“Prevention of Transmission of the ‘Superbug’ Carbapenem-Resistant Enterobacteriaceae (CRE) during Gastrointestinal Endoscopy”

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Objectives

Today’s objectives are to:

1. Discuss “CRE,” or carbapenem-resistant *Enterobacteriaceae*:
   - What are they?

2. Discuss the details of some recent outbreaks of CRE linked to contaminated gastrointestinal (GI) endoscopes;
   - What factor(s) were to blame?

3. Provide some recommendations for the prevention of CRE transmissions during GI endoscopy.
   - What measures reduce the risk of CRE outbreaks?

Email your questions to: Larry@LFM-HCS.com
Part 1: CRE and Related Superbugs

1. “What is a superbug?”
   — According to the Centers for Disease Control and Prevention (CDC):
     › “superbugs”
       ✓ are certain “nightmarish bacteria” that pose a public health threat primarily
         ▪ because of 3 specific traits:
           1) superbugs are resistant to many --- some are resistant to virtually all --- classes of antibiotics;
2) Some superbug infections are associated with high mortality rates.

✓ For example, bloodstream infections caused by some superbugs
  – have a mortality rate of:
    ⇒ as high as 40% - 50%; and

3) Some superbugs can exchange their genetic material with other bacteria

✓ causing antibiotic-susceptible strains
  – to become antibiotic-resistant strains.
2. “What are ‘CRE’?”

— “CRE,” or

› carbapenem-resistant *Enterobacteriaceae* (pronounced: \,ent-ə-rō-,bak-,tir-ē-ˈā-sē-,ē\),

⇒ are an important superbug that has recently emerged, with implications to gastrointestinal (GI) endoscopy.

— For background, *Enterobacteriaceae*

✓ is a family of more than 70 genera of non-spore-forming bacteria.

✓ *Escherichia coli* and *Klebsiella sp.* are members of this family.
— Other traits of *Enterobacteriaceae*:

- They may be found in water and soil
  - as well as in human intestinal flora.
- Many are opportunistic, primarily infecting ill patients.

— A most important trait of CRE is their resistance to virtually every antibiotic drug

  - including --- *notably* --- carbapenems.

  - These are a type of β-lactam antibiotic that is
    - used as a “last defense” or “last resort” against serious bacterial infections.
3. “When were CRE first discovered?”

— Only recently have some *Enterobacteriaceae* developed resistance to carbapenems.

 o One strain of CRE --- namely, *Klebsiella pneumoniae* *(pronounced: nōō-mō’nē-ē’)* ---

  was first identified in a hospital (unrelated to GI endoscopy) in North Carolina in 2001.

✓ Since then, CRE have been identified in healthcare facilities throughout the U.S.
4. “How significant a threat is CRE?”

- In one word: Very.
  
  — More and more strains of Enterobacteriaceae in hospitals are becoming CRE.
  
  — According to USA TODAY, CRE are “the biggest threat to patient safety in the hospital” (March 6, 2013).
  
  — According to the CDC, CRE is responsible for more than 9,000 healthcare-associated infections annually in the U.S.

- Indeed, CRE outbreaks recently linked to GI endoscopes are now a national concern.
5. “In what *settings* have CRE been confirmed?”

— CRE are primarily found in:

  › hospitals;
  › long-term care facilities; and
  › nursing homes (but not ordinarily in the community).

  ○ And as we said, reports have recently linked CRE outbreaks to

     ⇔ contaminated GI endoscopes

     ▪ causing a national stir.
6. “What are some examples of CRE?”

— Specific strains of *Enterobacteriaceae* that are resistant to carbapenems (i.e., CRE) include:

  - *E. coli*
  - *Klebsiella pneumoniae*

⇒ An important mechanism by which CRE can become resistant to carbapenems is through their production of enzymes called:

  ✓ carbapenemases

    › which chemically degrade carbapenems.)
7. “What are some examples of carbapenemases enzymes?”

— The best example is “KPC,” or *Klebsiella pneumoniae* carbapenemase, which

  - was first reported in North Carolina in 2001;
  - is the most common carbapenemase in the U.S.; and
  - is encoded by the $bla_{KPC}$ gene.

— Another example of a carbapenemase enzyme produced by some CRE is:

  - “NDM,” or the New Delhi metallo-β-lactamase,

    $\Rightarrow$ which is encoded by the $bla_{NDM}$ gene.
8. “What is a ‘β-lactam antibiotic’? And what is a ‘β-lactam ring’”?

— There are many different types of antibiotics,

  ▪ one type of which is called a:

    › β-lactam antibiotic.

  ✓ These antibiotics necessarily feature

    — a β-lactam ring in their molecular structure.

  ⇒ As noted earlier, carbapenems are a type of β-lactam antibiotic.
The β-lactam ring of a β-lactam antibiotic looks like this:

⇒ Note the 4-membered β-lactam ring, above, in the core structure of a carbapenem, below:

⇒ Other examples of β-lactam antibiotics include:

✓ penicillins (e.g., penicillin G, methicillin);
✓ cephalosporins (e.g., Keflex); and
✓ monobactams (e.g., Azactam).
9. “CRE cause what types of infections?”

— CRE can cause many types of infections, including:

✓ urinary tract infections (UTIs), which are the most common type of CRE infections in hospitals;

✓ bloodstream infections
  › which are associated with a mortality rate of as high as 50%;

✓ GI tract infections (e.g., biliary tract infections); and

✓ ventilator-associated pneumonia.
Part 2: CRE Transmission during GI Endoscopy

10. “Prior to the recent emergence of CRE, GI endoscopes primarily transmitted which types of bacteria?”

— Previously, outbreaks linked to contaminated GI endoscopes, although rarely reported, were often (but not always) due to:

⇒ side-viewing duodenoscopes (also called “ERCP endoscopes”)

✓ transmitting *Pseudomonas aeruginosa*. 
11. “What were some of the common causes of these past reports of GI endoscopes transmitting bacteria?”

- The common causes of these outbreaks documented primarily in the 1980s and 1990s were reported to be:
  
  ✓ insufficient cleaning;
  
  ✓ inadequate high-level disinfection; and/or
  
  ✓ improper drying (and/or storage)

  – of the GI endoscope’s internal channels,

  o often of the ERCP endoscope’s elevator wire channel

    ▪ which in older models of ERCP endoscopes was always open, exposed.
12. “What are some examples of past reports of ERCP endoscopes transmitting disease prior to 2001 (when CRE first emerged)?”

— Some prototypical examples of past reports of ERCP endoscopes transmitting disease (prior to CRE’s emergence in 2001) include:

✓ Allen et al. (1987);
✓ Alvarado et al. (1991); and
✓ Struelens et al. (1993), among others.*

* These references are available upon request.
13. “Since 2001, have GI endoscopes transmitted CRE?”

— Yes. Several outbreaks of CRE (or a related superbug) linked to a GI endoscope have been reported in the U.S. --- the first in 2008.

— Examples of these published reports include:

  ✓ Alrabaa et al. (2013) (Florida, USA):
    ⇒ this was the 1st report in the U.S. to link a CRE outbreak in 2008 to a contaminated GI endoscope;

  ✓ Aumeran et al. (2010) (France);

  ✓ Bajolet et al. (2013) (France); and

  ✓ Carbonne et al. (2010) (France).*

* These references are available upon request.
For example, Alrabaa et al. (2013)* report that 7 patients in Florida between 2008 and 2009 were infected or colonized with CRE following ERCP.

- An ERCP endoscope was found to have transmitted the CRE.
  - These authors report that the “elevator area” of the ERCP endoscope remained contaminated with CRE resulting in disease transmission.

14. “What do these several recent reports share in common?"

— Most of these “superbug” outbreak reports share in common:

i. the infectious agent: \( \Rightarrow \) CRE (or a related superbug);

ii. the mode of transmission: \( \Rightarrow \) an ERCP endoscope, which remained contaminated

  • despite reportedly being manually cleaned and disinfected consistent with manufacturers’ instructions; and

iii. the same clinical outcome: \( \Rightarrow \) patient morbidity, mortality. ...

— Reports of CRE outbreaks now routinely conclude that:

  › the duodenoscope's complex design --- which hinders thorough cleaning --- was the primary cause of patient infection.
15. “Can you discuss some of the U.S. cities where reports have linked outbreaks of CRE to contaminated ERCP endoscopes?”

- “Hospital X’s” superbug outbreak in 2013 near Chicago
  - was the first to cause CRE infections linked to contaminated duodenoscopes to be placed
    - under a powerful regulatory and political microscope.

- Since then, hospitals in the following U.S. cities have similarly linked CRE outbreaks to ERCP:
  - Seattle (WA)
  - Los Angeles (CA)
  - Pittsburgh (PA)
  - Philadelphia (PA)
  - and Florida (in 2008), among a few other cities.
16. “How have hospitals terminated their CRE outbreaks?”

- **CDC**: “Hospital X” near Chicago ended its CRE outbreak by changing the reprocessing protocol for its ERCP endoscopes from automated high-level disinfection to ethylene oxide (EtO) gas sterilization.

- Alternatively, some hospitals have employed the “test-and-hold” surveillance policy (to prevent CRE infections), whereby:
  - endoscopes are reprocessed, microbiologically sampled, and then quarantined for 2 days until the culture’s results are “CRE-negative.” …

- Both of these actions, however, remove the endoscope from service for 1-2 days, likely requiring the purchase of more ERCP endoscopes.
17. “Does disinfection destroy CRE?”

1) **Yes.** Aumeran et al.* (2010) report that a peracetic acid-based high-level disinfectant (sold in Europe)

   - was “fully effective”

   - against a multidrug-resistant strain of *K. pneumoniae*.

2) Further, several EPA-registered intermediate-level disinfectants

   - are labeled to destroy CRE in 1-2 minutes.

   ⇒ Therefore, high-level disinfection is expected to destroy CRE even more rapidly.

18. “What are some recommendations to prevent CRE outbreaks via contaminated GI endoscopes?”

— Recommendations include:

› For now, consider using EtO gas to sterilize ERCP endoscopes.

• For its part, the CDC has not yet recommended a “wholesale switch” to sterilization (of ERCP endoscopes). *

› Also consider the merits and cost-effectiveness of employing the previously mentioned “test-and-hold” surveillance policy.

— Also practice the following steps:

› **Manually clean or flush (with detergent) the ERCP endoscope’s:**
  ✓ **elevator wire** channel (if it’s open and exposed); and
  ✓ **forceps elevator mechanism and recess**, which requires **additional, rigorous** manual cleaning with a brush and syringe.

  › **Remember:** Reports suggest that even manual cleaning may not be entirely effective to prevent CRE infections.

› **Manually clean and flush the exposed elevator wire channel** of “EUS” (ultrasound) endoscopes, too.

› **Manually clean** these complex endoscope models

  ✓ **even if** using an “AER” cleared by the FDA to “eliminate manual cleaning and brushing.”

› **Consider manually disinfecting** these endoscope models, too (not using an AER).
Attention:

— Download for free an article I wrote in the “World Journal of Gastrointestinal Endoscopy” (October, 2014):

  › “Risk of transmission of carbapenem-resistant Enterobacteriaceae and related ‘superbugs’ during gastrointestinal endoscopy.”

— Visit: http://goo.gl/N6YxHB (this article is free thanks to an educational grant provided by an endoscope manufacturer).

  › This peer-reviewed article provides additional recommendations to prevent CRE transmissions during GI endoscopy.
Completed Objectives

Completed objectives:

1. We discussed “CRE”;
2. We discussed some of the details and causes of recent outbreaks of “CRE” linked to contaminated GI endoscopes; and
3. We discussed some recommendations for the prevention of CRE transmission during GI endoscopy.
The End

*Thank you* for your attention to and interest in these topics.

Contact me if you have any questions:

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