

## **Ever Evolving Enterobacteriaceae**

*Enterobacteriaceae* are a group of gram negative non spore forming bacilli. This group consists of organisms like *Citrobacter*, *Enterobacter*, *Escherichia coli (E.coli)*, *Klebsiella*, *Morganella*, *Proteus*, *Providencia*, *Serratia*, *Salmonella*, *Shigella*, and *Yersinia*. Most of these organisms cause clinically significant infections of which *E.coli* and *Klebsiella* are commonly associated with Healthcare Acquired Infections (HAI).

Multiple resistance mechanisms could be present in these organisms simultaneously. As per the popular quote “Antimicrobial resistance follows antimicrobial use as surely as night follows day”. These mechanisms are due to excessive production of plasmid derived AmpC beta-lactamase or plasmid mediated extended-spectrum beta lactamses (ESBL). These ESBL producing organisms, mostly seen in *E.coli* and *Klebsiella* species, are typically resistant to penicillins, cephalosporins, and monobactams, sometimes to Aminoglycosides. Recently, resistance has been seen to the most potent available class of  $\beta$ -lactam, the Carbapenems, (Doripenem, Imipenem, Meropenem and Ertapenem).

*Enterobacteriaceae*, mainly the *E.coli* and *Klebsiella* species, which are resistant to Carbapenems, or Carbapenem-resistant *Enterobacteriaceae* (CRE) are an emerging, important health care challenge, resistance to almost all available current antibiotics. CRE infections include pneumonia, wound or surgical site infections, blood stream infections and meningitis. Currently, Carbapenem - resistant *Klebsiella pneumoniae* (CRKP) is the CRE species commonly seen in United States.

Health care providers should be concerned about CRKP infections as they are associated with high rates of morbidity and mortality, treatment challenges, increased length of stay, and increased cost. CRKP is seen among patients who are critically ill, have a prolonged hospitalization and are exposed to invasive devices. Outbreaks have been seen in long term acute care hospitals (LTACH) and long term care facilities (LTC) in the US. The mechanism of resistance for CRKP is production of carbapenamase enzyme known as *bla<sub>kpc</sub>* or KPC. The newly found mechanisms were production of New Delhi metallo-beta-lactamase (NDM-1) likewise, newer mechanisms have been found all around the world in different *Enterobacteriaceae* species.

Due to the threats and challenges posed by these emerging organisms, strict infection prevention and control measures are necessary to manage and limit further emergence of resistant organisms. CDC and Healthcare Infection Control Practices Advisory Committee (HICPAC) guidance can be found at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5810a4.htm> and in table below.

The Communicable Disease Reporting Rule, 410 IAC 1-2.3, requires the reporting of diseases caused by drug-resistant organisms and emerging infectious diseases (410 IAC 1-2.3-49 (2)(f)(2)). Contacts at ISDH include, S. Kariyanna, 317-233-7329 or J. Svendsen, 317-233-7825.

**BOX. Infection prevention and control guidance for carbapenem-resistant *Enterobacteriaceae* (or carbapenemase-producing *Enterobacteriaceae*) in acute care facilities — CDC and the Healthcare Infection Control Practices Advisory Committee**

### **Infection Prevention and Control**

- All acute care facilities should implement contact precautions for patients colonized or infected with carbapenem-resistant *Enterobacteriaceae* (CRE) or carbapenemase-producing *Enterobacteriaceae*. No recommendation can be made regarding when to discontinue contact precautions.

### **Laboratory**

- Clinical microbiology laboratories should follow Clinical and Laboratory Standards Institute guidelines for susceptibility testing (1) and establish a protocol for detection of carbapenemase production (e.g., performance of the modified Hodge test).
- Clinical microbiology laboratories should establish systems to ensure prompt notification of infection prevention staff of all *Enterobacteriaceae* isolates that are nonsusceptible to carbapenems or *Klebsiella* spp. or *Escherichia coli* isolates that test positive for a carbapenemase.

### **Surveillance**

- All acute care facilities should review clinical culture results for the preceding 6–12 months to determine whether previously unrecognized CRE have been present in the facility.
  - If this review identifies previously unrecognized CRE, a point prevalence survey (a single round of active surveillance cultures) should be performed to look for CRE in high-risk units (e.g., intensive care units, units where previous cases have been identified, and units where many patients are exposed to broad-spectrum antimicrobials).
  - If this review does not identify previously unrecognized CRE, monitoring for clinical infections should be continued.
- If CRE or carbapenemase-producing *Klebsiella* spp. or *E. coli* are detected from one or more clinical cultures **OR** if the point prevalence survey reveals unrecognized colonization, the facility should investigate for possible transmission by:
  - Conducting active surveillance testing of patients with epidemiologic links to a patient with CRE infection (e.g., patients in the same unit or who have been cared for by the same health-care personnel).
    - Continue active surveillance periodically (e.g., weekly) until no new cases of colonization or infection suggesting cross-transmission are identified.
    - If transmission of CRE is not identified after repeated active surveillance testing, consider altering the surveillance strategy by performing periodic point prevalence surveys in high-risk units.
  - In areas where CRE are endemic, an increased likelihood exists for importation of CRE, and the procedures outlined might not be sufficient to prevent transmission. Facilities in such areas should monitor clinical cases and consider additional strategies to reduce rates of CRE as described in the 2006 Tier 2 guidelines for management of multidrug-resistant organisms in health-care settings (2). Recommendations for rate calculations have been described previously (3).

### **References**

1. Clinical and Laboratory Standards Institute. 2009 performance standards for antimicrobial susceptibility testing. Nineteenth information supplement (M100-S19). Wayne, PA: Clinical and Laboratory Standards Institute; 2009.
2. CDC, Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings, 2006. Atlanta, GA: US Department of Health and Human Services, CDC, Healthcare Infection Control Practices Advisory Committee; 2007. Available at <http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroguideline2006.pdf>.
3. Cohen AL, Calfee D, Fridkin SK, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper. *Infect Control Hosp Epidemiol* 2008;29:901–13.

## Additional CRE Resources

1. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5810a4.htm>
2. [http://www.cdc.gov/ncidod/dhqp/ar\\_kp.html?zbrandid=3032&zidType=CH&zid=1693961&zsubscriberId=751517065](http://www.cdc.gov/ncidod/dhqp/ar_kp.html?zbrandid=3032&zidType=CH&zid=1693961&zsubscriberId=751517065)
3. <http://www.infectioncontrolday.com/news/2010/10/survey-shows-rise-in-new-antibiotic-resistant-bacteria-in-chicago-area.aspx>
4. <http://www.infectiousdiseaseneews.com/print.aspx?id=70587>
5. <http://www.bio-medicine.org/biology-news-1/Press-statement-on-new-CDC-MMWR-on-Klebseilla-pneumonia-Carbapenemase-producing-organisms-7568-1/>
6. <http://www.medscape.com/viewarticle/713709?src=mp&spon=24&uac=96567PY>
7. [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5937a4.htm?s\\_cid=mm5937a4\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5937a4.htm?s_cid=mm5937a4_w)
8. [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5924a5.htm?s\\_cid=mm5924a5\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5924a5.htm?s_cid=mm5924a5_w)
9. <http://www.cdc.gov/mmwr/pdf/wk/mm59e0921.pdf>
10. CDC, Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings, 2006. Atlanta, GA: US Department of Health and Human Services, CDC, Healthcare Infection Control Practices Advisory Committee; 2007. Available at <http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroguideline2006.pdf>.
11. Clinical and Laboratory Standards Institute. 2009 performance standards for antimicrobial susceptibility testing. Nineteenth information supplement (M100-S19). Wayne, PA: Clinical and Laboratory Standards Institute; 2009.