New Test for Respiratory Season 2017-18

Molecular testing for respiratory pathogens has provided new insight into the epidemiology of upper & lower respiratory infections. For example, in addition to influenza, RSV (respiratory syncytial virus) and rhinovirus are now known to cause severe illness in selected patient populations. Besides infants and young children, older adults and adults with chronic medical conditions are at risk for complications from RSV infections. Specifically, adults with chronic lung or heart disease, who are immunocompromised or aged 65 or older should be considered high risk according to CDC guidelines. RSV infection may also exacerbate underlying chronic disease including asthma, COPD, and congestive heart failure.

Saint Luke’s Laboratories offer a variety of test options for detection of influenza and RSV. Rapid antigen testing is performed by all testing sites. The major disadvantage of rapid antigen testing is low sensitivity of 60-80%. Sensitivity of rapid influenza antigen tests is variable from season to season, depending on the predominant strain. Likewise, RSV antigen testing has poor sensitivity in adults, compared to children.

Specimens can also be sent to the central Microbiology laboratory at Saint Luke’s Hospital for respiratory PCR testing. Beginning in December 2017, a combination influenza A/B/RSV PCR will be available in addition to the multi-organism respiratory panel and influenza A/B PCR. Specimen type for the influenza A/B/RSV PCR is a nasopharyngeal swab submitted in universal transport media.

The respiratory PCR panel detects influenza A, influenza B, and differentiates A subtypes H1 & H3. Additional pathogens detected by the panel include coronavirus (not MERS co-V), human metapneumovirus, rhinovirus, parainfluenza, RSV, adenovirus, Bordetella pertussis, Mycoplasma pneumoniae, and Chlamydia pneumoniae. Respiratory panel testing can be performed on bronchoscopy specimens in addition to nasal swabs or washes. Optimal utilization of the multi-organism panel is for severely ill, immunocompromised, or transplant patients.

The Microbiology laboratory also performs PCR testing for influenza viruses only. In addition to influenza B, the flu A/B PCR detects influenza A H1 and H3 subtypes and differentiates 2009 H1N1. Sensitivity averages 90% with specificity near 100%. During seasons when rapid antigen sensitivity is low, influenza PCR testing is recommended for patients needing hospitalization for respiratory illness, at the time of admission. Nasopharyngeal or nasal swabs submitted in universal transport media or nasal washes are the only acceptable specimen types for influenza A/B PCR.

Interpretation of Benzodiazepines in Urine Drug Screen Testing

There are two types of urine drug testing (UDT) - screening and confirmatory tests. The screening test performed in both the laboratory and onsite as point of care testing (POCT), is based on immunoassay technology and provides rapid results in a cost-effective manner. Antibodies constituting the immunoassays are directed towards either drug metabolites or class of drug metabolites present in the urine. Unfortunately, presence of substances with similar characteristics will result in cross-reactivity and a false positive reaction. All positive results on screen testing therefore are presumptive and need confirmation using gas chromatography/mass spectrometry (GC-MS) or liquid chromatography-tandem mass spectrometry (LC-MS/MS). In addition to clinical judgement and patient history, a basic knowledge of urine specimen characteristics is helpful in interpretation of drug screen testing results. The majority of commercially available drug screen testing panels include amphetamine, cocaine,
marijuana, opiates, benzodiazepine, and phencyclidine.

Traditionally, drug screen testing for barbiturates and benzodiazepines have been performed for hospital emergency department and workplace or forensic purposes. Increasingly, pain management clinics and/or primary care physicians are requesting barbiturates and benzodiazepines UDT to monitor therapy compliance and/or substance abuse. In the United States, more than 15 benzodiazepines are commercially available with clonazepam, lorazepam, and alprazolam among the top drugs prescribed. Interpretation of benzodiazepine UDT can be complex due to its metabolic pathway, half-life, potencies, and inability to differentiate between individual benzodiazepines.

False positive benzodiazepine screen testing due to presence of drugs such as oxaprozin is well known. However, there is a general lack of understanding regarding the possibility of false-negative results with the benzodiazepine immunoassays. Two major factors that may contribute to false negative screen tests include –

1. the inability of antibodies present in the immunoassay to detect conjugated metabolites. Most of the benzodiazepine immunoassays are designed to detect free or unconjugated forms of oxazepam or nordiazepam (common metabolites of several benzodiazepines eg, diazepam, chlordiazepoxide, and temazepam). However, many currently prescribed benzodiazepines such as lorazepam and alprazolam are excreted as glucuronide conjugates and may not be detected on the screening test. Similarly, clonazepam which is metabolized to 7-aminoclonazepam may produce false negative screening test, and

2. high cutoff concentrations of 200 or 300 ng/mL for positive results. Initially, these values were based on standard dosage of older benzodiazepines such as diazepam, oxazepam, and flurazepam (ranged between 5-20 mg/d). Benzodiazepines such as lorazepam, alprazolam, and triazolam, however are more potent and prescribed at much lower doses. A study performed demonstrated that lowering the cutoff concentration for alprazolam and triazolam to 100 ng/mL with enzyme hydrolysis of the urine specimen reduced false-negative results (Fraser AD and Meatherall R. et. al. Anal Toxicol. 1996;20(4):217-223 and Ther Drug Monit. 1998;20(3):331-334).

At Saint Luke’s Laboratories all positive benzodiazepine immunoassays are reflexively sent out for confirmation testing. The current benzodiazepine confirmation testing includes alprazolam, clonazepam, flurazepam, lorazepam, midazolam, nordiazepam, oxazepam, temazepam, and triazolam (effective since 10/24/17). In rare cases, if there is a suspicion for false negative screen results on patients with benzodiazepine prescription, consultation with a clinical pathologist for requesting benzodiazepine confirmation testing may be considered.

**Reference Range Change for Alkaline Phosphatase**

At Saint Luke’s Laboratories, the reference ranges for alkaline phosphatase (ALK), an age dependent analyte, are published under two age groups - 0-19 years and >20 years. The development and growth spurts in children can profoundly influence numerous circulating biochemical markers. A study performed to establish reference ranges of various biochemical markers in healthy children and adolescents was published to help guide test interpretation. Accordingly, a new reference range of 50 – 500 IU/L for 0-19 yrs age group has been established for Saint Luke’s Laboratories, and became effective November, 29th 2017.

**New C. difficile PCR Rejection Criteria**

The Microbiology laboratory has rejected formed stool specimens for *C. difficile* testing for some time due to the risk of false-positive results. Effective immediately, inpatient stool specimens will also be rejected if the patient has received laxatives in the past 48 hours prior to specimen collection, or if the patient has not had ≥ 3 watery/loose stools in the past 24 hours. Additionally, a positive *C. difficile* in the last 14 days, or a negative result in the last 7 days may result in test cancellation. These rejection criteria are based on recent literature guidelines. A best-practice alert in Epic alerts clinicians to these new test conditions.