Clinical Validation of Fecal Electrolytes for Chronic Diarrhea
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Introduction: Fecal electrolytes are measured to help narrow the differential diagnosis for chronic diarrhea, defined as symptoms lasting more than 4 weeks. Our laboratory offers a comprehensive panel that includes measurement of chloride, magnesium, osmolality, phosphorous, sodium, and calculated osmotic gap (OG) using published interpretive information for identifying osmotic (OG >50 mmol/L), secretory (OG <50 mmol/L), and magnesium-induced (Mg >110 mg/dL) diarrhea. The objective of this study was to determine the diagnostic accuracy of calculated osmotic gap and magnesium in our patient population to optimize the testing algorithm.

Methods: Fecal electrolyte results between August 7, 2013, and December 22, 2017, were extracted from the electronic medical record for 435 unique patients (male = 153, female = 282, mean age = 57) at Mayo Clinic Rochester, MN. Random liquid fecal specimens submitted for testing were centrifuged for 1 hour at 14,000 rpm, transferred to a new tube, stored refrigerated, and tested in daily batches. Electrolytes were measured using Roche Cobas c501 (Roche Diagnostics, Indianapolis, IN). Osmotic gap was calculated as 290 mOsm/kg - [2|Na] + 2|K]. Chart review was conducted to document the cause of diarrhea and medications containing magnesium and other laxatives. Receiver operator curve (ROC) analysis with area under the curve (AUC) was calculated using AnalyzeIT (Microsoft Excel). This study was conducted with Mayo Clinic IRB approval.

Results: Chronic diarrhea was classified as osmotic (n = 27), secretory (n = 107), inflammatory (n = 85), steatorrhea (n = 14), and of unknown etiology (n = 202). The prevalence of magnesium-induced diarrhea in our population was only 1.4%. OG differentiates osmotic from nonosmotic causes of diarrhea with an AUC of 0.866, having an optimal decision limit for OG >82 mOsm/kg, sensitivity = 83%, and specificity = 83%. OG differentiates secretory from nonsecretory causes of diarrhea with an AUC of 0.545. A decision limit with sensitivity = 50% is <22 mOsm/kg and has specificity = 37%, while the OG having sensitivity = 95% is <30 mOsm/kg and specificity = 11%. Mean (±SD) results of magnesium were 0.579. The optimal decision limit is Mg >106 mg/dL, having sensitivity = 15% and specificity = 97%. Mg was >106 mg/dL in 3.3% of those tested, resulting in a negative predictive value (NPV) = 98.8%. With one exception, all samples with Mg >106 mg/dL had OG >50 mOsm/kg, suggesting 62% of Mg testing would not identify Mg-induced osmotic diarrhea.

Conclusion: These data demonstrate OG should have a single cutoff to differentiate osmotic from nonosmotic causes but not secretory from other causes. The diagnostic utility of Mg measurement is its negative predictive value.

Diagnosing Harvey: A Laboratory Medicine Department’s Response to a Disaster Situation
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Objective: There are limited published data pertaining to a laboratory medicine department’s preparedness and response to natural or manmade disaster situations. Therefore, the goal of this project is to share lessons learned during a recent disaster, Hurricane Harvey, and provide recommendations on preparedness, action, and recovery efforts that can be universally applied to laboratory medicine departments throughout the world.

Methods: A PubMed literature search was performed using the terms pathology, laboratory medicine, and disaster response. The authors reviewed existing hospital and departmental policies regarding disaster preparedness, as well as debriefing assessments of both the hospital and laboratory performance during and following Hurricane Harvey. Personal accounts of the experience were obtained from technologists, supervisors, trainees, medical directors, and other physicians.

Summary: The Texas Medical Center (TMC), greater Houston area, and surrounding counties were devastated by one of the most catastrophic national disasters in US history. However, due to extensive implementation of planning and preparedness procedures developed following Tropical Storm Allison in 2001, the hospital and laboratory were able to maintain operations, with few interruptions, throughout the entirety of Hurricane Harvey. All of the organization’s facilities both within and outside the TMC were able to maintain sufficient personnel staffing, with many employees and directors spending multiple nights in the hospital. Flooded roadways created difficulties in transportation of specimens, delayed performance of services rendered in central laboratory locations, and resulted in longer than expected turnaround times for some areas. The primary goals during the catastrophe were to be able to provide medical care and the preservation of the safety of both patients and staff. These goals were achieved throughout the event; however, the recovery period that followed was mentally, emotionally, and physically grueling for many staff, patients, and their families, especially for those with personal losses of homes and cars. This created significant challenges in the following days, weeks, and months.
Conclusions: The effects of a catastrophic disaster situation, such as the one during and following Hurricane Harvey, cannot be avoided or understated. The impact of a disaster situation affects all areas of health care; however, little to no literature exists that provides insight into preparations and guidelines specific to laboratory medicine. It is impossible to predict when a disaster, natural or manmade, will occur or to know the extent of damage and destruction it will bring. It is thus imperative for laboratory medicine departments to be vigilant and have actionable policies and procedures in place that ensure the safety of patients and staff, the quality and integrity of the laboratory’s performance, and measures to recover following a catastrophic event.

Novel Chitohexaose Compounds to Treat Abdominal Peritonitis Leading to Sepsis
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Gastrointestinal perforation and appendicitis are the common cause of leakage of alimentary contents into the peritoneal cavity, leading to sepsis with a mortality rate between 14.7% and 29.9%. Besides its clinical challenge, the treatment of sepsis and its complications impose an enormous economic burden on health care systems worldwide. In sepsis caused by gram-negative bacteria, the bacterial endotoxin, lipopolysaccharide (LPS), activates the immune system through signaling the MD2-toll like receptor 4 complex (TLR4) to initiate the infection process for production of inflammatory cytokines (TNF-α, IL-1β, IL-6) that are responsible for hyperinflammation. Thus, development of antagonists that block these receptors either by inhibition of activation of TLRs or downstream signaling pathways would be beneficial in ameliorating the hyperinflammation if introduced early in the therapy.

At AyuVis Research, we have designed a series of dual-acting small molecules (AVR-25, 48) that block TLR4 receptor, which inhibits the production of proinflammatory cytokines; stimulate production of macrophages leading to organ protection; and limit tissue injury. Our lead compound, AVR-25, has efficaciously demonstrated survival, organ protection, downregulation of inflammatory cytokines, and upregulation of M2 markers and cytokines such as arginase-1 and IL-10 in vivo in a cecal ligation and puncture (CLP) sepsis mouse model via intravenous (IV) dosing. Our published and unpublished in silico modeling experiment has demonstrated that our compounds have a unique binding mode where they either bind to the dimerization site or to the middle of the TLR4 protein restricting the dimerization of protein, which is a critical step in downstream signaling. In our CLP model of both young and aged mice, compounds AVR-45 and AVR-48 efficaciously protected them against CLP-induced death and organ dysfunction at a 10-mg/kg (q8h) IV dose. These compounds also possess modest antibacterial activities against both gram-positive and gram-negative bacteria, as well as synergistic/additive activity in combination with standard of care antibiotics such as primaxin (PRM, Imipenem + cilastatin), indicating good potential for adjuvant antimicrobial therapy.

We are the first and only key investigator team to observe the effects of AVR-25 and AVR-48 natural oligosaccharide-derived small molecules in preventing sepsis-induced death in the murine CLP-induced peritonitis model. We believe that development of this class of compounds will lead to a paradigm shift and could become a very high-gain project in the treatment management of inflammation and organ dysfunction in intra-abdominal sepsis. These significant research capabilities will open a new facet to combination therapy with antibiotic and standard antihypotensive agents for critically ill patients.

Apheresis Ports: The Houston Methodist Experience
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Background: Therapeutic apheresis cannot be performed without adequate vascular access and the ability to achieve inlet flow rates of approximately 50 to 100 mL/min. Central venous catheters (CVCs), which are dialysis capable, are intravascular devices used in apheresis and are capable of such performance. However, their use has several associated risks that include localized and systemic infections, as well as catheter occlusions and thrombosis. Some of these risks can be mitigated if peripheral venous access can be established. However, in some patients, peripheral vascular access is not an option for long-term apheresis treatments. In such situations, totally implantable venous access systems or ports are increasingly being utilized for vascular access. Ports offer several perceived advantages over CVCs, including low rates of infection, long-term usage, patient comfort, and improved quality of life.

Methods: We recently sought to evaluate implantable ports in our apheresis patient population. Houston Methodist Hospital’s apheresis service is a large, 2,000-bed community and tertiary care system that performs approximately 3,400 apheresis procedures per year. We collected data on two apheresis ports, the TidalPort (Norfolk Medical Products) and the PowerFlow (Bard Peripheral Vascular). The construction of these two ports is different; the TidalPort is cylindrical while the PowerFlow is funnel shaped. Given these design differences, we reviewed the safety and efficacy of these ports for long-term apheresis care.

Results: In our apheresis population during 2016 to current, four patients were implanted with the TidalPort and four patients were implanted with the PowerFlow. For