Welcome Dr. Mathur, Transfusion Medicine

Dr. Gagan Mathur will soon join the clinical pathologists at Saint Luke’s Laboratories. He received clinical pathology training at University of Iowa. Additionally, he completed a fellowship in transfusion medicine in June 2016, for which he recently received board certification. While training in pathology, Dr. Mathur also completed a Master’s in Business Administration. His joining date at Saint Luke’s Hospital is Oct 31st. Saint Luke’s Pathology welcomes Dr. Mathur to the team.

Calprotectin Levels in IBD

Calprotectin, a heterodimer of S100A8/A9, is a small calcium-binding protein and a member of the S100 family of zinc-binding proteins. It constitutes approximately 60% of the cytosolic protein content in neutrophils and is also present in low concentrations in monocyte/macrophage cytosol. During active intestinal inflammation, calprotectin derived from neutrophils migrating from the circulation to the inflammation site, leaks into the gut lumen and is subsequently excreted into feces. The fecal concentration of calprotectin is therefore directly proportional to the intensity of intestinal inflammation. Since it is stable in feces for up to 7 days at room temperature and has a homogeneous distribution, calprotectin has emerged as a new noninvasive, simple, and cost-effective diagnostic tool for detection of intestinal inflammation.

Patients with inflammatory bowel diseases (IBD) and irritable bowel syndrome (IBS) share many clinical symptoms, including abdominal pain, diarrhea and generalized malaise. In many cases, IBD and IBS cannot be separated on the basis of clinical symptoms alone. The majority of these patients, until recently underwent colonoscopy to rule out IBD. Initial studies performed in 1992, showed increased fecal calprotectin levels in IBD compared to IBS. Depending on the prevalence of IBD, the positive predictive value has been shown to vary between 70% and 100% and negative predictive value between 51% and 91% in the adult population. In children, the fecal calprotectin has a comparable sensitivity of 100% but a lower specificity of 68% for diagnosis of IBD. Limitations of fecal calprotectin levels is the lack of specificity and increased levels reported in different organic diseases such as colorectal carcinoma, bacterial or viral gastroenteritis, diverticulitis, food intolerance, non steroidal enteropathy, and after pelvis radiation. In addition, calprotectin concentration depends on age, clinical co-morbidities, and may also show day-to-day variation. A validated cut-off value to discriminate IBS from IBD, active IBD and clinical remission has not been defined in the literature. Most of the published studies have used a cutoff concentration of 50ug/g, as suggested by manufacturers of the immunoassay kit. A study using fecal calprotectin cut-off of 30ug/g showed improved sensitivity for discrimination of IBS from IBD (Tibble et. al. 2000b).

A more recent study evaluated calprotectin levels in serum for accurate prediction of inflammatory burden in IBD (Kalla et. al. Am J Gastroentrol 2016). In contrast to feces, serum calprotectin has a short half-life (5 h) and may provide a more dynamic alternative to the conventional serum inflammatory markers (half-life of CRP 18 h, albumin 19 days). Other advantages of serum calprotectin levels include less daily concentration variability and lack of hurdles associated with fecal material collection. The study concluded that in combination with other serum inflammatory markers, calprotectin may help in accurate prediction of inflammatory burden of IBD. Additional large multicenter cohorts based studies, however are warranted.

At present, fecal calprotectin testing is available as a send-out test. Interpretation of these results should be done with caution and in context of the clinical picture.

Anaerobic Cultures

Anaerobic infections are usually caused by leakage of normal flora into a sterile body site, following disruption of a mucosal barrier. The most
commonly isolated gram-negative anaerobic pathogens include Bacteroides, Fusobacterium, Prevotella, and Porphyromonas. Gram-positive anaerobic pathogens include Anaerococcus and a variety of Clostridium species. The most frequent sites of infection include skin and soft tissue, pleuropulmonary and abdominal spaces, and female genital tract. Anaerobic infections are characterized by suppuration or abscess formation and tissue necrosis. When anaerobes are suspected to be the causative agent of an infection, physicians must specifically request an anaerobic culture.

Specimens for anaerobic culture should be collected only from an acceptable site and appropriately to avoid contamination with normal flora. This is best accomplished by aspiration with a needle and syringe or with tissue/biopsy samples. Swabs are strongly discouraged since they provide a limited quantity of specimen, allow exposure to oxygen that is lethal to anaerobes, and are often contaminated with normal flora. For these reasons, swabs should only be used during surgery and only when aspiration or biopsy is not possible. In the instance that a swab must be collected, the eSwab transport system should be utilized.

**C. difficile Strain Differentiation**

*Clostridium difficile* is a Gram-positive, spore-forming, anaerobic bacillus that is associated with pseudomembranous colitis, and is the most common cause of health care-associated diarrhea. *C. difficile* infection (CDI) ranges in severity from mild diarrhea to fulminant colitis. Risk factors for CDI include antibiotic use within three months prior to symptom onset, exposure to a health-care setting, and age greater than 65. Colonization with *C. difficile* is common in hospitalized patients (20-40%), while only 3% of healthy adults are colonized. The propensity of the organism to form spores results in contamination of environmental surfaces, potentially resulting in transfer of the organism to patients via hands of health care workers. Community-acquired infections, many without identifiable risk factors, are reported as well.

Alterations of normal gut flora, resulting in overgrowth of *C. difficile*, are believed to initiate CDI. Production of exotoxins A & B by the organism subsequently results in colonic mucosal damage, and detection of these toxins is the basis for diagnostic laboratory tests. PCR testing for the presence of toxin producing genes has largely replaced enzyme immunoassay due to unacceptable sensitivity and specificity of the latter.

A hypervirulent strain of *C. difficile* was recognized several years ago and has now been reported in most areas of the U.S. This strain results from a sequence variation in the tcdC gene that usually suppresses toxin A & B genes. Consequently, significantly higher amounts of toxin may be produced. The hypervirulent organism is commonly designated as NAP1/BI/027. Effective in November, the presence of the hypervirulent strain will be reported when detected by *C. difficile* PCR testing. The following comment will alert the clinician to the presence of the hypervirulent strain: "This patient is positive for *C. difficile* strain NAP1/BI/027. This strain is hypervirulent and has the capacity to produce significantly larger quantities of toxin, and should be treated promptly."

*C. difficile* PCR testing is performed daily by Saint Luke’s Microbiology. Due to the complexity of PCR tests for *C. difficile* toxin testing, there are published guidelines for test frequency designed to limit the false diagnosis of *C. difficile* infection in colonized patients. It is suggested that only patients with 3 or more loose stools per day for at least 1-2 days be tested. The specimen should be loose enough to take the shape of the container. In addition, “test of cure” is imprudent, as the PCR test will remain positive for several days to weeks following treatment. Likewise, testing is not done on formed stool, due to the likelihood of false-positive results.

**Serum Cancer Markers**

Starting Oct 26, 2016 CA15.3 will replace the CA27.29 tumor marker test. At present, concurrent CA15.3 levels are being reported on all specimens received for CA27.29 testing for correlation and to facilitate the transition. In addition, Saint Luke’s laboratory has retained all specimens received for serum CA27.29 levels for the last two months. If indicated, serum CA15.3 levels can be requested on these saved specimens for correlation and patient management at no extra cost.

Serum complexed PSA (cPSA) test will be discontinued starting October 26. A directly measured total PSA (tPSA) and free PSA (fPSA) will be available with no change in the reference ranges.