The ABC’s of ESBL: Extended-Spectrum Beta-Lactamases
(everything you wanted to know but were either too scared or too lazy to ask!)

Gonzalo Bearman MD, MPH
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Epidemiology

• Today, 30 – 50% of E. coli are resistant to ampicillin and amoxicillin due to a beta-lactamase
• 90% of S. aureus produce a beta-lactamase which produces resistance to penicillin
• S. aureus still susceptible to semi-synthetic penicillins, cephalosporins, and carbapenems
• ESBLs have been reported for E. coli, Klebsiella Enterobacter, Proteus, Pseudomonas, Salmonella, Serratia
Beta-Lactamases: What are they?

- Enzymes produced by certain bacteria that provide resistance to certain antibiotics
- Produced by both gram positive and gram negative bacteria
- Found on both chromosomes and plasmids
Beta-lactamases

- Are primary mode of resistance to beta-lactam antibiotics
- Produced by some gram positive bacteria and virtually all gram negative bacteria
ESBL?

• Resistance that is produced through the actions of beta-lactamases.
• Extended spectrum cephalosporins, such as the third generation cephalosporins, were originally thought to be resistant to hydrolysis by beta-lactamases!
• Not so!
  – mid 1980's it became evident that a new type of beta-lactamase was being produced by *Klebsiella & E coli* that could hydrolyze the extended spectrum cephalosporins.
  – These are collectively termed the
  • 'extended spectrum beta-lactamases' (ESBL's)
Mechanism of Action

• Hydrolysis of beta-lactam ring of basic penicillin structure
• Hydrolysis = adding a molecule of $\text{H}_2\text{O}$ to C-N bond with enzyme action
  – This opens up the ring, thus making the drug **ineffective!**
Plasmids

- Rings of extrachromosomal DNA
- Can be transferred between different species of bacteria conjugation
- Carry resistance genes
- Most common and effective mechanism of spreading resistance from bacteria to bacteria
Beta-lactam Antibiotic Examples

- **Penicillins:**
  - Penicillin, amoxicillin, ampicillin

- **Cephalosporins:**
  - Ancef, Rocephin, Keflex, Cefotan

- **Carbapenems:**
  - Imipenem, meropenem
Beta-lactamase inhibitor

- Clavulanic acid + amoxicillin = Augmentin
- Clav. Acid + ticarcillin = Timentin
- Sulbactam + ampicillin = Unasyn
- Tazobactam + piperacillin = Zosyn

**Good News:** Beta-lactamase inhibitors inhibit the beta-lactamase thereby not allowing the molecule to hydrolyze the antibiotic. Most ESBLs remain susceptible to Beta-lactamase inhibitors

**Bad News:** some ESBL producing bacteria produce large amounts of beta-lactamase thereby overwhelming the beta-lactamase inhibitors
The story is more complicated….

- Multiple antimicrobial resistance is often a characteristic of ESBL producing gram-negative bacteria.
  - Ceftazidime
  - Cefotaxime
  - Ceftriaxone
  - Aztreonam

- Genes encoding for ESBLs are frequently located on plasmids that also carry resistance genes for:
  - Aminoglycosides
  - Tetracycline
  - TMP-SULFA
  - Chloramphenicol
  - Fluoroquinolones
Take home message: ESBLs are harbingers of multidrug resistance
However: ESBL producing organisms are still susceptible to:

- Cephamycins:
  - Cefoxitin
  - Cefotetan
- Carbapenems:
  - Meropenem
  - Imipenem

Carbapenems are becoming the therapeutic option of choice
What are the clinical implications?

- Can result in treatment failure
  - Morbidity and mortality
- Several outbreaks have occurred
- If an ESBL is detected, all penicillins, cephalosporins, and aztreonam should be reported as “resistant”, regardless of in vitro susceptibility test results
Screening for ESBLs

- Organisms most commonly tested:
  - *K. pneumoniae*, *K. oxytoca*, *E. coli*
  - Drugs used: cefpodoxime, *ceftazidime*, aztreonam, cefotaxime, *ceftriaxone*
Infection Control?

As infection control nurses your job is to ensure that adequate precautions are taken to minimize the risk of cross transmission!

– Contact precautions
  • Cohort patients during outbreaks
– Promote meticulous hand hygiene practices
– Reminders to HCW staff
  • Electronic flagging of medical record
  • Placing stickers on charts
– When are contact precautions discontinued?
The End!