Saint Luke's Regional Laboratories
Clinical Laboratory Letter

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GI Pathogen Panel Performance Characteristics

The new molecular GI Pathogen Panel is now being performed by Saint Luke's Microbiology. This assay detects 22 targets from a single stool specimen including bacteria, viruses, parasites, and toxins. A recently published comparative evaluation of 500 diarrheal stool specimens performed at Mayo Medical Laboratories (J. Clin. Microbiol. 2014, 52(10):3667) found this Panel's sensitivity >90%, and specificity >97% for 243 previously characterized positive samples. Another 230 specimens not previously tested yielded 19 positives (8.3%) from conventional testing and 65 positives (28%) from the GI Pathogen Panel, which were confirmed by alternate methods. The Panel identified mixed infections in 27% of confirmed positive samples, compared to 8% tested by conventional means.

A major advantage of the GI Pathogen Panel is identification of organisms not detected by conventional testing. Key characteristics of these pathogens are as follows:

- Diarrheagenic E. coli/Shigella, 5 major types:
  - Enteroaggregative E. coli (EAEC). Inflammatory diarrhea, sometimes bloody. May have low-grade fever and/or vomiting. Common in the U.S., second most common cause of travelers' diarrhea and causes large outbreaks worldwide.
  - Enteropathogenic E. coli (EPEC). Non-bloody diarrhea. Mostly children. Seasonal peaks in summer/early fall. No toxin production.
  - Enterotoxigenic E. coli (ETEC). Watery diarrhea due to toxins that bind to epithelial cells. Most common cause of travelers' diarrhea.
  - Shiga-like toxin-producing E. coli (STEC). Bloody diarrhea. Can progress to hemolytic-uremic syndrome. Foodborne (ground beef), contaminated water, peron-to-person or animal contact. In addition to E. coli, shiga toxin is also produced by Campylobacter, Shigella, Salmonella, and Yersinia.
  - Shigella/Enteroinvasive E. coli (EIEC). Bloody or non-bloody watery diarrhea. Highly contagious, low infectious dose. EIEC believed rare in US but molecular target is indistinguishable from Shigella.
- Viruses
  - Adenovirus F 40/41. Common in children under 2, and can cause outbreaks. Resistant to disinfectants. Mild illness of several days duration with prolonged shedding of virus in feces.
  - Astrovirus. Mild symptoms lasting ~72 hours. High seroprevalence in school-age children, therefore very common.
  - Norovirus. Highly contagious, low infectious dose. Moderate to severe vomiting and diarrhea with fever. Outbreaks common. Most common cause of foodborne GI illness in US. Peaks in winter.
  - Sapovirus. Similar to norovirus but infects children more than adults. Fever & vomiting with diarrhea. Also very contagious, causes outbreaks, peaks in winter.

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.

Restrictive Transfusion Strategy Reduces Risk of Healthcare Associated Infection

The association between transfusion strategies and healthcare-associated infection was recently assessed in a meta-analysis that included 18 randomized trials with a total 7,593 patients that were assigned to either a restrictive or liberal transfusion strategy. The definition of restrictive and liberal transfusion strategies varied amongst

individual studies, but most defined a restrictive strategy as the transfusion of red blood cells once hemoglobin falls below either 7.0 or 8.0 grams per deciliter and a liberal strategy as transfusion once hemoglobin falls below 10 grams per deciliter.

The main outcomes of these studies were serious healthcare-associated infections such as pneumonia, mediastinitis, wound infection, and sepsis. The pooled risk of all serious infections was 11.8% in patients treated under a restrictive strategy and 16.9% in patients treated under a liberal strategy. Risk ratio for the association between transfusion strategies and serious infection was 0.82 (95% CI 0.72-0.95). The number needed to treat with a restrictive strategy to avoid one infection was 38 (Rohde JM, et al. *JAMA* 2014; 311(13): 1317-1326). In the subset of those studies with the most restrictive hemoglobin strategy of <7.0 g/dL, risk ratio remained at 0.82, but the number needed to treat decreased to 20.

When the analysis was stratified by patient type, researchers found that a restrictive strategy in patients undergoing orthopedic surgery and in patients presenting with sepsis significantly reduced the chance of infection, with risk ratios of 0.70 and 0.51, respectively. There were no significant differences in the incidence of infection by hemoglobin threshold for patients with cardiac disease, the critically ill, those with acute upper gastrointestinal bleeding, or low birth weight infants.

More than 80% of patients in this meta-analysis were transfused with leukocyte reduced red blood cells, which are believed to reduce the risks of transfusion associated immunomodulation.

About one in every 20 inpatients develops a nosocomial infection, with estimated annual direct medical costs to U.S. hospitals ranging between $28 billion and $45 billion. Transfusion is associated with immunomodulation, which may affect infection risk. This meta-analysis suggests that adoption of restrictive transfusion strategies might prevent 26 healthcare-associated infections for every 1000 patients in which red blood cell transfusion is under consideration.

Lower Transfusion Thresholds do not Harm Septic Shock Patients

An international, multicenter, randomized trial recently assessed the best transfusion threshold for 998 critically ill patients with septic shock (Holst etal. NEJM 2014;37:1381). Patients in the ICU were randomized to receive 1 unit of leukocyte reduced red blood cells when the hemoglobin was 7 g/dL or less (restrictive group) or when the hemoglobin was 9 g/dL or less (liberal group). The restrictive group received a median of 1 unit of blood, while the liberal group received a median of 4 units.

By 90 days after randomization, 43% (216/502) of patients in the restrictive transfusion group had died compared to 45% (223/496) of the liberal transfusion group (relative risk, 0.94; 95% confidence interval, 0.78-1.09). There was no difference in mortality, the number of ischemic events, severe adverse reactions, or numbers of days in the hospital between patients in the restrictive group (7 g/dL) compared to those in the liberal group (9 g/dL). A restrictive transfusion strategy not only reduced blood use by half but also did not cause harm.

New Pregnancy Test

A new pregnancy test is available that can test either serum or urine. Once a specimen is applied to the device, results are available in 3 minutes for urine and 5 minutes for serum. Sensitivity is 10 IU/mL for serum and 20 mIU/mL for urine. hCG concentrations reach 10 to 25 mIU/mL by 7 to10 days after conception.

The most common cause of a falsely negative urine pregnancy test is a dilute urine specimen. The lab performs a specific gravity with each urine pregnancy test. If urine is too dilute, a chartable comment is added to negative urine pregnancy test results. Unless urine is too dilute or the patient may have conceived in <10 days of testing, a urine pregnancy test is sufficient to rule out pregnancy.

Both the urine and serum hcG are qualitative tests, reported as positive or negative. This serum test should not be confused with hCG quantitative that requires approximately 30 minutes to perform.