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 H_2O 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

Bacterial Conjugation

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

NCCLS ESBL Screening

- **For isolates:**
  - ***K.pneumoniae, E.coli and K.oxytoca :***
  - 1st step- screen using:
    - Ceftazidime, ceftriaxone, cefotaxime, cefpodoxime, or aztreaonam
  - 2nd 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 3rd 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!