On September 15th, 2016 the BJH Laboratory discontinued serologic testing for *Helicobacter pylori*. The recommended alternative for testing for *H. pylori* infection is stool antigen testing.

Gastric biopsy has long been regarded as the gold standard for *H. pylori* diagnosis, though this approach is invasive, requiring endoscopy. As such, several noninvasive tests are more commonly used for routine diagnostic screening. 1) In the urea breath test (UBT) the patient ingests urea comprised of a carbon isotope and there is subsequent measurement of the isotope in exhaled CO2. The amount of exhaled isotope increases if infection is present due to the urease activity of the organism. 2) The detection of *H. pylori* antigen in stool can be performed directly on fresh stool specimens. Both the UBT and stool antigen tests show favorable performance when compared to histology and are recommended by the American Gastroenterological Association (AGA) and the American College of Gastroenterology (ACG) for routine noninvasive diagnostic testing http://gi.org/guideline/management-of-helicobacter-pylori-infection/.

Although detection of antibodies against *H. pylori* in serum is another noninvasive diagnostic approach, the diagnostic performance of this test is poor. False positives are common since patients can test positive for years following resolution of infection. An internal review of *H. pylori* IgG results at BJH suggests a positive predictive value of only 62.5% when compared to biopsy. These results are consistent with those from other institutions and support the AGA and ACG recommendations of the avoidance of *H. pylori* serology, favoring the use of other noninvasive *H. pylori* tests for diagnosis. In light of this, *H. pylori* serology testing is being discontinued at major reference laboratories throughout the United States.

The recommended alternative test, *H. pylori* stool antigen, is available as an orderable in COMPASS, Allscripts, and HMED. Stool specimens submitted for testing should be formed, collected in a sterile plastic container, and delivered to the laboratory within 48 hours of collection. Testing will be sent to Mayo Medical Laboratories and the turnaround time is ~3-5 days. Falsely negative results may be obtained within 1 month of treatment with antimicrobials, bismuth, or proton pump inhibitors. For patients on active *H. pylori* therapy, a negative test should be followed...continued on pg 2
Helicobacter pylori Serology....continued from page 1.

up with a repeat test at least 1 month after discontinuing therapy.
If you have any questions, please contact Neil Anderson, M.D., (362-1307) or the microbiology lab medicine resident (747-1320).

Revised Transfusion Consent

By George Despotis

In June, BJH implemented a revised Transfusion Consent. The previous consent was not compliant with regulations that require patients the ability to refuse transfusion of some or all blood components. The new BJH consent provides patients with options to accept or refuse all or some of the four main blood components by initialing next to the appropriate options.

Check one:

☐ I CONSENT TO ALL blood products, blood derivatives or blood-related treatments
☐ For personal, religious or other reasons, I CONSENT TO ONLY SOME blood or blood products:

Red Blood Cells  Accept____  Refuse____  Platelets  Accept____  Refuse____
White BloodCells  Accept____  Refuse____  Platelets  Accepts____  Refuse____

I understand that because I refuse some of these products, I could die or suffer very serious problems.

☐ I DO NOT CONSENT TO ANY blood or blood products. I understand that because I refuse all of these products, I could die or suffer very serious problems.

The additional pages that accompany the consent summarize the risks of transfusion and provide a description of blood and blood components. The Transfusion Consent will always be a SEPARATE consent and cannot be included as part of a surgical or other procedure consent.

Physicians and physician extenders (i.e., PAs or NPs) must still explain the risks of blood components, obtain and document consent (i.e., execution of the consent or a note in the chart if a consent is not readily available), and patients should have ample time during the discussion to ask questions.

In addition, the BJH consent form does not include multiple other blood-related interventions that should be addressed independently. For example, a patient who refuses one or more of the four blood components may consent to use of other interventions such as:

• Pooled human blood derivatives like albumin or factor concentrates.
• Recombinant factor concentrates that may also contain albumin.
• Other therapeutic/diagnostic techniques that involve use of either autologous or allogeneic blood derivatives or
• Techniques that involve processing or circulation of patient blood within extracorporeal methodologies (e.g. cell salvage, apheresis, dialysis or cardiopulmonary circulatory devices).

Clinicians involved with the management of patients who are refusing blood and may benefit from other interventions should discuss the risks and benefits of these interventions and document their discussions and patient preferences. Direct questions to George Despotis, MD gidespotis@wustl.edu.
Characterization of Carbapenem-Resistant *Enterobacteriaceae*

by: Carey-Ann Burnham

The rapid emergence and expansion of carbapenem resistant *Enterobacteriaceae* (CRE) is a global public health problem; the CDC classifies CRE as one of the three highest priority, or "urgent" antimicrobial resistant threats in the US (http://www.cdc.gov/drugresistance/threat-report-2013/). Carbapenemases, or enzymes that can degrade broad spectrum β-lactams including carbapenems, can be located on mobile genetic elements, facilitating the spread of resistance genes between organisms. Although numerous carbapenemase genes have been described to date, the most common determinants conferring carbapenem resistance in the US include KPC, NDM, and OXA-48; clinical strains harboring these resistance determinants have been isolated at BJH. Detection and characterization of CR-GNB is important to optimize antimicrobial therapy and to facilitate infection prevention efforts; enhanced methods for this characterization have recently been implemented in the BJH Microbiology laboratory. Isolates of *Enterobacteriaceae* that test resistant to meropenem will be characterized with a phenotypic assay to detect carbapenemase production--the Carbapenemase Inactivation Assay (CIA) (McMullen et al, *Clinical Chemistry*, 2016). Isolates that test positive by the CIA (i.e. confirmed carbapenemase producing strains) will be further characterized using the Xpert CARBA-R assay. This assay detects and differentiates 5 genes commonly conferring carbapenem resistance: KPC, NDM, OXA-48, VIM, and IMP. If you have any questions about this update, please contact Carey-Ann Burnham, PhD, Medical Director of Clinical Microbiology for BJH (eburnham@path.wustl.edu).

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**Update: Electronic Decision Support to Reduce Unnecessary Repeat Testing for *Clostridium difficile***

by: Jennie H. Kwon and Carey-Ann Burnham

*Clostridium difficile* is the most common cause of antibiotic-associated diarrhea, and *C. difficile* infection (CDI) is the most common healthcare associated infection in the US. CDI is a clinical diagnosis supported by laboratory and/or endoscopic findings. BJH utilizes the Wampole/TechLab Toxin A/B II enzyme immunoassay, which has a negative predictive value (NPV) of 97.4-99.2%. Despite the excellent NPV of one *C. difficile* test, at BJH historically 41% of patients who had an initial negative test had second test requested within 7 days of initial testing. There are no data to support this practice, and this leads to a decrease in the positive predictive value from ~80% from the first test, to ~20% by the third test. The consequences of a false positive test include unnecessary CDI treatment, drug side effects, a paradoxical increased risk in CDI after drug exposure, and increased length of stay and cost of hospitalization.

To improve *C. difficile* testing practices at BJH, in May 2015, an electronic decisions support intervention via COMPASS was introduced. After implementation of this hard-stop decision support tool, it was not possible to order a repeat *C. difficile* test within 96 hours of an initial negative test or within 10 days of an initial positive test. If the index of suspicion for *C. difficile* remained high, this hard-stop could be bypassed after discussion with the Laboratory Medicine Resident.

Interim analysis of the initial lock-out period (June 2015 to August 2015) demonstrated a 21% reduction in the number of *C. difficile* tests repeated within 96 hours of an initial negative (Figure 1), and the mean number of tests per admission decreased from 1.42 to 1.25 (p <0.01). The reduction in the number of *C. difficile* tests performed was sustained one year after the initiative was implemented (Table 1). On average, the laboratory receives two to six requests to by-pass the lock-out each month.

The overall percentage of positive tests was not affected by the intervention. Importantly, there were no adverse events reported as a result of this intervention, and there were no significant differences in patient discharge location or increases in 30-day patient mortality in the interim analysis of the lock-out period. These data suggest that the intervention successfully reduced unnecessary *C. difficile* testing without having a negative impact on patient care or outcomes.
Table 1: C. difficile EIA Testing at Barnes-Jewish Hospital

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Figure 1: C. difficile EIA Assay Utilization at Barnes-Jewish Hospital 2014-2015
EDTA pretreatment improves anti-HLA antibody detection

by: Chang Liu

In August the BJH HLA Laboratory implemented ethylenediaminetetraacetic acid (EDTA) pretreatment of serum samples for anti-HLA antibody detection by the LABScreen single-antigen bead assay. Complement interference is a major source of false negative results for this assay. Activation of complement factors on anti-HLA antibodies can lead to falsely low mean fluorescence intensity (MFI) values. Pretreatment of serum with EDTA can abolish the interference by chelating calcium cations required for complement activation.

The HLA lab compared test results with neat serum to EDTA-pretreated serum and observed a change from negative to positive results based on the cutoff value of 2000 MFI in 1% of the 18240 beads tested. In 18 samples with strong complement interference, the sensitivity of EDTA pretreatment was verified by dilution studies at 1:25, which is an alternative method to abolish complement interference. The figure illustrates an example of an antibody against DQ7 which would have been missed by testing neat serum alone, as only two out of five DQ7 beads seem to be reactive. The strong reactivity on all five DQ7 beads after EDTA pretreatment indicates the presence of anti-DQ7, which is consistent with the dilution study.

In summary, EDTA pretreatment prevents false negative results caused by complement interference during routine testing for anti-HLA antibodies. If you have any questions, please contact Chang Liu, MD, PhD, Medical Director of HLA at cliu32@wustl.edu, or the HLA Laboratory Supervisor Donna Phelan at 314-362-6527.

**Did You Know?**

You can follow Pathologists Overseas @path_overseas on Twitter.
Outstanding Laboratory Medicine Posters

This summer, two posters by LGM division trainees, received recognition at the annual meeting of the American Association for Clinical Chemistry.

Mitch McGill, a clinical chemistry fellow, presented a poster under the direction of Dr. Mitchell Scott, entitled “Pseudohypercreatininemia due to a monoclonal IgM kappa paraprotein” which received a Distinguished Abstract Award from the National Academy of Clinical Biochemistry.

Khushbu Patel, also a clinical chemistry fellow, presented a poster under the direction of Dr. Ann Gronowski, entitled “Establishing reference intervals for hCG in postmenopausal women” which received 3rd place in the student poster contest.

On-line Laboratory Medicine Resources

There are plenty of free, on-line laboratory medicine resources and the LGM faculty help make them possible!

http://transfusionnews.com/ (click the link)  Dr. Ron Jackups is Co-Founder & Co-Editor of Transfusion Medicine Questions & Associate Editor of Transfusion News

Blood banking, transfusion medicine, tissue transplantation, blood policies, hematopoietic stem cells, cellular therapies & related fields. “Question of the Day” every Monday, Wednesday and Friday.

https://pathquestions.com/cgi-bin/q.fpl?c=2 (click the link)  Dr. Carey-Ann Burnham is a Founder and Co-Editor.

Medical microbiology questions focused on clinical microbiology and infectious diseases are sent to subscribers with a personalized e-mail link three times each week.

https://labmedicinesblog.com/ (click the link)  Dr. Sarah Brown is a monthly contributor.

A blog for lab medicine professionals. Topics range from microbiology case presentations to quality issues to day-to-day practice of lab medicine. Anyone can follow the blog!

http://www.pregnalcab.net/ (click the link)  Dr. Ann M. Gronowski is co-founder & frequent contributor.

A blog resource for anyone interested in gaining a better understanding of laboratory testing during pregnancy.