

# **Let's Win the Race of Resistant Infections vs Antibiotics**

Nancy Balch, PharmD, BCCCP  
nbalch@mgh.harvard.edu

# Disclosure Statement

- I have no personal or financial conflicts of interest relating to this presentation

# Objectives

- **Analyze patient's previous cultures for appropriate antibiotic therapy**
- **Identify situations where antibiotics may not be indicated**
- **Differentiate antibiotics with serious cross-sensitivity reactions vs antibiotics safe to administer when a patient has an allergy to a specific antibiotic**

# FYI

- **NOT a discussion on treatments of infections**
  - Too large a topic for a single discussion
  - Best method = a different discussion for each type of infections (cellulitis, urinary, sepsis, etc)

# US Antimicrobial Resistance

- Known in humans since at least 1942
- Some infections = no current antimicrobial options
- According to CDC in 2019:
  - ❖ > 2.8 million antimicrobial resistant infections yearly
  - ❖ > 35,000 Americans die yearly due to resistant infections
- Covid caused a setback in the fight against antimicrobial resistance

# Antibiotic vs Antimicrobial

- Often used interchangeably, should not be
- Antibiotics treat bacterial infections
- Antimicrobials treat bacteria, fungi, viruses, parasites
- This discussion will focus on antibiotic resistance

# What Is Resistance?

- Infection overcomes therapeutic ability of medication(s)
- Occurs in microbes
  - Natural occurrence
  - Overuse and misuse of medications increases resistance

# Mechanisms of Antibiotic Resistance

- Microbe mutations
- Microbe to microbe
- Pathogenic microbes kill colonized, 'useful', bacteria



# Inappropriate Antibiotic Use

- More broad spectrum than necessary
- Upper Respiratory Tract Infection
  - Viral vs other
  - Colonized with bacteria
- Antibiotics not discontinued when no longer indicated
- Patient treated longer than recommended

# Appropriate Antibiotic Use

- Follow national guidelines when available
  - Infectious Disease Society of America (IDSA)
  - Global Initiative for Chronic Obstructive Lung Disease (GOLD)
  - Surviving Sepsis Guidelines
- Appropriate antibiotic, dose and duration
- Does your facility have an antibiogram?

# Cultures

- Obtain, when possible, before starting therapy
  - Normal flora vs contamination vs colonized
  - Ensure proper technique of all staff
  - Bacteremia r/o: 2 different culture sites
  - Proper patient technique for urinary tract infection
- Monitor cultures returned after patient seen
  - Ensure appropriate antibiotic choice
  - Ensure appropriate dose and length of therapy

# Culture History

- Usually do not go back further than a year
  - May not be applicable to current infection
  - May be patient or institution specific
  - May be instances where is warranted, but must ensure not overtreating infection

# Culture History

- Previous culture data accurate?
  - ‘clean catch’ for urinary tract infection?
  - Colonized bacteria cultured?
- Correct culture for current infection?
  - Resistance of sputum culture should not be used for toe infection
  - Urinary tract culture beneficial if patient being ruled out for urosepsis

# Patient Understanding

- Variable, but largely misunderstood
  - Some believe cannot happen to them: their body is healthy, would not become resistant
  - Lack of understanding microbes develop resistance
- Lack of understanding of how Global or US resistance affects they or their family

# Patient Education

- Explain how pertains to them, not Society
- May be beneficial to practice with family, friends, etc
  - Determine their initial understanding
  - Educate how resistance would affect them and those around them
  - Evaluate understanding after, ask for feedback on anything not clearly understood

# Allergic vs Intolerant

- Patients may state allergic when intolerant
- Nausea, vomiting, diarrhea = intolerances
- Dizziness, 'felt funny', 'didn't get better'
- Intolerance should not prevent use of antibiotic unless severe
- Intolerance to one antibiotic in class does not always preclude use of all antibiotics in class



# Allergic?

- May benefit from allergy testing
  - “I was told I’m allergic”
  - “Someone in family is allergic so I was told to never take it”
  - “I had a bad reaction when I was a child”
  - “I don’t remember which antibiotic it was”
  - “I’m allergic to all antibiotics”
- Review antibiotics received since allergy listed
- Skin testing shows significant number patients not actually allergic

# Outdated

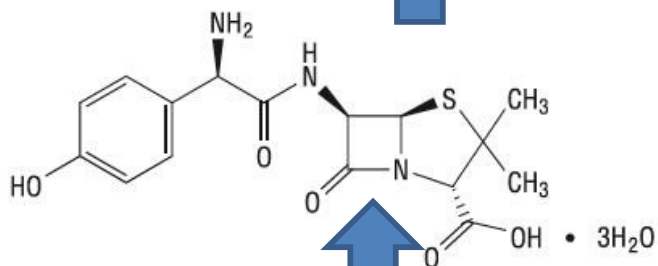
- Patients with 'allergy' to penicillins can never have them again
- Unsafe for patients with 'allergy' to penicillins to be treated with cephalosporins
- Beta lactam ring causes cross reactivity

# Chemical Structures

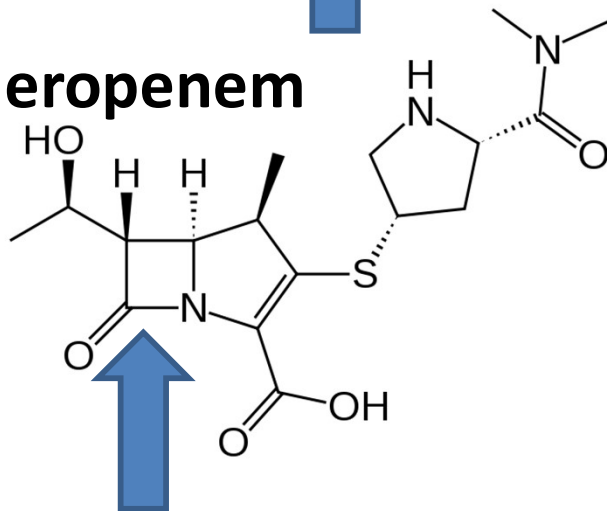
## Cephalexin



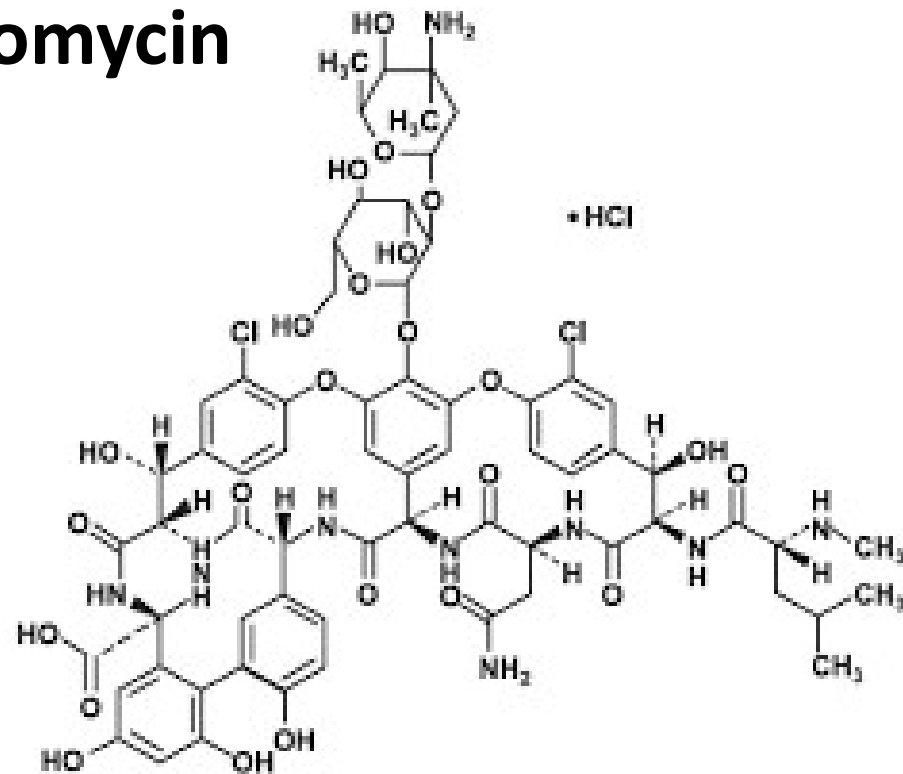
## Amoxicillin



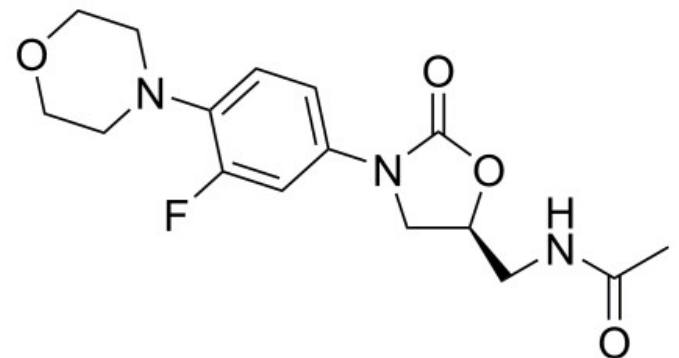
## Meropenem



## Vancomycin



## Linezolid

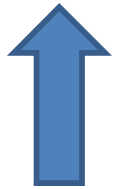
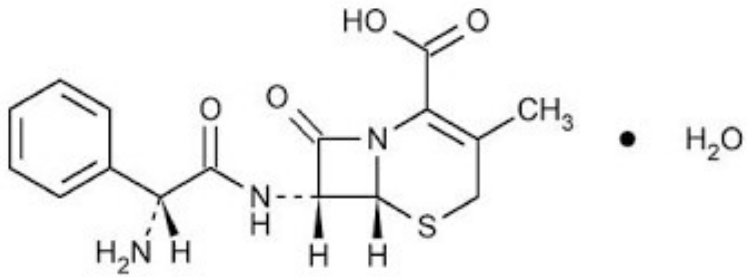


# Current Data

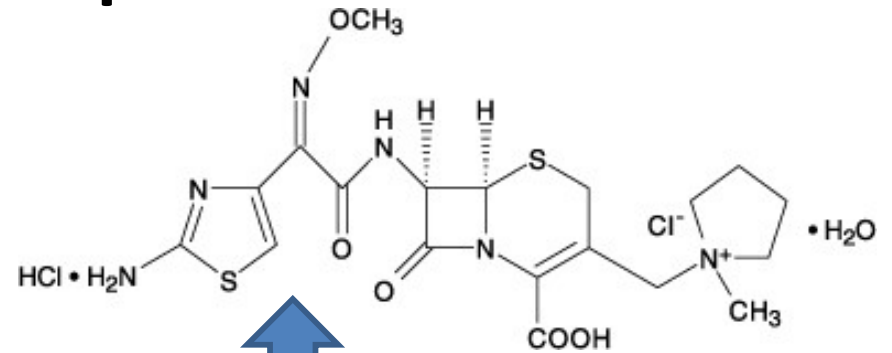
- Patients with penicillin allergy more likely to tolerate cephalosporins
  - 3<sup>rd</sup> and 4<sup>th</sup> generation unlikely to have reaction
  - 1<sup>st</sup> and 2<sup>nd</sup> generation lower cross-reactivity than previously thought
- Side chains more important than beta lactam ring
- Worth retesting patients to determine if still allergic

# Chemical Structures

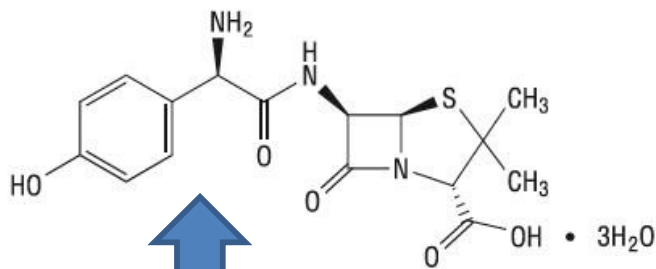
## Cephalexin



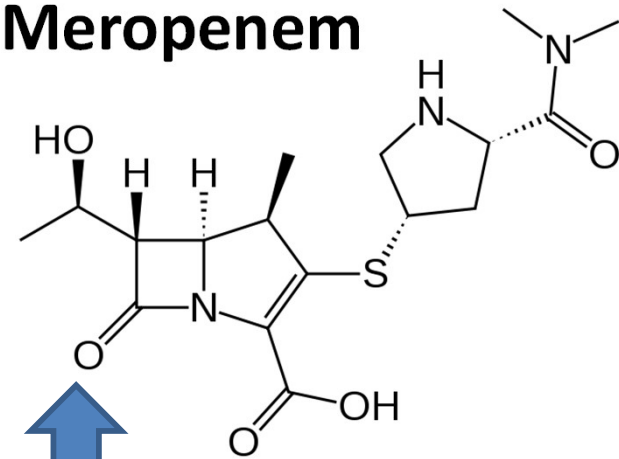
## Cefepime



## Amoxicillin



## Meropenem



# Concerns for Cross Reactivity

- Test dose protocols for less severe reactions (rash, etc)
- Involve Allergy Services for more severe reactions
  - Desensitization if required, but cannot miss doses
  - Testing, to determine if cross reactivity
  - Verify, with Allergy Service, if may have false negative skin test

# Penicillins

- Anaphylaxis to one, avoid all
  - Anaphylaxis to amoxicillin avoid ampicillin-sulbactam (Unasyn), nafcillin, etc
- All Penicillins too similar in chemical structure to administer for moderate to severe reactions, unless tested first

# Cephalosporins

- Side chains most likely cause of reaction
- Avoid others in same generation
- Data lacking between generations
- Monitor for future studies- NOT YET PROVEN:
  - May be safe to receive cephalosporin with different side chain
  - May even be safe if same side chain



# Vancomycin

- Current MRSA screening?
- NOT for 24 to 48 hours of therapy
  - NO oral equivalent for IV -> oral antibiotics
- No cross-reactivity with other antibiotics
- ‘Infusion Related Syndrome’
  - ‘Red Man Syndrome’ inappropriate
  - Usually tolerated with slower infusion rate
  - May require diphenhydramine, can administer orally, if given an hour before vancomycin dose

# Other Classes

- Macrolides and Lincomycins
  - ❖ Cross-reactivity within class
  - ❖ Cross-resistance within class has been seen
  - ❖ Resistance increasing Worldwide
- Sulfamethoxazole-trimethoprim (Bactrim)
  - ❖ Resistance seen
  - ❖ Ensure dosing appropriately (single strength: SS vs double strength: DS)
  - ❖ Cross-reactivity with erythromycin-sulfisoxazole (Pediazole)

# Tetracyclines

- Resistance with each in class
  - Use culture data for use
  - Antibiogram, if available, pending culture data
- Tigecycline boxed warning, risk vs benefit
- Cross reactivity within class not yet determined
  - Avoid others in class if patient is allergic

# Fluoroquinolones

- Boxed warning limits use
- Increased resistance further limits use
- Cross reactivity within class

# Take Home Tips

- Educate patients: direct to how may affect them and those they love
- Use current guidelines, antibiograms, to guide therapy
- Determine allergy vs intolerance
  - Allergy testing if possible and insurance covers
  - ‘Unknown’ has the power to increase antibiotic resistance

***Questions?***

***Nancy Balch, PharmD, BCCCP***

***[nbalch@mgh.harvard.edu](mailto:nbalch@mgh.harvard.edu)***

# References

- Smith-Martinez, L.A., Chatham, L.N., Muthukanagaraj, P. (2019, March) Intramuscular Ketamine Protocol as an Alternative to Physical Restraints for Electroconvulsive Therapy Administration in a Psychotic Patient. *The Journal of ECT*, 35 (1) e1-e2 doi: 10.1097/YCT.0000000000000522
- Giuliano C, Patel CR, Kale-Pradhan PB. A Guide to Bacterial Culture Identification And Results Interpretation. P T. 2019 Apr;44(4):192-200. PMID: 30930604; PMCID: PMC6428495
- Chardavoyne PC, Kasmire KE. Appropriateness of Antibiotic Prescriptions for Urinary Tract Infections. *West J Emerg Med*. 2020 Apr 13;21(3):633-639. doi: 10.5811/westjem.2020.1.45944. PMID: 32421512; PMCID: PMC7234695
- Valerie M Vaughn, Tejal N Gandhi, Vineet Chopra, Lindsay A Petty, Daniel L Giesler, Anurag N Malani, Steven J Bernstein, Lama M Hsaiky, Jason M Pogue, Lisa Dumkow, David Ratz, Elizabeth S McLaughlin, Scott A Flanders, Antibiotic Overuse After Hospital Discharge: A Multi-hospital Cohort Study, *Clinical Infectious Diseases*, Volume 73, Issue 11, 1 December 2021, Pages e4499–e4506, <https://doi.org/10.1093/cid/ciaa1372>
- Dellinger, R. Phillip MD, MSc, MCCM<sup>1</sup>; Rhodes, Andrew MB BS, MD(Res)<sup>2</sup>; Evans, Laura MD, MSc<sup>3</sup>; Alhazzani, Waleed MD<sup>4</sup>; Beale, Richard MB, BS<sup>5</sup>; Jaeschke, Roman MD<sup>6</sup>; Machado, Flavia R. MD, PhD<sup>7</sup>; Masur, Henry MD<sup>8</sup>; Osborn, Tiffany MD, MSc<sup>9</sup>; Parker, Margaret M. MD<sup>10</sup>; Schorr, Christa DNP, RN, FCCM<sup>11</sup>; Townsend, Sean R. MD<sup>12</sup>; Levy, Mitchell M. MD, MCCM<sup>13</sup>. Surviving Sepsis Campaign. *Critical Care Medicine* 51(4):p 431-444, April 2023. | DOI: 10.1097/CCM.0000000000005804
- Trubiano JA, Stone CA, Grayson ML, Urbancic K, Slavin MA, Thursky KA, Phillips EJ. The 3 Cs of Antibiotic Allergy- Classification, Cross-Reactivity, and Collaboration. *J Allergy Clin Immunol Pract*. 2017 Nov-Dec;5(6):1532-1542. doi: 10.1016/j.jaip.2017.06.017. Epub 2017 Aug 23. Erratum in: *J Allergy Clin Immunol Pract*. 2018 Jan - Feb;6(1):323. Erratum in: *J Allergy Clin Immunol Pract*. 2022 Dec;10(12):3346-3347. PMID: 28843343; PMCID: PMC5681410
- Khan DA, Banerji A, Bernstein JA, Bilgicer B, Blumenthal K, Castells M, Ein D, Lang DM, Phillips E. Cephalosporin Allergy: Current Understanding and Future Challenges. *J Allergy Clin Immunol Pract*. 2019 Sep-Oct;7(7):2105-2114. doi: 10.1016/j.jaip.2019.06.001. PMID: 31495420; PMCID: PMC6955146
- Jahantigh M, Samadi K, Dizaji RE, Salari S. Antimicrobial resistance and prevalence of tetracycline resistance genes in *Escherichia coli* isolated from lesions of colibacillosis in broiler chickens in Sistan, Iran. *BMC Vet Res*. 2020 Aug 3;16(1):267. doi: 10.1186/s12917-020-02488-z. PMID: 32746815; PMCID: PMC7397602

# References

- <http://dx.doi.org/10.1080/20961790.2017.1285219>
- <https://doi.org/10.7326/M19-1696>
- [http://escholarship.org/uc/uciem\\_westjem](http://escholarship.org/uc/uciem_westjem) DOI: 10.5811/westjem.2019.10.43067
- [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2018/209481s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/209481s000lbl.pdf)
- <https://www.ebmconsult.com/articles/penicillin-allergy-cross-reactivity-cephalosporin-antibiotics>
- [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/207131s006lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207131s006lbl.pdf)
- [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2018/050405s107lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/050405s107lbl.pdf)
- [https://www.idsociety.org/practice-guideline/practice-guidelines/#/+0/date na dt/desc/](https://www.idsociety.org/practice-guideline/practice-guidelines/#/+0/date%20na%20dt/desc/)
- <https://goldcopd.org/clinicians/>
- <https://goldcopd.org/2023-gold-report-2/>
- <https://www.cdc.gov/drugresistance/about.html>