Saint Luke's Regional Laboratories
Clinical Laboratory Letter

September 2014

Blood Culture ID by PCR Improves Care

Two recent patients of Saint Luke's Health System hospitals have had blood cultures positive for multiple organisms. Due to utilization of PCR blood culture identification by Microbiology, these organisms were identified by species the same day their blood cultures turned positive. Furthermore, valuable susceptibility information was available the same day based on detection of resistance genes including *van A/B* (vancomycin-resistant enterococcus).

One of the patients was bacteremic with two different Gram-negative enterics plus vancomycin-susceptible enterococcus. Conventional testing would only have demonstrated a Gram-negative rod along with Gram-positive cocci by stain the day the culture became positive. Full identification would not have been available for 1 to 2 more days, with vancomycin susceptibility results unknown for 2 to 3 days.

The second patient was bacteremic as well as fungemic with both vancomycin-resistant enterococcus and Candida albicans. Only the enterococcus was visible by Gram stain, so that conventional testing would have missed the yeast initially. Additionally, the yeast did not grow on the culture plates for four days, which would have further delayed appropriate anti-fungal therapy.

These anecdotes demonstrate the value of new technology in targeting appropriate antimicrobial therapy and initiating isolation precautions sooner.

Molecular Detection of Gastrointestinal Pathogens

Gastrointestinal pathogens include a variety of bacteria, parasites, and viruses all of which may cause serious, and sometimes life-threatening, diarrhea. Conventional testing for diarrhea-causing pathogens is a mishmash of bacterial culture, viral culture, microscopy, special stains, antigen detection, toxin immunoassay, and single target PCR. This testing is expensive, time-consuming, labor-intense, generally of very low yield, requires multiple samples to improve detection, and has variable sensitivity and specificity. Diagnostic algorithms designed to provide test-ordering guidance for clinicians are of limited usefulness due to the similarity of symptoms caused by these organisms.

Multiplex PCR/array panels are optimal for diagnosis of infectious diarrhea, due to improved sensitivity for common pathogens and detection of more unusual pathogens that are not identified by conventional means.

In October, Saint Luke's Microbiology will have available a molecular gastrointestinal pathogen panel that detects 22 targets from a single stool specimen. Pathogens detected by this assay include the following bacteria, viruses, and parasites:

Campylobacter species
Salmonella
Vibrio species (V. cholerae differentiated)
Yersinia enterocolitica
Plesiomonas shigelloides
Clostridium difficile (toxin A & B)
Shiga-like toxin producing E. coli (STEC)
E. coli O157
Enteroaggregative E. coli
Enteropathogenic E. coli
Enterotoxigenic E. coli
Shigella/Enteroinvasive E. coli
Adenovirus
Astrovirus
Norovirus
Rotavirus
Sapovirus
Cryptosporidium
Cyclospora cayetanensis
Entamoeba histolytica
Giardia lamblia

This assay should be ordered as 'Gastrointestinal Pathogen Panel' and requires submission of a fresh diarrheal stool sample from inpatients. Outpatient samples should be submitted in Cary-Blair transport media. The panel will not be available on inpatients that have been hospitalized for more than three days, for whom Clostridium difficile toxin PCR is still the most appropriate initial test. Time to result from initiation of testing in the laboratory is approximately one hour.

Due to the enhanced sensitivity & specificity provided by this technology, conventional diarrheal stool testing with suboptimal performance characteristics (including ova/parasite stains, bacterial stool culture, and viral stool culture) will be phased out early in 2015. Single-target PCR testing for Clostridium difficile toxin, as well as Giardia/Cryptosporidium and Rotavirus antigen testing will remain available in addition to the panel.

Drugs of Abuse Detection Intervals

The laboratory often receives phone calls asking how long a particular drug of abuse can be detected in urine. The detection window for the most common drugs of abuse is summarized below.

Drug	Detection Window
Amphetamine	1-3 days occasional use 7-10 days chronic use
Methamphetamine	1-3 days occasional use 7-10 days chronic use
Barbiturates	4-6 days
Cocaine	2-3 days occasional use 4 days chronic use
Fentanyl	1-3 days
LSD	1-5 days
Marijuana	3-5 days occasional use 8 weeks chronic use
Methadone	2-3 days
Opiates	2-3 days
PCP	7-14 days
Propoxyphene	1-7 days

N-Telopeptide Bone Marker

Bone remodeling allows for bone growth, bone repair and elimination of microfractures. Osteoclasts resorb old bone, while osteoblasts synthesize new protein, known as osteoid. Within several months, osteoid becomes calcified. After the age of 40 years, bone destruction begins to exceed formation, leading to osteoporosis. For every 10% of bone that is lost, the risk of fracture doubles.

The medications most commonly used to treat osteoporosis are estrogen, calcitonin and biphosphonates (etidronate, alendronate, risedronate). Their mechanism of action is to inhibit osteoclastic activity and decrease bone resorption. Treatment with biphosphonates must be continuously monitored because overdosage can eventually weaken bone.

More than 90% of the osteoid matrix of bone consists of type I collagen. Noncollagenous proteins, such as osteocalcin, comprise the remaining 10%. Type 1 collagen is synthesized as procollagen precursor molecules. Prior to insertion into the osteoid matrix, the N and C terminal peptides of procollagen are cleaved and released into the circulation. The N terminal peptide is commonly referred to as N-telopeptide and is one of the most sensitive indicators of bone resorption.

Following initiation of treatment, bone resorption markers can detect early changes much sooner than bone mass density measurements. N-telopeptide levels undergo significant change by 3 months, while changes in spinal bone mass density are noticeable only after 24 months.

A baseline N-telopeptide level should be measured in all patients before beginning anti-resorptive therapy. In general, biphosphonates are administered until N-telopeptide levels fall to 50% of baseline. They are then discontinued and N-telopeptide concentration is measured every 3 months. Treatment is reinstated when the level returns to baseline.

Reference range is 5.4-24.2 nM BCE for adult males and 6.2-19.0 nM BCE for premenopausal women. Results are expressed in bone collage equivalents (BCE).

Specimen requirement is a red top tube of blood.