

**September 2016**

### **Carbapenem-Resistant Enterobacteriaceae (CRE) Update**

The Enterobacteriaceae are a large family of gram-negative bacilli that includes *Escherichia coli*, *Klebsiella* species, and *Enterobacter* species. They are normal inhabitants of the gastrointestinal tract of humans and animals and a common cause of community-acquired and health-care-associated infections (HAI). They have gradually developed resistance to broad spectrum antibiotics through several mechanisms. In the United States, these resistant strains are usually treatable with carbapenem antibiotics including imipenem, meropenem, doripenem, and ertapenem. However, new classes of enzymes that hydrolyze & inactivate the carbapenems are being detected in the United States. Carbapenem-resistant Enterobacteriaceae (CRE) were uncommon in the United States before 2000, but have increased in hospitals over the past 16 years. Invasive bloodstream infections with CRE have mortality rates as high as 50%. Therefore, they have become a serious infection control concern.

The most common carbapenemase to date is found in *Klebsiella pneumoniae*, and is hence referred to as KPC. This carbapenemase is plasmid-mediated, which facilitates transfer between bacteria. Other enteric bacteria in which this type of plasmid-mediated carbapenemase has been reported include *E. coli*, *K. oxytoca*, *S. marcescens*, *E. cloacae*, *E. aerogenes*, *C. freundii*, and *Salmonella*. *Klebsiella pneumoniae* carbapenemase (KPC) is encoded by a highly transmissible gene that has now spread widely throughout the United States and around the world. In addition to KPC, other carbapenemases have emerged among Enterobacteriaceae outside the United States. The best known example is the New Delhi metallo-beta-lactamase (NDM). The unfortunate clinical significance of these carbapenemase-producing organisms is that they are usually resistant to most other anti-microbials, including all classes of beta-lactam agents, and often aminoglycosides and quinolones as well.

More recently, other mechanisms besides carbapenemase enzymes that may render Enterobacteriaceae resistant to carbapenems have been recognized. Most commonly this would include production of AmpC beta-lactamase in combination with porin mutations of the bacterial cell membrane. Saint Luke's Microbiology has recently identified ertapenem-resistant *Enterobacter cloacae* isolates that appear to have this resistance mechanism.

Due to recognition of multiple types of carbapenem resistance, the CDC recently revised its definition of CRE to include any Enterobacteriaceae that is resistant to imipenem, doripenem, meropenem, or ertapenem OR is found to produce a carbapenemase. Effective immediately, Saint Luke's Microbiology susceptibility reports will include the following comment to alert physicians when a CRE isolate is identified: "This enteric organism is resistant to one or more carbapenems (CRE). Inpatients require contact isolation."

### **New Hepatitis A IgG Replaces Hepatitis A Total Antibody**

Effective in early October, hepatitis A total antibody (IgM & IgG combined) will be replaced with a newly available hepatitis A IgG assay. Hepatitis A IgG antibodies are detectable early in the convalescent phase of an acute infection or post-vaccination. Hepatitis A IgG antibody is detectable for decades following vaccine or infection, and a reactive result is indicative of protective immunity. Hepatitis A IgM antibody is detectable at the time of symptom onset and generally remains detectable for 3 to 6 months following an acute infection. Occasionally hepatitis A IgM may persist for years or be false positive.

Hepatitis A is transmitted by the fecal-oral route, either through person-to-person contact or ingestion of contaminated food or water. Outbreaks of food borne hepatitis A have been reported in the U.S. due to imported produce and food products. Blood-borne transmission is possible, but rare. The

incidence of hepatitis A in the United States has dropped substantially due to availability of an effective vaccine, although globally over 1 million acute infections occur per year. According to CDC data, there were twelve cases of acute hepatitis A reported in Missouri and Kansas for the year 2015 (six cases each). Symptoms of hepatitis A infection include nausea, vomiting, abdominal pain, fever, jaundice, & pruritus.

Hepatitis A is generally a self-limited infection that does not have a chronic phase. There is a 1% incidence of fulminant liver failure due to acute hepatitis A infection, predominantly in patients with underlying liver disease. The incubation period for an acute infection averages 28 days. The virus can be shed in feces for up to six months, and is transmissible for 2 weeks prior to the onset of symptoms. Travelers to areas of the world with high transmission rates of hepatitis A (e.g. Central and South America, Eastern Europe, and parts of Asia) should consider vaccination, if not previously immune.

For detection of acute hepatitis A infection, physicians should order both hepatitis A IgM and hepatitis A IgG antibodies. For confirmation of immunity, hepatitis A IgG antibody is the test of choice. Hepatitis A serology is performed Monday through Friday. Specimen requirement is one red top serum gel tube of blood.

### **Peripheral Blood Eosinophilia**

Absolute eosinophil count refers to the number of circulating eosinophils in the peripheral blood (in cells/ $\mu$ L) and can be mild (500-1500 eosinophils/ $\mu$ L), moderate (1500-5000 eosinophils/ $\mu$ L), or severe (>5000 eosinophils/ $\mu$ L). The evaluation of peripheral blood eosinophilia is important due to the complications of associated end-organ damage, which are usually unrelated to the etiology and severity of eosinophil count. A patient with mild peripheral blood eosinophilia may present with significant organ involvement. Two terms commonly used to describe eosinophilia include – Hypereosinophilia, defined as moderate to severe eosinophilia (>1500 eosinophils/ $\mu$ L) with or without end-organ damage, and Hypereosinophilic syndrome (HES), defined as hypereosinophilia demonstrated on at least two

different occasions along with associated end-organ damage.

Etiology of absolute eosinophilia varies from benign conditions (allergic and infectious) to neoplastic disorders (myeloproliferative and lymphoproliferative neoplasm). The primary goal of initial evaluation is to identify disorders requiring specific treatments such as parasitic infections, drug-hypersensitivity or leukemia. The following laboratory tests should be part of initial evaluation –

- CBC with differential and smear review for abnormalities in other cell lines and dysplastic features
- Serum chemistries, creatinine, urine analysis (for renal insufficiency)
- Serum B12 level (elevated in myeloproliferative disorder)
- Serologic testing for parasites especially in immigrant population, patients with travel history and/or dietary history of consumption of raw/incompletely cooked food (Strongyloides, Toxocara, Trichinella, Schistosomiasis, Ancylostomiasis, Ascariasis and Filariasis)
- Stool studies for ova and parasites
- Liver function tests (for hepatic involvement)
- Troponin levels (for cardiac involvement)
- Flow cytometric analysis for lymphocyte subsets

Exposure history including occupational/recreational activities, medications and over the counter remedies and food are important in the initial evaluation. Examples include a risk for strongyloides infection in miners, a risk for ascariasis in slaughterhouse workers, and a risk for schistosomiasis in river rafters. Drug reaction to penicillins, cephalosporins, NSAIDs, ranitidine, allopurinol, phenytoin, aspirin, hydrochlorothiazide, and carbamazepine may present with eosinophilia. Referral to a specialist is appropriate if a thorough evaluation has been conducted and the cause of persistent eosinophilia is not found.