<u>Sherlock Holmes:</u> β-lactamase edition

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Wound culture and sensitivity (C&S)

Susceptibility

	Enterobacter cloacae
	Not Specified
Amikacin	Sensitive
Amoxicillin/Clavulanic Acid	Resistant
Aztreonam	Sensitive
Cefazolin	Resistant
Cefepime	Sensitive
Cefoxitin	Resistant
Cefpodoxime	Sensitive
Ceftriaxone	Sensitive
Cefuroxime	Resistant
Ciprofloxacin	Sensitive
Gentamicin	Sensitive
Levofloxacin	Sensitive
Meropenem	Sensitive
Nitrofurantoin	Intermediate
Piperacillin/Tazobactam	Sensitive
Tetracycline	Sensitive
Tobramycin	Sensitive
Trimethoprim/Sulfamethoxazole	Sensitive

First thoughts:

- May be an increasingly resistant *Enterobacter cloacae*
- Need adequate tissue penetration

ID attending antibiotic of choice:

• Meropenem, of course!

"Never trust to general impressions, my boy, but concentrate yourself upon details."

-Sherlock Holmes

Antimicrobial Resistance Mechanisms

Intrinsic

• Bacterial genes that encode antimicrobial properties

Acquired

 β-lactamase production, diminished cell membrane permeability, changes in PBP, loss of porins, presence of antibiotic-modifying enzymes, target site mutations increase efflux pump expression

Adaptive

• A form of induced resistance that occurs in the presence of specific antibiotics and environmental stressors

β-lactamase production: Ambler Classification System



ESBL and AmpC producers (most common)

• ESBL

- Klebsiella pneumoniae
- Klebsiella oxytoca
- Escherichia coli
- Proteus mirabilis
- AmpC
 - Enterobacter spp.
 - Citrobacter freundii
 - Klebsiella aerogenes
 - Serratia marcescens



Rapid ID/AST Technology





What if your site does not have Rapid ID/AST Technology?



Identifying the β -lactamase from C&S Results

ESBLs

- Extended-spectrum β-lactamases
- Not inducible from resistance genes exchanged through horizontal gene transfer
- Hydrolyze penicillins, late-generation cephalosporins, and carbapenems
- Partially inhibited by clavulanate and tazobactam
- No effect on cephamycins

AmpC

- Inducible upon exposure to β-lactams
- Potent inducers
 - Aminopenicillins
 - Amoxicillin-clavulanate
 - Narrow-spectrum cephalosporins
 - Cephamycins
- Weak inducers*
 - Piperacillin-tazobactam
 - Aztreonam
 - Third-generation cephalosporins

*Weak inducers: can be hydrolyzed if enough β-lactamase is produced – correlated to increased drug-specific minimum inhibitor concentrations

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Susceptibility



What do you observe from the C&S above?



"You see, but you do not observe. The distinction is clear."

Sherlock Holmes

C&S Breakdown

Enterobacter cloacae	Known AmpC producer
Resistant to cefoxitin	AmpC producers resistant to cephamycins, ESBLs are not
Resistant to amoxicillin/ clavulanic acid	ESBLs can be inhibited by clavulanate creating intermediate sensitivity, AmpC producers typically result as resistant

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What antibiotic do you recommend?



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