ESBL, AmpC, and CPO Bacteria

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BACKGROUND

- Some Gram-negative bacilli produce enzymes (β-lactamases) that hydrolyze penicillins and cephalosporins (i.e. β-lactams), making the broad-spectrum β-lactamase-producing organisms
- There are many β-lactamases, making classification and terms confusing
- The common classes of broad-spectrum β-lactamases are:
  - **ESBL**s (extended spectrum β-lactamases)
  - **AmpC β-lactamases** (those produced by "SPACE/SPICE" organisms)
  - **CPO** (carbapenemase-producing organisms)
- There is little evidence that these organisms are more virulent than their susceptible counterparts

ESBL

Genes that encode for ESBLs are always on and found on transmissible plasmids in all enterobacteriacease, especially *E. coli* and *K. pneumoniae*.

AmpC

SPACE or SPICE are acronyms for gram-negative bacteria that have inducible (i.e. not always on—they get turned on or induced after exposure to β-lactam antibiotics) chromosomal **AmpC** β-lactamase genes

Organisms in this group include: ***S****erratia*, ***Pseudomonas***, ***A****cinetobacter*/**I**ndole-positive Proteae (i.e. Morganella, Proteus, and Providencia), ***C****itrobacter*, and ***E****nterobacter* species.

CPO

A collection of organisms with differing mechanisms of resistance (e.g. *Klebsiella pneumoniae* plasmid-borne (KPC), and New Delhi metallo-β-lactamase-1 (NDM-1))

EMPIRIC CHOICES

- Penicillins (with or without β-lactamase inhibitors) and cephalosporins should generally be avoided.
- Carbapenems are favoured for ESBL and AmpC organisms empirically: ertapenem can be used for most ESBLs, although may not be sufficient for all AmpC bacteria (e.g. *Pseudomonas aeruginosa* is uniformly resistant to ertapenem)
- Fosfomycin can be used for UTIs
- Fluoroquinolones and TMP-SMX can often be used, but should be prescribed only after microbiology lab susceptibility is demonstrated

ALTERNATIVES FOR ALLERGIES

- Cross-reactivity for penicillin allergies with carbapenems is ~ 1% (see Clinical Summary on β–lactam allergy)

RISK FACTORS AND OTHER TREATMENT CONSIDERATIONS

- Consider coverage for broad-spectrum β-lactamase-producing organisms in empiric treatment regimens for patients with risk factors and severe, life-threatening infections; however, if no ESBL/AmpC/CRO organism isolated, switch to less broad-spectrum coverage
- Risk factors for infections caused by multidrug-resistant β-lactamase-producing organisms include:
  - Previous and/or prolonged hospital stay
  - Hemodialysis
  - Prior and/or prolonged antibiotic use
  - Prior infection or colonization with these organisms within past 3 months
  - Travel to areas with high rates of resistance
  - NB: There are relatively high rates of CROs in some pockets of the Greater Toronto Area with a high population originating from South Asia.

Reference:
Harris PNA, Tambyah PA, Lye DC, et al. Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance: A Randomized Clinical Trial. *JAMA.* 2018;320(10):984–994. doi:10.1001/jama.2018.12163