preparing an antibiogram?**
    - a. M39
    - b. M52
    - c. MM18
    - d. MM24

12. **Which area(s) in the hospital contribute(s) to the assembly of the antibiogram?**
    - a. Pharmacy only
    - b. Antimicrobial stewardship team only
    - c. Pharmacy and antimicrobial stewardship team
    - d. Microbiology laboratory, pharmacy, and antimicrobial stewardship team

13. **This term is used when treatment with an antibiotic is started before the data from the standardized susceptibility tests are known.**
    - a. Susceptibility-guided therapy
    - b. Empiric therapy
    - c. Cumulative data therapy
    - d. None of the above

14. **Which of the following best describes an antibiogram?**
    - a. A hospital's annual cumulative susceptibility test results
    - b. A report including susceptibility data from only gram-positive organisms
    - c. A report including only blood and urine isolate susceptibility test results
    - d. A report including susceptibility data from only gram-negative organism

15. **Antibiograms have no impact on containing the spread of antimicrobial-resistant infections in the hospital setting.**
    - a. True
    - b. False

16. **What organization has made using updated breakpoints a requirement in the microbiology laboratory.**
    - a. Food and Drug Administration (FDA)
    - b. World Health Organization (WHO)
    - c. College of American Pathologists (CAP)
    - d. Centers for Disease Control and Prevention (CDC)

17. **Which statement best describes WHONET?**
    - a. A software program which must be purchased to aid in developing antibiograms
    - b. A software program that can download data from automated susceptibility testing methods
    - c. A software program unable to export data to surveillance systems
    - d. A software program that is not capable of importing disk diffusion data from spread sheets

18. **How often does it take for automated susceptibility testing systems to incorporate any new interpretive criteria in the instrument's software once updated criteria are approved by the U.S. Food and Drug Administration?**
    - a. Few days
    - b. Few weeks
    - c. Few months
    - d. Few years

19. **Tracking carbapenemase-producing organisms (CPOs) has become a major public health priority.**
    - a. True
    - b. False

20. **Which of the following is NOT a metallo-carbapenemase?**
    - a. NDM
    - b. IMP
    - c. KPC
    - d. VIM

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Plague take it! What's new in viral infectious diseases?

By Linda L. Williford Pifer, Ph.D., SM(ASCP), GS(ABB)

"Plague take it!" was an expression employed by 19th and early 20th century Christians to convey anger, disgust, or frustration in a manner that would circumvent profanity.[1] It simultaneously reflects the centuries-old angst and terror arising from a generational memory of plagues passed down through the centuries. But despite medical advances such as stem cell therapy, cloning, and having the total human genome at our fingertips, plagues are with us still, in ever-changing outbreaks of infectious diseases.

Highly pathogenic avian influenza virus (HPAI-H5N1)

Influenza is like "déjà vu all over again"[2] and comes in more "flavors" (potential antigenic recombinants) than Baskin-Robbins ice cream. Although SARS-coronavirus-2 (SARS-CoV2) has held the lion's share of the spotlight since late 2019, we need to remember that highly pathogenic avian influenza (HPAI-H5N1) has 16 possible expressions of hemagglutinin and 9 types of neuraminidase surface glycoproteins that could undergo antigenic shift, making it more highly transmissible and/or pathogenic. Although avian influenza viruses do not often infect humans, the amazing versatility of the agent presents a serious potential threat, and we are all too familiar with zoonotic viruses making the "leap" to humans.

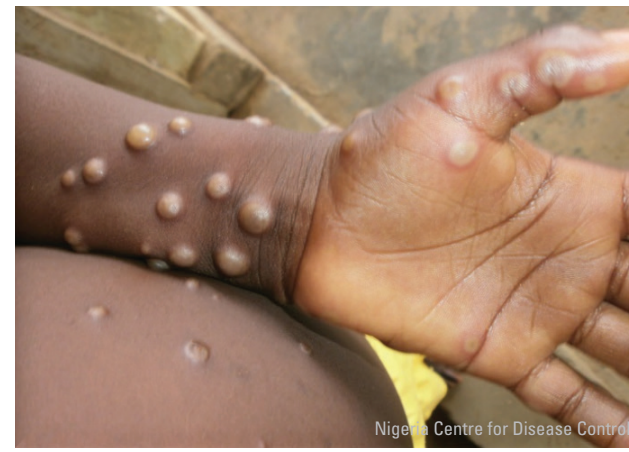
In 2021–22, four humans (Ohio, Oklahoma, Colorado, and California) contracted four different antigenic variants of novel influenza. Three were found to have a swine-derived virus while one (a poultry worker in Colorado) had an avian subtype.[3] To date, at least 49 million chickens and turkeys have been euthanized to try to limit the spread. However, it is already present in at least 44 states in domestic fowl and 46 states in wild birds. In many poultry husbandry facilities, birds are being kept in barns or structures with roofing to minimize the risk of transmission of highly pathogenic avian influenza (HPAI) from wild bird populations.[4]

Avian influenza "flies in" aboard migratory birds sweeping it from east to west across the continental United States. Influenza virus circulates and recombines to produce epidemics and pandemics due to its means of transmission and the relatively large number of potential hosts and antigenic drift and shift. We need full cooperation and communication among diagnostic laboratories, immunization sites/programs, domestic poultry producers, the U.S. Department of Agriculture, and the Centers for Disease Control and Prevention (CDC) to keep a watchful eye on this potential threat.

The 2022–23 egg-derived vaccine was developed against the following: an A/Victoria/2570/2019 (H1N1)pdm09-like virus; an A/Darwin/9/2021 (H3N2)-like virus; a B/Austria/1359417/2021-like virus (B/Victoria lineage) and a B/Austria/1359417/2021-like virus (B/Victoria lineage); and a B/Phuket/3073/2013-like virus (B/Yamagata lineage).[3]

Monkeypox virus

Monkeypox (mpox) viral infections in humans in Africa were first recognized in 1970. However, 2022 saw it skyrocket to World Health Organization (WHO) global emergency status.[6]



Monkeypox in (pustular) stage

At that time, only circulating vaccine-derived oral poliovirus (cVDPV) and COVID had achieved that status.[7] The first case in the United States was in a man from Texas who had just returned from Nigeria via Mexico.[8]

Following an incubation period of 5–21 days, symptoms develop including exhaustion, fever, muscle or back aches, swollen lymph nodes, and chills. Painful dermal lesions progress from papule to pustule finally ending in crusted sores. Lesions do not always spread to many areas of the body and the patient may display a few lesions or only one. According to the CDC, lesions frequently occur "in the genital/anogenital regions or in the mouth. In some patients, monkeypox symptoms include rectal bleeding, pain, and purulent or bloody stools."[9] According to research published in the *New England Journal of Medicine*, "Transmission was suspected to have occurred through sexual activity in 95% of gay or bisexual men with the infection."[9]

It should be noted that anyone can contract this infection via skin-to-skin contact or by contact with contaminated towels, surfaces, or inanimate objects.[10] In Brazil, a nurse contracted the virus from a patient via a needlestick procedure while attempting to obtain a specimen from a lesion for confirmation by laboratory professionals.[10] According to the CDC, needles or other "sharps" should never be used to collect specimens from suspected mpox patients. CDC describes in detail what PPE are advised when working with mpox patients and specimens.

Worldometer data as of November 4, 2022, reflect that there have been 78,229 cases of monkeypox and six deaths caused by the virus. Vaccines (Jynneos and ACAM2000) against monkeypox are currently being stockpiled by the federal government in quantities sufficient for vaccinating millions of Americans against monkeypox.[11,12]

Ebolavirus disease

Ebolavirus disease (EVD), formerly known as Ebola Hemorrhagic Fever, is a rare but extremely severe viral infection with a complex clinical course. The mortality rate ranges from 70–90%.[13,14] It has caused the deaths of thousands of residents of the Democratic Republic of Congo (DRC), Sierra Leone, Liberia, Gabon, and countries in central and west Africa in about 40 outbreaks since it was discovered in 1976 simultaneously in Nzara, South Sudan and in Yambuku, DRC.[13]

EVD interferes with coagulation, which often gives way to both internal and external bleeding. Other symptoms include fever, headache, muscle pain, sore throat, rash, vomiting,

and diarrhea. Severe dehydration potentiates the mortality rate.[15] It is characterized by bleeding from every orifice of the body and formation of bullous skin lesions filled with blood. EVD is a sylvatic, zoonotic virus and humans contract it from fruit bats, small antelopes, primates, and numerous animals bagged as "bush meat," which is highly prized, although the capture and consumption of bush meat is illegal for obvious health reasons.

The most recent outbreak of EVD occurred in a man from Uganda who presented with fever and bleeding from the eyes on September 11, 2022. Over the next four days, his condition worsened with muscle aches and bloody diarrhea. EVD caused by the Sudan virus (one of five subtypes of Ebola virus) was confirmed by PCR, and he died on September 19, 2022. By October 26, 2022, there had been a total of 115 confirmed and 21 probable cases of Ebola Sudan virus infection with 32 confirmed and 21 probable deaths. The case fatality ration among confirmed cases was 27.8%.[16]

EVD can be diagnosed by antibody-capture, enzyme-linked immunosorbent assay (ELISA), antigen-capture tests, serum neutralization, reverse transcriptase polymerase chain reaction (RT-PCR), electron microcopy, and virus isolation in cell culture.[17,18]

On October 6, 2022, the United States announced that travelers from Uganda would be screened for EVD at one of five U.S. major airports. These include JFK (NY), Washington-Dulles (VA), Newark Liberty (NJ), Chicago-O'Hare (IL), and Hartsfield-Jackson Atlanta (GA).[19]

Circulating vaccine-derived poliovirus

On September 13, 2022, the CDC confirmed that circulating vaccine-derived poliovirus (cVDPV2) (antigenically similar to Sabin-like 2 virus) is in the Rockland and surrounding counties in New York. A case of paralytic polio was detected in an unvaccinated adult, and the virus was present in several samples of wastewater from the same location. Additionally, cVDPV2 has also been found in wastewater samples from the Jerusalem district in Israel and in London and Ireland indicating community transmission.[20] This is a sobering fact because the wild type was eliminated from the United States in 1979 thanks to vaccine diligence.

Photo by Minacarson @ Dreamstime.com

Two failures enabled the re-emergence of this virus: 1. failure to adhere to good health practices by ignoring polio vaccination and 2. the instability of the RNA polioviruses that are used in live, attenuated vaccines and their tendency to back-mutate in nature and regain enough of the original pathogenicity to induce illness (and more rarely, paralysis). Live attenuated oral poliovirus vaccine is still given in many countries due to its ease of use, low economic impact, and efficiency in halting outbreaks.

As Saint Francis de Sales (1091–1153) reportedly stated, "The road to Hell is paved with good intentions."[21] Those of us who knew the threat of polio before killed injectable vaccine or live attenuated polio vaccine were available are particularly frustrated. Senior laboratory professionals will remember the tragic photos of dozens of children in "iron lung" devices that prevented them from dying of asphyxiation following a paralytic course of poliovirus infection. Even children who seem to fully recover can develop new muscle pain, weakness, or paralysis as adults, 15 to 40 years later. This is called post-polio syndrome.[22]

Poliovirus is highly contagious and readily spreads via person-to-person contact. It can be detected in a patient's throat and intestinal tract, illustrating that it is transmitted by a fecal-oral route. Coughs and sneezes by an infected individual can also spread the virus, although less efficiently. Unfortunately, poliovirus can be spread by asymptomatic persons.

Inactivated poliovirus vaccine (IPV) is administered via injection, and this type of vaccine has been used in the United States since 2000. Oral polio vaccine (OPV) is still used throughout much of the world.[22]

Parechovirus

From April to May 2022, 23 infants aged 5 days to 6 months were admitted to the Monroe Carell Jr. Children's Hospital at Vanderbilt University in Nashville, TN with parechovirus (PeV) infection.[23] Twenty-one of these infants recovered without residual health issues, but one was left at risk for blood clots and hearing deficits.[24] Another young patient was at serious risk for developmental delays and had experienced persistent seizures.

This comprised an "unusually large cluster" and the CDC determined that the PeV involved was circulating on a nationwide basis since May 2022. The virus is so common that doctors suggested that PeV be considered in infants with seizures and fever. Very little distinguishes it from common rhinovirus infections other than its intensity.[23,24] PeV is dangerous in newborns, but causes milder symptoms that often go undiagnosed in older kids and adults.

Respiratory syncytial virus

In Memphis, Tennessee at Le Bonheur Children's Hospital, cases of respiratory syncytial virus (RSV) are skyrocketing in pediatric patients this fall. By October 27, there were no beds left in the pediatric intensive care (ICU) unit. The vast majority of these children were suffering from RSV or influenza. The hospital reported 290 admissions due to respiratory viruses in September, and in November, influenza was on the rise, with 8–10 admissions daily due to either influenza or RSV. The emergency department averaged about 50 admissions per day due to RSV or influenza and 187 resulting from asthma.[25]

RSV can cause illness in persons of any age, but it presents the greatest risk of life to premature infants and those with pulmonary pathology due to a variety of elements. It causes damage in the bronchioles where large syncytial cells form containing multiple nuclei. The result is "plugging or occlusion of bronchiolar airway lumens by sloughed necrotic and irregular epithelium, combined with peribronchiolar infiltration and submucosal edema."[26] In adult and older pediatric patients, RSV can cause mild cold-like symptoms, including

congested or runny noses, low-grade fever, sore throat, sneezing, and headache.

Severely affected infants exhibit gasping, shallow and slow breathing, coughing, poor feeding, and unusual tiredness and irritability.[25,26] High-risk patients can be treated with Synagis, which is an RSV F protein inhibitor monoclonal antibody. It is not a vaccine but can be administered to high-risk pediatric patients by injection at monthly intervals throughout the peak RSV season.[27]

Conclusion

Our battle with viruses is very old and is yet almost completely new when one considers the late trend in emerging agents. We need to be very watchful of zoonotic agents that have "jumped" from various animals to infect humans. The SARS group of viruses arose from pangolins (scaly anteaters, bats, etc.), HIV (chimpanzees), EBV (fruit bats, primates, etc.), avian influenza (migratory birds), and monkeypox (monkeys, sylvan rodents, etc.). These have caused major health disasters, and we have not even gotten into rabies (mammals), Hantavirus (rodents), and Nipah virus (fruit bats).

Emerging virus "sentinel" labs and medical facilities around the world, in conjunction with the CDC, WHO, ProMed, Epicore, the National Institutes for Health (NIH), and the International Society for Infectious Diseases (ISID), continually monitor and produce reports about "new" viruses. We can never be too careful. As the anonymous saying goes, "What doesn't kill you mutates and tries again."

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Virtually uninterrupted: A virtual learning success

Tips on how to develop a successful virtual learning program

By Stephanie Post

Until the COVID-19 pandemic, many laboratories depended on the classic train-the-trainer model for teaching staff how to operate their new instruments. Select laboratorians were sent to a vendor's location to receive the training necessary. Pressured to know everything from system operations to maintenance to troubleshooting, these laboratorians were responsible for the transfer of knowledge to their coworkers, for the life of that system.

The train-the-trainer model has its limitations. The laboratorian sent to training may have learned a great deal but may fail as a trainer. Can he or she explain both the what and the how in a meaningful and understandable manner? Can he or she teach concepts to those with varying levels of experience and understanding? Coworkers may not feel comfortable asking questions or sharing ideas. Overall, the model can be a very difficult and time-consuming process.

When travel and in-person training came to a halt in March 2020, manufacturers were forced to shift gears and create virtual training programs to ensure laboratories could continue to carry out the valuable role they play in supporting the healthcare system. What started as a temporary fix, became a major shift for many manufacturers accustomed to the train-the-trainer model. For Sysmex America, which has had Virtual Instructor-Led Training (VILT) in place since 2014, it was an opportunity to further leverage its virtual training knowledge, experience, and technology. Within the first two weeks of the COVID-19 pandemic, Sysmex America was pushed to expand, pivot, and innovate solutions faster than ever before around customer training, customer care, sales, and even training its own staff. Some of these solutions included the following, which allowed broader engagement in many respects than the classic, in-person models:

- Pre-COVID, 90% of the training for Sysmex's service, scientific applications, and technical assistance center associates was conducted in person. The curriculum was completely reinvented to VILT in just a few weeks to ensure no interruption in customer service.
- Sales associates were no longer allowed in hospitals to meet their customers' needs, so sales associates conducted virtual demonstrations, presentations, and symposia, allowing healthcare staff to remain in their laboratories with minimal disruption.
- An advanced training course for laboratorians, previously offered only face-to-face, was broken into two-hour increments for delivery via VILT to ensure ongoing learning.
- A Virtual Event Platform was built to ensure a positive experience for participation in industry conferences, customer meetings, and product demonstrations. These leadership communications were streamed live to customers from Sysmex America's Center for Learning studios, which allowed live engagement among participants.

Tips on developing a virtual learning program

Public health emergencies, extreme weather situations, or acts of God that prohibit travel demand the availability of uninterrupted, diverse, and effective

distance learning options for public health and clinical laboratory professionals. Here are tips on how to develop a successful virtual learning program to serve both clinicians and internal staff.

Infrastructure and technology: The infrastructure and technology items to carefully consider include studio space, camera and lighting equipment, communication tools (e.g., microphones, earpieces), content delivery platforms (e.g., Microsoft Teams, Zoom), and learning management systems for course registration and completion tracking. Be sure to consult with broadcast and studio professionals for their expertise. Instructional designers need to be aware of both the classroom setting, as well as the participant's virtual environment when developing a virtual learning course, with technology acting as the bridge between the two.

Instructors: Select credible and experienced instructors and studio production specialists. Give the instructors an opportunity to practice on-camera. They will need to learn the technology, run through scripting and timing, and test transitions. There are outside training organizations that specialize in virtual and on-camera presence. Using two instructors in the studio, one who is on camera and the other who is behind the scenes monitoring online discussions and managing learner questions, ensures a smooth class flow.

Course development and delivery: Laboratories will maximize learning and engagement by taking the time to consider the following steps in course development and delivery:

- Curriculum design: Take the necessary time to consider the content, sequence of course delivery, and knowledge checkpoints. Provide any support tools such as worksheets or exercises prior to class.
- Senior leadership involvement: Whether it's new hire or annual staff training, virtual training makes it a lot easier to involve senior leadership. Senior leaders can welcome participants or serve as guest speakers.
- Keep participants engaged: Like face-to-face training, it is important to keep participants engaged with a highly interactive learning experience. This may include lecture, break-out room teamwork, hands-on lab exercises, and time for individual feedback and Q&A. Sysmex courses are designed with built-in retention questions to ensure the learner is at their computer and completing exercises. In addition, Smart Boards have been incorporated into virtual classrooms to further engage the learners through live annotation tools.
- Lab experiences: Sysmex follows a series of tell, show, do — Tell the learner; show the learner; and then learners do the exercise on their own instrument, in their own laboratory.
- Prepare learners: Although many learned to use technology to stay connected during the pandemic, you will need to provide clear instructions on how to register, prepare, and get the most out of class. Provide participants with a list of what will be needed for the class such as quiet space, computer, bandwidth, earphones, and telephone. Provide checklists for internet troubleshooting and how to get familiar with collaboration tools that will be used during the course. Reinforce the course learning objectives and how to communicate with the instructor prior to or on the day of class.


Photo courtesy of Sysmex

Continuous improvement: At the conclusion of the course, measure and improve by gathering and using feedback. Debrief sessions with the production team and instructors, as well as participant surveys, interviews, and focus groups are key to identifying opportunities for improvement.

Conclusion

While virtual learning may have been a temporary fix during the height of the COVID-19 pandemic and is a great back-up plan for future extreme weather situations, the training is here to stay for many. Virtual learning blends the social learning benefits of classroom-based training with the speed, agility, and cost-effectiveness of e-learning. It is a flexible option for staff and organizations that can be delivered in a variety of configurations. A two-day virtual training course may be delivered in four, four-hour sessions with time in between for practice, homework, and blended e-learning content.

In addition, learners can access e-learning from almost anywhere with an internet connection and on any device. There are also many accommodation options to make virtual training sessions as accessible for as many learners as possible. For example, virtual training offers opportunities for auto-captioning to support learners who are deaf or hard-of-hearing.

"I took the course with two of my employees (one just hired with no Sysmex familiarity) and the "go do it" exercises were very helpful. We were able to figure it out together and that was maybe more beneficial than having a trainer right beside us walking through it step-by-step. I think we were more engaged in the training. No one seemed bored, even with the basic stuff. The time frame was right on, too. It was long enough to cover a lot of material, but not so long that we lost interest."

—VILT participant in June 2020

Stephanie Post is Senior Director, All Americas Marketing Communications, Center for Learning & Program Management at **Sysmex America, Inc.** Through the demonstrated success of Sysmex Virtual Instructor-Led Training (VILT) classes, Stephanie designed a strategic vision that led to a multi-million-dollar expansion buildout, allowing Sysmex to expand its virtual offerings enabling customers to be trained across the Americas. Stephanie is a board-certified Clinical Laboratory Scientist and holds certifications in the training field as a Training Director, Instructor/Facilitator, Sales Trainer, and Performance Consultant.


Photo by sanjeri @ gettyimages

Preparing point-of-care testing for the long journey

By Harvey W. Kaufman, MD

Driving a motor vehicle involves real-time inputs of road conditions and hazards. The same is true in healthcare: medical professionals need real-time inputs to guide decisions affecting patient outcomes. Point-of-care tests (POCT) are an option when providing this real-time insight, helping the clinician navigate the care pathway. Like driving, POCT requires skill and attention to avoid both "potholes and accidents" and losing time on the journey.

What is point-of-care testing (POCT)?

POCT refers to testing technologies and methods that provide test results at the place, or point, where care is delivered to the patient, versus in a separate laboratory. POCT is typically valued for providing timely test results for conditions requiring rapid treatment. As an example, in surgical pathology, frozen tissue sections are analyzed while patients are being operated on, to provide surgeons with crucial information about the type and extent of disease and to identify if surgical margins are free of disease. Other examples include arterial blood gases in the intensive care unit, providing near real-time critical information about respiratory and metabolic disorders and determining adequate hemoglobin levels in blood donors just prior to their donation. Many are familiar with home POCT applications, including urinary human chorionic gonadotropin (hCG) as the first laboratory confirmation of pregnancy, glucose testing for people with diabetes, and rapid antigen testing for SARS-CoV-2 to diagnose COVID-19.

POCT can add value when utilized properly

A recent situation highlights the value of POCT. In response to the outbreak of Ebola virus disease in Uganda, some hospitals in the United States prepared intensive unit beds to accept incoming high-risk patients, especially those arriving at airports from international cities. This involved creating an extensive test menu using POCT that could be performed by either laboratory or intensive unit personnel in an area adjacent to the patient's hospital room. This approach sought to limit the transfer of potentially infectious specimens to others on the healthcare team.

POCT options continue to expand, driven largely by the value of quick results allowing for timely medical decision making. POCT can also eliminate specimen transportation and storage issues, although confirmatory testing (of the same specimen) may often be warranted. Having near real-time POCT results allow the clinician and patient to discuss diagnoses or next steps in the moment. This capability can be critical in ensuring patients receive results and are adequately directed into care.

For instance, in the case of HIV testing, some patients offered anonymous testing never retrieved test results when testing was sent to a core or reference laboratory, including patients who had positive test results. This suggests that POCT would have provided immediately actionable results. Likewise, testing for sexually transmitted infections (e.g., chlamydia and gonorrhea) following treatment offerings may be more effective when results are nearly immediately available. Thus, POCT can provide timely test results while patients are engaged in their own health.

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POCT – Screening versus confirmation

Most POCT tests are designed to screen for potential health risks. Sophisticated laboratory methods may follow to confirm a result. For instance, POCT urine tests may help screen for the presence of controlled drugs as part of a clinical drug monitoring program. But unlike confirmatory lab methods, these POCT devices have certain limitations that can affect clinical decision making. For instance, POCT devices may be unable to differentiate a prescribed opioid from non-prescribed fentanyl. COVID-19 is also a case in point. While rapid POCT antigen tests should be taken serially to confirm a result; molecular laboratory techniques are preferred to confirm a specimen as positive for SARS-COV-2. Laboratory professionals should understand the strengths and limitations of POCT and more sophisticated laboratory methods to ensure they complement, rather than duplicate, each other.

POCT versus in-laboratory testing: Challenges and opportunities

POCT differs from in-laboratory testing through interferences, precision, sensitivity, specificity and different targets (especially immunoassays). Most POCT is less precise than laboratory testing, which is typically performed on more expensive and sophisticated analyzers. As an example, hemolysis may affect a laboratory-based test but not a whole blood-based POCT. However, the greater imprecision and inaccuracy of POCT methods may be acceptable for select clinical applications that benefit from rapid results, such as those outlined above.

POCT assays are classified based on complexity. The Clinical Laboratory Improvement Amendments of 1988 (CLIA) defined waived testing as a simple test with low risk of patient harm resulting from incorrect results (presuming the test is used as described in the FDA labeling including robust quality system). That definition would hardly apply to the plethora of currently performed waived tests, which some POCT fall under. Some POCT results can have huge consequences on diagnoses and treatments especially if performed improperly. Laboratorians face continued challenges and opportunities in providing guidance on the value and limitations of POCT and support for its proper performance and oversight.

Those performing waived testing must follow manufacturers' instructions. Moderately and highly complex tests are considered nonwaived tests and are subject to laboratory inspection and must comply with CLIA quality system standards including proficiency testing, semi-annual calibration/verification, quality control, personnel requirements, and documentation. Whereas hospital core laboratorians have largely mastered CLIA '88 requirements, POCT remains more challenging to manage because it is performed in diverse settings outside of the clinical laboratory.

POCT's areas of improvement

Many clinicians have outlined four main areas where POCT programs could seek to improve. These include:

- Coordination
- Connectivity
- Control
- Costs

Coordination (See Table 1 for a sample coordinator job description.)

Successful hospital-based POCT programs typically have strong coordinators. Individuals assigned to this role must be qualified, have sufficient time to dedicate to the role, and have the authority to lead and control all aspects of testing. Many hospitals come up short when POCT coordinators lack the complete competency for this role.[1]

The POCT coordinator must also be part of a governance structure that includes nursing, the emergency department, the clinical laboratory, and other stakeholders of the institution to foster clear communication and an alignment of interests. As technology changes, the governance structure should provide a basis to decide which tests to perform, when to replace equipment, and how to address chronic issues.

Qualifications:	
1.	Meets the minimum qualifications of testing personnel in a highly complex laboratory, as defined in 493.1489 of CLIA '88.
2.	Understands applicable Clinical Laboratory Standards Institute (CLSI) documents pertaining to POCT.
3.	Ability to communicate effectively and diplomatically within a multi-functional team.
4.	Strong organizational skills.
Functions:	
1.Personnel	
a) Follow the testing personnel responsibility standard as defined in 493.1495 of CLIA '88.	
2.Training and Performance:	
a) Ensure that all hospital staff using POCT devices are adequately trained and competent for test performance, troubleshooting, maintenance, and documentation.	
b) Review policies and procedures and adherence at least once annually.	
c) Perform and record all required instrument maintenance and calibration activities.	
d) Follow the established POCT procedures whenever test systems are not within the POCT established acceptable levels of performance.	
3. Quality:	
a) Collaborates with other departments to develop methods and/or systems for improving quality and controlling costs associated with POCT.	
b) Collects and evaluates quality assurance and quality control data from POCT sites and reports data collected to clinical service and laboratory directors.	
c) Resolves technical problems and ensures that remedial actions are taken whenever test systems deviate from established performance specifications.	
d) Be capable of identifying problems that may adversely affect test performance or reporting of test results.	
e) Documents all actions taken to correct problem(s).	
f) Enrolls in proficiency testing program for all required POCT systems. Maintains records that demonstrate that proficiency testing specimens are tested in the same manner as patient specimens. Follow-up to identify root causes of unacceptable proficiency testing results and implement appropriate corrective and preventative measures.	

Table 1. Sample coordinator job description.

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[1] Brown, H. *Improving the Diagnosis of Vulvovaginitis.* Population Health Management. Vol. 23, suppl 1, 2020

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Control

The ideal way to assure quality performance is to begin before the quality control materials are utilized; that is through training, analyzer maintenance, and documentation.[2,3,4]

POCT procedures should generally follow those in the core clinical laboratory. These procedures include storing all supplies at the right temperature — specifically, refrigerators and freezers must be monitored daily even when POCT is not performed. New lots of reagents or test strips must be evaluated prior to their use. A common approach is to check reagents and test strips upon delivery and run quality control samples at least monthly to check storage conditions and operator performance. Electronic instrument checks may be inadequate in establishing if the whole system functions properly. In POCT, some of the moderately complex testing may have both internal and external controls.

Recording only "in control" quality control results would be like a sports team recording only its wins. This is an unacceptable practice, hiding true assay performance. My observations are that many non-laboratorians do not understand quality control principles and procedures. Staff education on quality control principles and procedures must be key elements of training prior to initiating new and ongoing POCT analyzers.

Additionally, quality assurance plans are often lacking, even though such plans are vital to addressing ongoing method validation; monitoring operator and document management; and identifying and addressing issues like excessive test failures, expired supplies, or user errors. Shifts and drifts in patient test results are nearly impossible for individual users to identify, but aggregate data analysis can spotlight test faults.

POCT has the option to comply with Individualized Quality Control Plan (IQCP) (see CLIA'88 42 CFR 493.1256(d)), the alternative CLIA quality control option that provides for equivalent quality testing for 42 CFR 493.1250. IQCP has been incorporated in Appendix C of the State Operations Manual.[5] IQCP is an all-inclusive approach to assuring quality. It includes many practices that a laboratory already uses to ensure quality testing beyond requiring that a certain number of quality control materials be tested at a designated frequency. IQCP applies to all nonwaived testing performed, including existing and new test systems.

Connectivity

Every test result must be appropriately documented to monitor quality control, proficiency testing, and patient care management.

Most POCT, even when appropriately enabled, is not connected to a hospital's electronic health record (EHR) system. This makes each of the pre-analytical, analytical, and post-analytical POCT steps prone to human error, from scanning patient wristbands for correct identification to reporting of the right results to the right patient. Although the POCT result may be written in the patient chart, without the appropriate additional documentation, the test may not be billed properly, and therefore, the true costs of patient care cannot be understood.

Costs

The true costs of POCT includes instruments, reagents, quality control, proficiency testing, personnel (training, performance, troubleshooting, maintenance, documentation), and oversight.

Whereas some POCT cannot be replaced by standard clinical laboratory testing, some can, and comparisons can be made between the total cost of testing in each setting. The costs of staff for POCT are generally grossly underestimated, in part because of the distributed nature of POCT.

As we begin 2023, one of the most pressing challenges for many health systems is staffing, both within the laboratory and among nursing and other staff who perform POCT. Adequate training and support can be difficult with high staff turnover, staffing on late shifts, and temporary contract staff filling vacant positions. Maintaining technical assessments on all POCT assays for each staff member is an additional and often overlooked major undertaking.

Furthermore, quality control testing must be performed at least once daily on days when testing occurs. This can be costly for hospitals that use some tests infrequently. Lack of adherence not only jeopardizes the quality of testing but also potentially the laboratory license and certification if not reliant on a separate CLIA certificate.

Each test must undergo a full verification procedure at least once every six months and with reagent/strip lot changes. Some hospitals purchase small supply volumes to control inventory costs but do not recognize the added costs associated with frequent reagent/strip lot changes.

As hard as it may be, expired reagents must be discarded or returned, if allowed. Given some tests are performed infrequently in some locations, rotating reagents before expiration can avoid reagent/strip wastage. The POCT coordinator must develop procedures to audit reagent inventories to reduce reagent waste due to expiration.

Conclusion

To prepare POCT for the long journey, many EMR systems now include software that facilitates the documentation and control of users who are current with training and technical assessments. These management systems reduce, but do not eliminate, the need to dedicate the necessary resources to perform POCT correctly.

By careful planning, including identifying and developing a strong POCT coordinator, maintaining effective quality control procedures, enhancing electronic connectivity with the EHR system, and strictly tracking costs, hospital laboratories can provide a highly valuable and reliable service that improves medical diagnoses and healthcare management for patients.

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How Northern Light Eastern Maine Medical Center phlebotomy team survived the pandemic

By Janelle Campbell, ASCP

The COVID-19 pandemic was a hard time not only for phlebotomy, but for all healthcare facilities in the nation with staffing shortages. Northern Light Eastern Maine Medical Center is the largest trauma hospital in northern Maine. It is also a teaching hospital. I had a department of 53 phlebotomists; I lost 15 in a very short time. A devastating loss. We had to think of ways to meet the needs of the hospital, outpatient labs, our patients, and our community. We eventually needed to reduce the hours of our outpatient lab and put out a call to our system teams for help. Medical assistants and nurses stepped up to offer their assistance to help us care for our patients.

My first priority was addressing staffing challenges. In the beginning of the pandemic, I started a "Phlebotomy On The Job" training program. Our department had relied heavily on the two phlebotomy schools in our area, but classes stopped as schools closed due to the pandemic. Applications stopped coming in, which presented an opportunity to go full force with my training program.

What better experience for a student than to have classroom time, trainings, and clinicals in the environment they will work in? We were able to provide real-life, real-time situations for these students. I was privileged to have great support from my organization and my colleagues, and my veteran phlebotomists were excited to help with the clinical portion of the class.

We interviewed many applicants, looking for specific skills and talents to fit the role of a phlebotomist working in a trauma center. When interviewing applicants, we were open and honest about the role of a phlebotomist, since many of them had no idea what it was like to work in a hospital, especially during a pandemic. They would be working with patients with COVID-19, trauma patients, and our smallest patients in pediatrics—it was essential to let all applicants know the reality of the environment they would be working in.

Upon entering the program, students sign a commitment agreement pledging to work in the phlebotomy department here at the Medical Center for two years after finishing their training. Northern Light Laboratory invested $5,000.00 to provide the employee with the skills and training necessary to pursue certification in the phlebotomy field in return for the two-year commitment. Over the course of two weeks, students completed 80 hours of didactive lectures with me, followed by four weeks of clinicals working on patient floors, the outpatient lab, or emergency department. Every day was different as they trained side by side with our senior phlebotomist. After clinicals, they were allowed to work on their own, but the training and learning continued.

Photo by Angellodeco@ Dreamstime.com

Students were hired as a phlebotomist II with the base pay of a phlebotomist II throughout the duration of the training period. Each time the employee was paid, a portion of their loan to Northern Light Laboratory was repaid. After six months of training, the students sit for the national phlebotomy exam through the American Society for Clinical Pathology (ASCP). So far, this training program has had a 100% success rate passing the ASCP exam!

I taught classes for months, bringing on new students every two weeks. I only took a certain number of students to ensure great training. I wanted to be sure our specimen quality and patient care stayed top notch. It took a long time to complete training and get each student up to speed—but we did it!

Our students have excelled. Many of them have become trainers and taken charge positions on the weekends and holidays. This has been a wonderful opportunity for the members of our community to gain education and skills in the medical field. Moreover, many were unable to take a class due to schools being closed because of the pandemic, or because they could not afford the class once schools opened back up.

For more information, or if you know someone who may benefit from this training program, contact me at jkcampbell@northernlight.org.

Janelle Campbell, ASCP is the Phlebotomy Supervisor at **Northern Light Eastern Maine Medical Center.** She has 22 years of phlebotomy experience working in a lab, teaching phlebotomy, and supervising teams within laboratory environments. She recently presented the success of her phlebotomy training program at the October 2022 Northeast Laboratory Conference.

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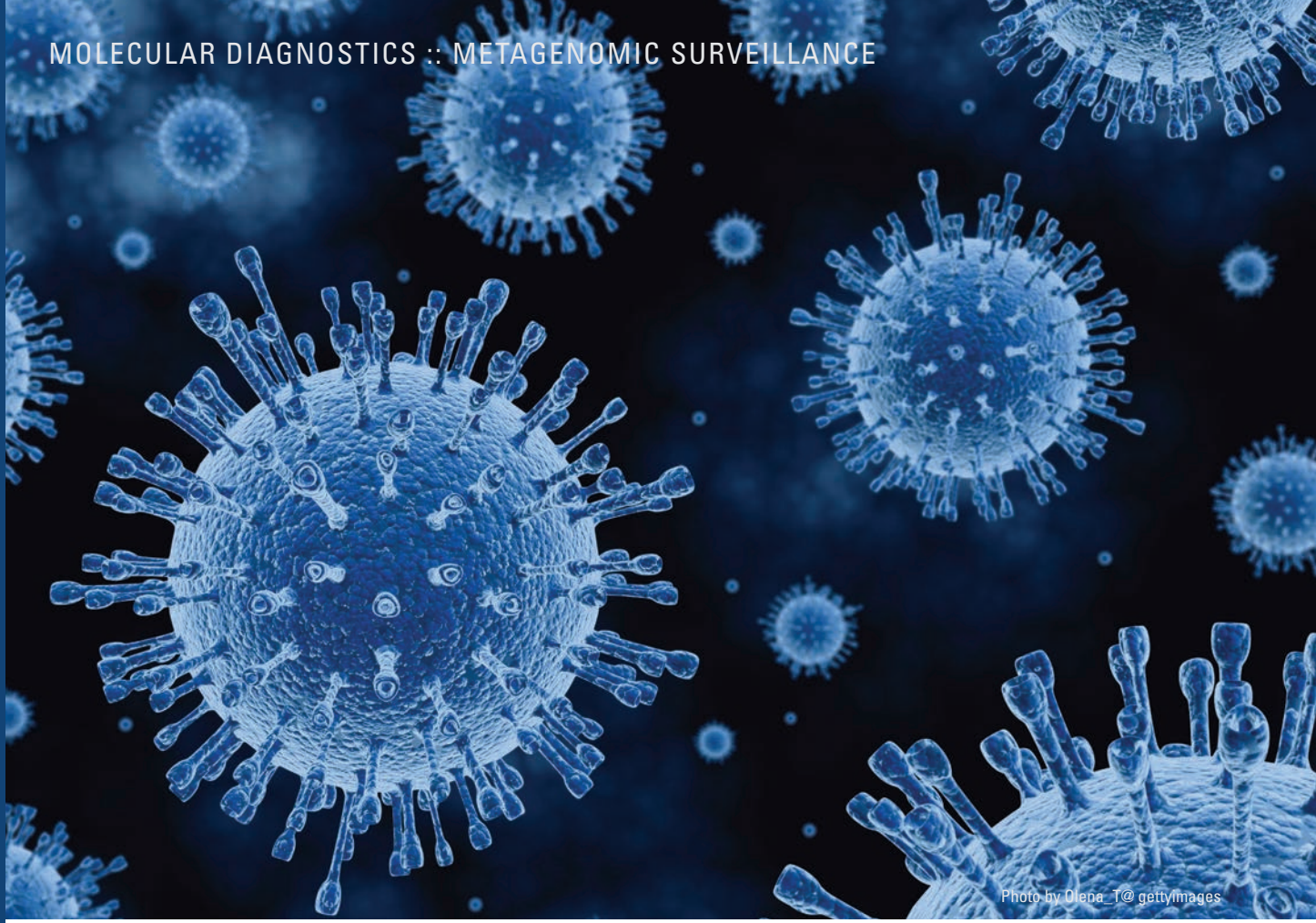

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Metagenomic surveillance for emerging diseases: An idea whose time has come?

By John Brunstein, PhD

At their root, human beings seem an eternally optimistic lot. While historians, epidemiologists, and to some extent the rest of us are at least vaguely aware of such things as the Black Death (Europe and North Africa, 1346–1353, with sporadic regional recurrences up to 1665/66 in London); the Spanish Flu (worldwide, 1918–1920) and subsequent Influenza A pandemics (1957, 1968, 2009); or SARS (2003), we'd like to think that vast strides in medical knowledge and practice have reduced the risk of emerging infectious diseases to ourselves as individuals and to our civilization as a whole. While that's undoubtedly true to some extent, the COVID-19 pandemic has served as a forceful reminder of how rapidly spreading and broadly disruptive an emerging pathogen can be even with the tools at our disposal. (Readers with a penchant for history are encouraged to find a copy of Daniel Dafoe's "Diary of a Plague Year;" its observations of human behaviors and infection control measures and their varied success during the 1665/66 London plague read shockingly similar to modern day and reinforce how little we have actually progressed in our reactions to these events.) Optimists or not, we must as a species face the reality that novel emerging and zoonotic pathogens, and perhaps ones of lab-derived origin, constitute a major threat to humanity and one which will be visited upon us with sporadic yet unceasing monotony.

Novel avian via swine to human reassortments of Influenza A have been recognized as a major potential of such pathogens, and since 1952 have been the target of a worldwide surveillance network. Now known as the Global Influenza Surveillance and Response System (GISRS), consisting of more than 140 National Influenza Centers plus other facilities, this loose organization works to collect, sequence, and analyze circulating Influenza A strains to provide (among other things) an early warning of appearance of novel, potential pandemic strains.[1] Such information is critical if we wish to be any better off at all than Dafoe's protagonist of 1665; so the question arises, "What if there was a way to do this with a capability to detect any new pathogen, not just one likely suspect?"

Such a capability is not only possible, it is technically achievable at relatively low cost and complexity with tools in hand at this very moment. At its front end, such an approach could rely on widely distributed, sample anonymized metagenomics. This is the molecular biology technique of taking a total nucleic acid sample (in this instance, from a person); using next generation sequencing methods to randomly sample and sequence elements of

all DNA and RNA present; then bioinformatically removing all of the expected host sequences and sieving through the leftover non-host material for whatever is present. The technique is agnostic as to relatedness to other known pathogens and can provide population-wide prevalence for any definable known or newly identified target. Below, let's consider some of the stages and processes involved along with the challenges to implementation.

Sample collection

Respiratory pathogens, due to their mode and ease of transmission, are the first priority here; so any such system should be integrated into collection from respiratory disease testing streams distributed around the world. Rather than reinvent the wheel, integration with the existing Influenza A network, but with a focus on samples testing negative for Influenza A, would seem to be an obvious starting point to build from as needed.

Challenges in this step include:

- Ensuring sample anonymization, bearing in mind that the unfiltered raw metagenomic data will include information traceable to source identity — so strong biosecurity measures to ensure removal of human sequences prior to data availability for analysis are essential.
- Ensuring enough geographically diverse sampling sites and unfettered access to a random sample of specimens from all sites. Put bluntly, political interference in the form of hiding or diverting anything from a broad and random sample stream will destroy the integrity of this approach. Among all the challenges considered in this article, this constitutes probably the biggest and hardest to address; only through an appreciation that collection of such information is in the long run in the best interests of all peoples and nationalities, can this be successful.

Technical process of raw data collection

DNA and RNA extractions, followed by library preparation as needed and next generation sequencing (NGS), can be done on a number of platforms.

Challenges in this step include:

- NGS devices, availability, and cost. At first blush, low-pass sequencing with relatively low per-base accuracy is likely "good enough" for this application. This combines the lowest cost approach with sample pooling (which, incidentally, would assist in ensuring sample anonymity). The exact mechanism and system for raw data collection is unlikely to be critical, meaning any designated collection center could use an available NGS infrastructure; where such is not available, the lowest cost systems such as currently embodied in nanopore-based technologies are a low barrier to entry.

> "Optimists or not, we must as a species face the reality that novel emerging and zoonotic pathogens, and perhaps ones of lab-derived origin, constitute a major threat to humanity and one which will be visited upon us with sporadic yet unceasing monotony."

Bioinformatic, computational, and databasing steps

The process suggested here is clearly computationally intense, and requisite hardware and expertise are likely out of scope for many smaller data collection sites. In addition, maintaining a single uniform process and data flow across multiple sites is desirable.

Challenges (and likely solutions) for this part include:

- Computational capacity. This would seem readily addressed by dynamic, scalable, off-site cloud computing capacity. This was demonstrated effective for both cost and purpose in analogous workflows more than a decade ago.[2] An additional benefit of a cloud computing–based approach would be enforced bioinformatics pipeline uniformity between data source sites.
- Ability to accept input from multiple systems, including both short-read and long-read NGS technologies, to a single cohesive data type. Strategies such as automated tiling of short-read data into longer reads are already normal practice and this point would not appear to be a significant hurdle with existing bioinformatics pipelines.
- Searching through masses of data for meaningful sequence signatures such as a new sequence variant of a known pathogenic organism and/or a spike in general population prevalence of a family of related sequence variants. This sounds like a perfect application of AI (artificial intelligence) routines — to search for and assess novelty sequence similarity to known pathogenic organisms and abnormal statistical variations in prevalence — all potential early warning signs of a wider and more dangerous emergence.
- Redundancy, data integrity, and accessibility of data: technically, this could be addressed through multiple mirrored database sites with appropriate access controls. The challenges here are less technical than again, political in nature.

Costs

Technical solutions to medical problems are great, but what does it cost to do something like this? A number of complex factors, including the depth of coverage needed for the process to be meaningful, would require thorough analysis to inform things such as level of pooling possible; but we can at least make some rough estimates. Presently, Illumina targeted 16S-based metagenomics suitable for bacteria only is estimated at $18/sample[3] while another source suggests whole genome shotgun sequencing (WGS), which is nontargeted, wide spectrum metagenomics can be done commercially at $150/sample.[4]

Taking these as upper and lower bounds and knowing the GISRS processes ~1 million samples per year, the cost of this program would be somewhere between $18 million and $150 million per year. Considering this upper bound is for a commercial service (including markup), and that some degree of sample pooling is likely viable, a true value towards the middle of this range or even a bit lower seems most plausible. A midpoint of $84 million per year, in perspective to other medical and research expenditures, for a worldwide target agnostic early warning system for new, emerging, or known but suddenly expanding pathogens sounds like a bargain. In fact, even a ten-fold increase on this (posited below with regards to detection scale) sounds like a very defensible public health cost.

Scale of detection and actionable responses

At an estimated 1 billion human Influenza A cases worldwide per year, the 1 million GISRS samples represents 0.1% of total cases so something on order of 1000 cases presenting similar to Influenza A would be needed before one would likely be inducted into this process. This could, however, be improved upon by including a nonrandom sampling com-

ponent; that is, preferential induction of samples in clusters and where a causal agent is not readily identified could be employed to bias these odds more favorably. A ten-fold increase in total sampling numbers would obviously improve on these numbers as well and seems within a reasonable cost scale.

Any expenditure is only justified if it can lead to some positive actionable outcome. In this system, appearance of a significantly novel sequence entity, almost certainly with recognizable similarity at least at the inferred protein sequence level to known pathogenic organisms, could be detected and flagged out. An immediate increase in sampling density in the geographic region could be undertaken, with aggregated sequence data used to generate a more complete picture of a full pathogen genome. Directed (RT)-PCR testing could be developed and deployed by reference centers, albeit with incomplete validation, yet still useful for rapid bulk screening of populations within weeks. The pathway of proceeding from this through aggregation of sequence, epidemiologic, and clinical presentation data is one well understood and recently practiced by the medical community worldwide for SARS, MERS, and COVID-19 to name just a few most recent examples. In other words, the use of widespread metagenomic surveillance would not change the pathway of response on detection of a novel agent; but it would perhaps speed it up by precious weeks to months at early stages. Notably, COVID-19 itself was initially identified by metagenomics techniques.[5]

Expansion beyond respiratory pathogens

While respiratory diseases are the most immediate application of this approach due to inherent transmission risk and a pre-existing surveillance network, other classes of infectious disease can be targeted through metagenomic surveillance as well. For those readers looking for more depth on application in other contexts, a recent review can be found in *Nature Microbiology*.[6]

Final thoughts

As a world, we have been using limited surveillance in the context of Influenza A and have reaped the benefits of this in early detection of novel pandemic potential strains and for guidance on vaccine composition. Expansion of this pre-existing network and inclusion of broader range detection technologies in the form of NGS is technically feasible and not cost prohibitive. Major hurdles exist but these are almost exclusively in the political will to allow transparency and unfettered random sample access. Overcoming these will require dialogue and resolve by entities at national and supranational levels. A recognition that diseases, particularly ones of an emergent pandemic nature, observe no national boundaries in today's highly mobile and connected world should help to convince all potential contributors to such a network that this form of surveillance is in their best interests. While this lesson of COVID-19 is fresh in our minds, it is an ideal time to consider whether adoption of generalized metagenomic surveillance might not be humanity's most immediately cost-effective defense against our next scourge — whatever it may be.

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John Brunstein, PhD is a member of the **MLO Editorial Advisory Board.** Among other roles, he previously served as President and Chief Science Officer for British Columbia-based PathoID, Inc., which provides consulting for development and validation of molecular assays, as CSO for the BC Provincial Health Service Authority's Center for Translational and Applied Genomics, and as a Clinical Assistant Professor in the University of British Columbia's Department of Pathology and Lab Medicine. Dr. Brunstein continues his avid interest in molecular diagnostics and providing ad-hoc consulting expertise.

Observatory continued from page 6

COVID-19 vaccine's effectiveness diminishes with age, UTSW research shows

The Pfizer-BioNTech COVID-19 vaccine limits transmission, hospitalization, and death from COVID-19 even among patients infected by variants of the virus, but the effectiveness of antibodies it generates diminishes as patients get older, according to a study by UT Southwestern researchers.

The emergence of new variants, including Delta and Omicron, left the vaccine less effective at neutralizing SARS-CoV-2 and resulted in increased rates of infection. However, vaccinated individuals, even when infected with COVID-19, continued to be protected against severe disease and death.

To understand how vaccines protect people without completely neutralizing the virus, blood samples were analyzed from 51 adults, ranging in age from 21 to 82, who had not been infected previously with COVID-19 and who each received two doses of the Pfizer-BioNTech vaccine between December 2020 and February 2021. From the samples, the researchers isolated antibodies specific to the SARS-CoV-2 spike protein.

The team showed that the antibodies generated in response to the vaccine were effective at neutralizing the original version of SARS-CoV-2 that emerged in 2019 but, as expected, were not as effective against the Delta and Omicron variants. In addition, the researchers found that these antibodies led to the activation of immune cells that can carry out a variety of antiviral effector functions after infection.

These antibody activities and functions differed by age, with people under 65 carrying significantly more of the activities and functions compared to those over 65. Dr. Lu's team discovered these observations could be attributed to different sugars attached to the antibodies. With age, these sugars change and antibody functions diminish.

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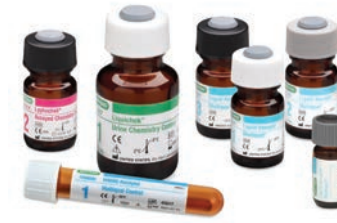

Automated, multiplex molecular diagnostic system

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Hardy Diagnostics

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The ZEUS Borrelia Modified Two-Tiered Testing (MTTT) algorithm improves detection of early Lyme disease by up to 30% compared to the Standard Two-Tiered Testing (STTT) algorithm. The STTT algorithm requires a 2nd tier immunoblot, which adds subjectivity in results interpretation and reduces sensitivity in measuring acute Lyme disease.

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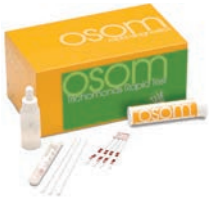

The OSOM® Trichomonas Rapid Test for the qualitative detection of trichomonas antigens from vaginal swabs is accurate (sensitivity 96%; specificity of 95%), fast (result in 10 minutes), simple (CLIA waived; no equipment needed), and cost-effective (collection swabs and QC included).

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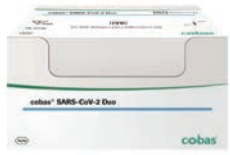

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LABORATORY INNOVATOR

Over 45 years of making a difference in the laboratory

By Christina Wichmann

Kathy Wilson, HT(ASCP) QLS, joined **COLA** in December of 2021 as Director of Pathology Accreditation. She is an ASCP-certified Histotech with the ASCP Qualification in Safety. She has over 45 years total experience in the laboratory, multiple disciplines. Prior to joining COLA, Ms. Wilson was the Anatomic Pathology Operations Manager, Safety Officer and Committee Chair, for a large reference laboratory, both local and regional operations, based in Austin, Texas. In addition, she managed multiple hospital frozen section and satellite laboratory locations. Ms. Wilson has managed multiple laboratory set-up, remodels, and build-out projects.

Kathy started her career in northern Michigan and has lived in many areas of the country to include Fairbanks, Alaska; Kansas City, Missouri; and Austin, Texas. Regulatory compliance, quality, safety, and project management have always been key areas of focus and interest.

In March 2022, COLA received deeming authority for the specialty of pathology. What should laboratories unfamiliar with COLA's Pathology Accreditation program know about it?

COLA has been accrediting clinical laboratories for over 30 years. COLA received deemed status to accredit pathology from CMS in March, and then in September we were approved to deem pathology laboratories in California compliant with that state's requirements. Laboratories performing testing in the specialty of pathology now have another choice for their accreditation.

COLA's pathology program is comprehensive, educational and meets or exceeds all CLIA regulatory requirements. We monitor the industry closely to ensure that our criteria reflect current industry guidelines and regulatory requirements. COLA's accreditation program is not just a list of criteria to comply with. Choosing COLA gives a laboratory access to multiple tools to assist with achieving compliance and applying best practices. The Accreditation Manual is well-organized and written clearly and simply, and COLA customers also have access to an entire library of educational Primers on critical topics such as safety, quality, personnel, and training. In addition to these tools, we have a COLAcentral customer portal, a comprehensive dashboard that makes it easy for laboratories and laboratory groups to manage their accreditation.

COLA can accredit histopathology, oral pathology, dermatopathology, and cytology laboratories. This includes full-service pathology laboratories as well as limited-service sites such as those performing Mohs surgery, frozen section, fine needle aspiration, or rapid on-site evaluation procedures. In addition, COLA provides coordinated laboratory surveys for health systems that have multiple laboratory sites.

I am very pleased to be part of the COLA family knowing that laboratories enrolling in the pathology accreditation program will be surveyed by knowledgeable, experienced COLA staff and subject matter experts with years of working experience in the laboratory.

Before becoming the Director of Pathology Accreditation at COLA, you were an Anatomic Pathology Operations Manager for Clinical Pathology Laboratories in Austin, Texas. Could you share your top five tips for being accreditation ready?

1. Ensure all staff are trained on all procedures and that the procedures are consistently followed.
2. Ensure that laboratory staff are familiar with what to expect during a survey. If staff is equipped with that knowledge, they won't be intimidated while the survey is in progress.
3. Schedule routine survey preparedness meetings throughout the entire accreditation cycle. When I was working in the laboratory, supervisors were all required to review criteria and participate in mock surveys to ensure they understood the survey process.
4. Perform departmental self-surveys regularly. This doesn't have to be a daunting task: rotate the responsibility so that everyone has a turn to audit laboratory processes in advance of biennial surveys. COLA has a self-assessment tool that makes this process easy.
5. Keep the laboratory prepared for a visit from any regulatory agency at all times. Keeping documentation well-organized and readily accessible can make surveys go much more smoothly.

What are some laboratory safety concerns you would like to bring awareness to for MLO readers?

What I found during my time as a safety officer is that staff sometimes thinks that safety is solely the company's responsibility. The organization develops safety policies and procedures and provides equipment intended to keep employees

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safe from exposure or injury. However, every employee also has a responsibility to work safely by being compliant with those policies and using equipment properly. OSHA's Laboratory Safety Guidance is an excellent resource.

Maintaining a safe laboratory workplace is everyone's responsibility. In some cases, staff may adhere to safety policies when managers are present, but be more lax about safety when there's no direct supervision. Employees must be trained on the importance of adhering to safety policies at all times.

Employees must feel empowered to report noncompliance with safety policies or any incidents or near-misses that they witness. Noncompliance could ultimately result in exposure or injury to laboratory staff and patients. The most common causes of safety incidents are employees not following safety policies, not wearing appropriate PPE, not paying attention to their surroundings, and being distracted or rushed in the workplace.

Incidents and accidents are costly! Medical treatment for injuries can be expensive and can also result in lost time if staff cannot work due to injury. Depending on the incident, there may also be a loss or waste of reagents, loss or damage to patient specimens, or damage to instruments. There are also hidden costs associated with safety incidents: feeling unsafe can affect staff morale and productivity.

In a recent survey on molecular testing, MLO readers shared that acquiring supplies is a lot more difficult in the past year. How has COLA seen laboratories addressing these supply issues?

It was amazing to see how teams from all areas of the laboratory came together to manage shortages and continue to deliver results for their patients. One way they coped was to validate duplicate methods, especially for SARS-CoV-2 testing. If one method's reagents weren't available, the laboratory could switch to the second validated platform or method without any delay in testing.

Laboratories also modified batch testing schedules to maximize efficiency; fewer, larger batches allowed them to stretch controls further. Personnel managed and maintained their PPE to reduce waste. Phlebotomists drew only what was necessary for testing to conserve on supplies. In histology, reagent use was monitored carefully. Modified procedures were implemented to minimize reagent use without sacrificing quality. They prioritized which tissues to process when reagents were low to ensure diagnostic specimens were not delayed. In addition, across all specialties, staffing schedules were adjusted to maximize efficiency.

I spoke with several of our surveyors recently, and they noted that while laboratories are still experiencing some supply issues, they are not as critical as they were during the height of the pandemic.

Pathology and laboratory medicine have important challenges in workforce capacity going into the future. What do you see the field doing to address these challenges?

The staffing shortage in the laboratory industry is affecting every position. Laboratories are short on clerical staff, couriers, phlebotomists, managers, and qualified and experienced technical and testing personnel. Addressing these challenges requires promotion, recruiting, and retention for all laboratory positions.

When choosing a "medical" field, most students think of nurses and doctors. Educating students on the types of laboratory careers available, including the various specialties, is crucial when students are making early career choices.

Partnering with schools can be a successful approach. For example, histology partnerships exist where a laboratory partners with a formally recognized training program. The student completes didactic and hands-on training per the program's requirements and then takes the program exam. Those who successfully complete the program are then eligible for ASCP certification. It's win-win for the company and the employee, especially if the arrangement includes a defined work commitment period following program completion.

COLA has also launched the Workforce Action Alliance, a diverse panel of experts developing strategies for addressing the laboratory workforce shortage. The group first met during COLA's Laboratory Enrichment Forum in May of 2022. These leaders will come together at COLA's Workforce Action Alliance Summit in Fort Worth, Texas in May of 2023 to continue the discussion and find actionable ways to work together to build the capacity and resiliency of the laboratory profession well into the future.

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

You have to love your job and what you are doing. A good employee has a good work ethic and goes above and beyond because they know that effort will benefit everyone. There are no handouts: you have to work hard, learn, and apply the knowledge and skills you've been taught.

I started working in a small community hospital when I was 18 years old. I didn't know a thing about laboratory testing or regulations, and I never dreamed that it would be my lifelong career. I worked for nearly four years performing clerical duties, making media for microbiology, and sending out tests. I greeted patients, drew blood, ran instruments, and performed manual tests under the supervision of the med techs. I was on the ER code team. I trained to be an EMT and took midnight calls for the hospital's ambulance service after working day shift in the laboratory.

Every few weeks a pathologist, our laboratory director, visited from the larger regional hospital. He offered to train me as a histotech if I would train to assist with autopsies. I said, "Well, if I can get through the autopsy, I'll do it." I trained and studied and in 1982 passed the ASCP boards to be a certified histotechnician, then remained in the field for 42 years. My record for not calling in sick is 9 years, and then I broke my leg! But that's another story!

My career has taken me from Michigan to Alaska, Oregon, Missouri, Texas and now back to Michigan. The pathologists and laboratory professionals I have worked with always encouraged me to do more. With each job, I have gained more knowledge, responsibility, independence, and trust.

The more you know and the more you use that knowledge, the more valuable you'll be to any employer. My career has been long and rewarding and one full of adventure. One of my goals in life has always been to make a difference. I hope that I have.

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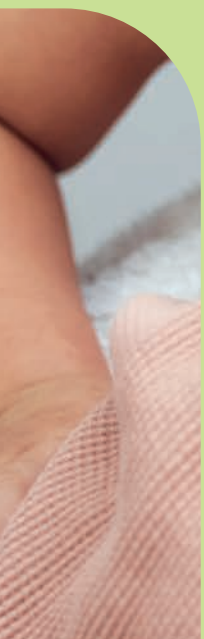

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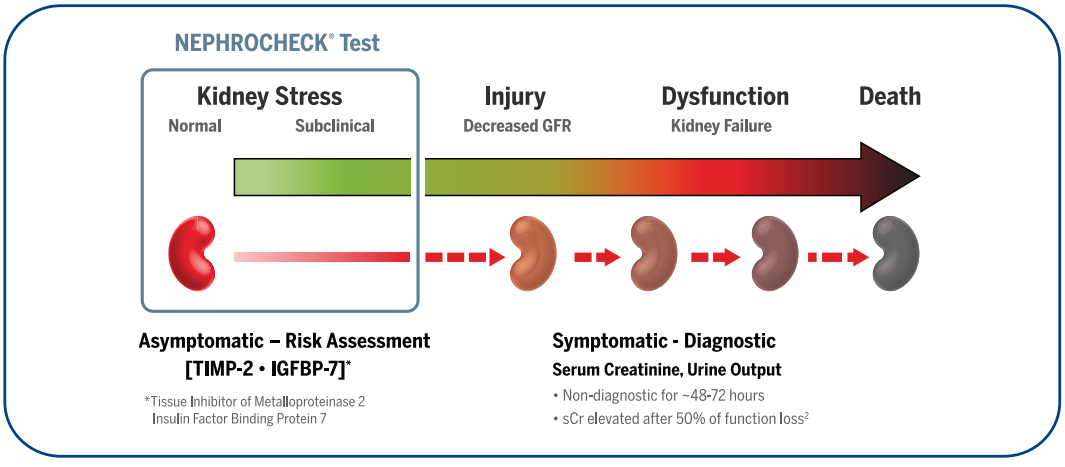

Identify kidney stress before damage occurs.

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INTENDED USE: The NEPHROCHECK Test System is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and/or respiratory compromise and are ICU patients as an aid in the risk assessment for moderate or severe AKI within 12 hours of patient assessment. The NEPHROCHECK Test System is intended to be used in patients 21 years of age or older.

1. NEPHROCHECK Test Package Insert.
2. Mårtensson J. Brit J Anaesth. 2012;109(6):843-850
3. Kashani K. Crit Care. 2013;17:R25.

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