

BACKGROUND

- ✦ Some Gram-negative bacilli produce “broad-spectrum” β -lactamases that can hydrolyze penicillins and cephalosporins
- ✦ The common classes of broad-spectrum β -lactamases are ESBLs (extended spectrum β -lactamases) and ampC beta-lactamases (those produced by “SPICE” organisms)
- ✦ While more challenging to treat (due to resistance issues), there is little evidence that these organisms are more virulent than susceptible Gram-negative bacteria

ESBL

- ✦ Genes that encode for ESBLs are primarily found on plasmids in some strains of *E. coli*, *K. pneumoniae*, and occasionally in *Proteus* species
- ✦ Although ESBLs may be inhibited by β -lactamase inhibitors (e.g. tazobactam) in vitro, there is concern of higher treatment failure when these agents are used in vivo

“SPICE”

- ✦ Colloquial acronym for gram-negative bacteria that have inducible, chromosomal β -lactamase genes known as AmpC
- ✦ Resistance may not be detectable initially but appears after a period of exposure to β -lactam antibiotics
- ✦ Organisms in this group include: *Serratia*, *Providencia*, “Indole-positive” *Proteus* species, *Citrobacter*, and *Enterobacter* species
- ✦ Other organisms in this class include: *Acinetobacter*, *Cronobacter*, *Edwardsiella*, *Hafnia*, *Morganella*, and rarely *Pseudomonas*

EMPIRIC CHOICES

- ✦ Penicillins (with or without β -lactamase inhibitors) and cephalosporins should generally be avoided
- ✦ Options for therapy (pending susceptibilities) include: nitrofurantoin (for cystitis only), trimethoprim-sulfamethoxazole, carbapenems, aminoglycosides and fluoroquinolones
- ✦ For severe or life threatening illness: meropenem 1g IV q8h (2g IV q8h for CNS infections) OR ertapenem 1g IV q24h (if not treating *Pseudomonas*, *Acinetobacter* or CNS infection)
- ✦ Oral options (e.g. TMP-SMX or fluoroquinolones) may be considered in stable or improving patients

ALTERNATIVES FOR ALLERGIES

- ✦ Cross-reactivity for penicillin allergies with carbapenems is ~ 1% (see Clinical Summary on β -lactam allergy)
- ✦ Carbapenems may, therefore, be used safely in most patients, unless documented anaphylaxis to penicillin

RISK FACTORS AND OTHER TREATMENT CONSIDERATIONS

- ✦ Consider coverage for these organisms in empiric treatment regimens for patients with risk factors and severe, life-threatening infections; however, if no ESBL/“SPICE” organism isolated, switch to less broad-spectrum coverage
- ✦ Risk factors for infections caused by ESBL and “SPICE” 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

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