

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?

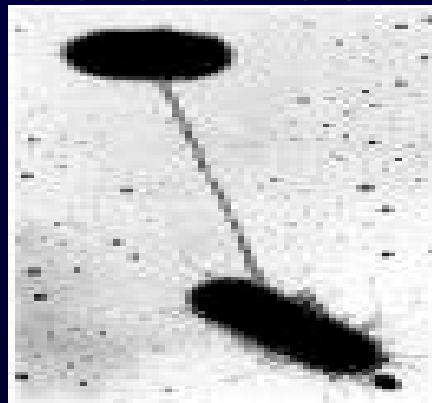
- Resistance that is produced through the actions of beta-lactamases.
- Extended spectrum cephalosporins, such as the third generation cephalosporins, were originally thought to be resistant to hydrolysis by beta-lactamases!
- **Not so!**
 - mid 1980's it became evident that a new type of beta-lactamase 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 H₂O 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 aztreonam
 - 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:

- Cephameycins:
 - 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!

