The ABC’s of ESBL for Infection Control Nurses:
-Extended-Spectrum Beta-Lactamases-

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Epidemiology

• Today, 30 – 50% of E. coli are resistant to ampicillin and amoxicillin due to a beta-lactamase
• 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 \textit{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
- **Carabapenems:**
  - 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
NCCLS ESBL Screening

• For isolates:
  – *K.pneumoniae, E.coli and K.oxytoca*:
  – 1\textsuperscript{st} step- screen using:
    • Ceftazidime, ceftriaxone, cefotaxime, cefpodoxime, or aztreonam
  – 2\textsuperscript{nd} Step: If MIC $>$ 2 mcg/ml then:
    • Ceftazidime and cefotaxime alone and in combination with clavulanate
    • Positive test: greater than a three-fold reduction in MIC for combination versus single agent
      – ESBL status of organism is now highly likely
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
Management of ESBL infections

• Pharmacotherapy
  – Avoid:
    • Ceftazidime, ceftriaxone, cefotaxime
    • Ticarcillin/Clavulanate, Ampicillin/Sulbactam
    • Aztreonam
    • Fluoroquinolones, aminoglycosides, TMP/SULFA, chloramphenicol and tetracyclines
Management of ESBL infections

• Pharmacotherapy:
  – Treatment of choice for serious infections
    • Carbapenems
      – Stable in the presence of most beta-lactamases
      – Examples
        » Imipenem
        » Meropenem
    • Restrict the use of 3\textsuperscript{rd} generation cephalosporins.
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 about Patient ESBL status
  - Electronic flagging of medical record
  - Placing stickers on charts
- When are contact precautions discontinued?
  - No specific guidelines:
    - Resolution of infectious process
The End!