

# More than Vancomycin: Practical Pearls for Prescribing Antimicrobials in the Hospital Setting

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# Disclosures

- Speaker's Bureau
  - Merck Pharmaceuticals

# Objectives

- Define the most common antimicrobials used in hospital practice
- Delineate practical pearls within each antimicrobial for optimized use
- Describe opportunities for antimicrobial stewardship within the hospital setting

# Where we are currently in ID

- *At least* 30-50% of antibiotic usage is unnecessary
- Antimicrobial prescribing is often more behavioral than scientific
- Fewer infectious diseases players in antibiotic research and development
- Duration of therapy has been largely made up for many infections
- Constantine in 321 A.D. decreed 7 days as a week
  - Hence how we have come to 7-14 days of therapy for many infections

# What is Antimicrobial Stewardship?

“Antimicrobial stewardship includes not only limiting inappropriate use but also *optimizing* antimicrobial selection, dosing, route, and duration of therapy to *maximize clinical cure* or prevention of infection while limiting the unintended consequences, such as the *emergence of resistance*, adverse drug events, and *cost*.”

- 5 “Rights”
  - Choice of antimicrobial
  - Route of administration
  - Dose
  - Time
  - Duration

# What are the risks of prolonged, unnecessary therapy?

- *C. difficile* infection
  - Adverse effects
  - Resistance emergence
  - Microbiome alteration
  - Increased costs
- 
- Bottom line: Defining appropriate DOT is an important antimicrobial stewardship issue. Many times zero is the right DOT...

Rooney AM et al. *Clin Infect Dis*. 2019 Aug 1. Ahead of Print  
Branch-Elliman W. et al. *JAMA Surg*. 2019;154:590-98.

# Discharge Rx Effect on DOT

- 3 centers
- ~45,000 inpatients admissions
- Discharge Rxs made up nearly 40% of total therapy
- Nearly 8 in 10 patients who received discharge Rx exceeded 7-day duration for most commonly seen infections
- **Patients with discharge Rxs had longer DOT than those who received all ABX inpatient**
- *Count all days of effective antibiotics before writing discharge Rx*
  - *Begin with end in mind*

Dyer A. et al. *Infect Control Hosp Epidemiol.* 2019;40:847-54.

# Summary of Disease States where Short Is In

<b>Stewardship: Shorter = Better</b>				
Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	12
Atypical CAP	1	3	Equal	1
VAP	8	15	Equal	2
cUTI/Pyelo	5 or 7	10 or 14	Equal	8*
Intra-abd	4	10	Equal	2
GNB Bacteremia	7	14	Equal	2**
Cellulitis	5-6	10	Equal	4 <sup>†</sup>
Osteomyelitis	42	84	Equal	2
Osteo with Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2 <sup>†</sup>
Septic Arthritis	14	28	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Neutropenic Fever	AFx72 h	+ANC>500	Equal	1
<i>P. vivax</i> Malaria	7	14	Equal	1
<b>Total: 14 Diseases</b>			<b>64 RCTs</b>	
<small>*1 RCT in males; **GNB bacteremia also in UTI/cIAI RCTs; †3 RCTs equal, 1 (low dose oral flucox)  <sup>†</sup>relapses 2° endpoint; †all patients debrided, in 1 study total bone resection (clean margins); refs at  <a href="https://www.bradspellberg.com/shorter-is-better">https://www.bradspellberg.com/shorter-is-better</a> </small>				

<https://twitter.com/BradSpellberg/status/1375468869100335108/photo/1>. Accessed 9/9/21.

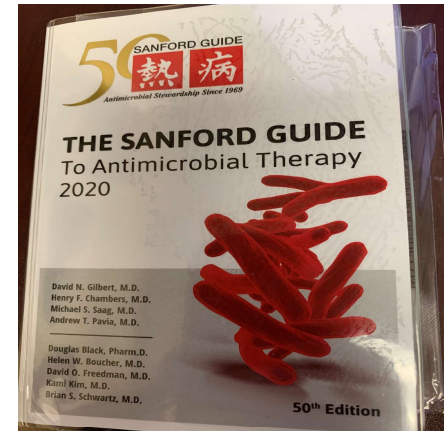


# Keys to Success

- Become familiar hospital formulary
  - But most drugs can be obtained if right situation
- Get to know antimicrobial stewardship team including pharmacists
  - Stewardship programs mandated at all hospitals
  - Pharmacists can help facilitate transitions in care
  - Also help with obtaining patient assistance for medications
- Become familiar with hospital antibiogram for empiric prescribing
  - Typically done annually
  - Will provide best agents by drug-bug combination
  - Some hospitals break down by unit (e.g. ICU vs. non-ICU cultures)
  - Incredibly helpful for knowing best *Pseudomonas aeruginosa* therapies

# Where to find antimicrobial drug information?

- Sanford Guide
  - Keep in mind this is “national” guide
  - Not substitute for local antibiogram
  - Good for the +/- Table in middle of book
  - Available as app for 29.95 annually
- Infectious Diseases Society of America (IDSA) guidelines
  - This is best place for empiric regimens including dosing
  - Broken down by syndrome or pathogen
  - Free
  - Go to [idsociety.org](http://idsociety.org)
  - Tables are your friend!



# Sample Antibiogram

Figure 1: Example Antibiogram

		Aminoglycosides			B-Lactams			Cephalosporins				Quinolones		Others		
Gram (-)	# of patients	Amikacin	Gentamicin	Tobramycin	Ampicillin	Imipenem	Piperacillin Tazobactam	Cefzolin	Cefoxitin	Ceftriaxone	Ceftazidime	Ciprofloxacin	Nitrofurantoin	TMP/SMX		
Echerichia coli	4	100	100	100		100	100				100	75				
Klebsiella sp	13	100	84.6	92.3	38.5	100	92.3	84.6	100	100	100	38.5	92.3	38.5		
Proteus sp	7	71.4	57.1	71.4		85.7	85.7			57.1	57.1		28.6	71.4		
Pseudomonas aeruginosa	13	100	83.3	92.3	91.7		100		81.8	100	100	30.8		69.2		
		Penicillins				Cephalosporins		Quinolones		Others						
Gram (-)	# of patients	Penicillins	Ampicillin	Oxacillin	Nafcillin	Cephalothin	Ceftriaxone	Ciprofloxacin	Moxifloxacin	Gentamicin	Linezolid	Rifampin	Tetracycline	TMP/SMX	Vancomycin	Nitrofurantoin
Staph aureus (all)	8	0		0	0			0	0	87.5	100	100	100	100	100	100
Methicillin Resistant (MRSA)	8	0		0	0				0	87.5	100	100	100	100	100	100
Methicillin Susceptible (MRSA)	0															
Enterococcus sp	4	100	100					50		75			25		100	100

[https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/quality-patient-safety/patient-safety-resources/resources/nh-aspguide/module2/toolkit1/cat\\_sources.pdf](https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/quality-patient-safety/patient-safety-resources/resources/nh-aspguide/module2/toolkit1/cat_sources.pdf)

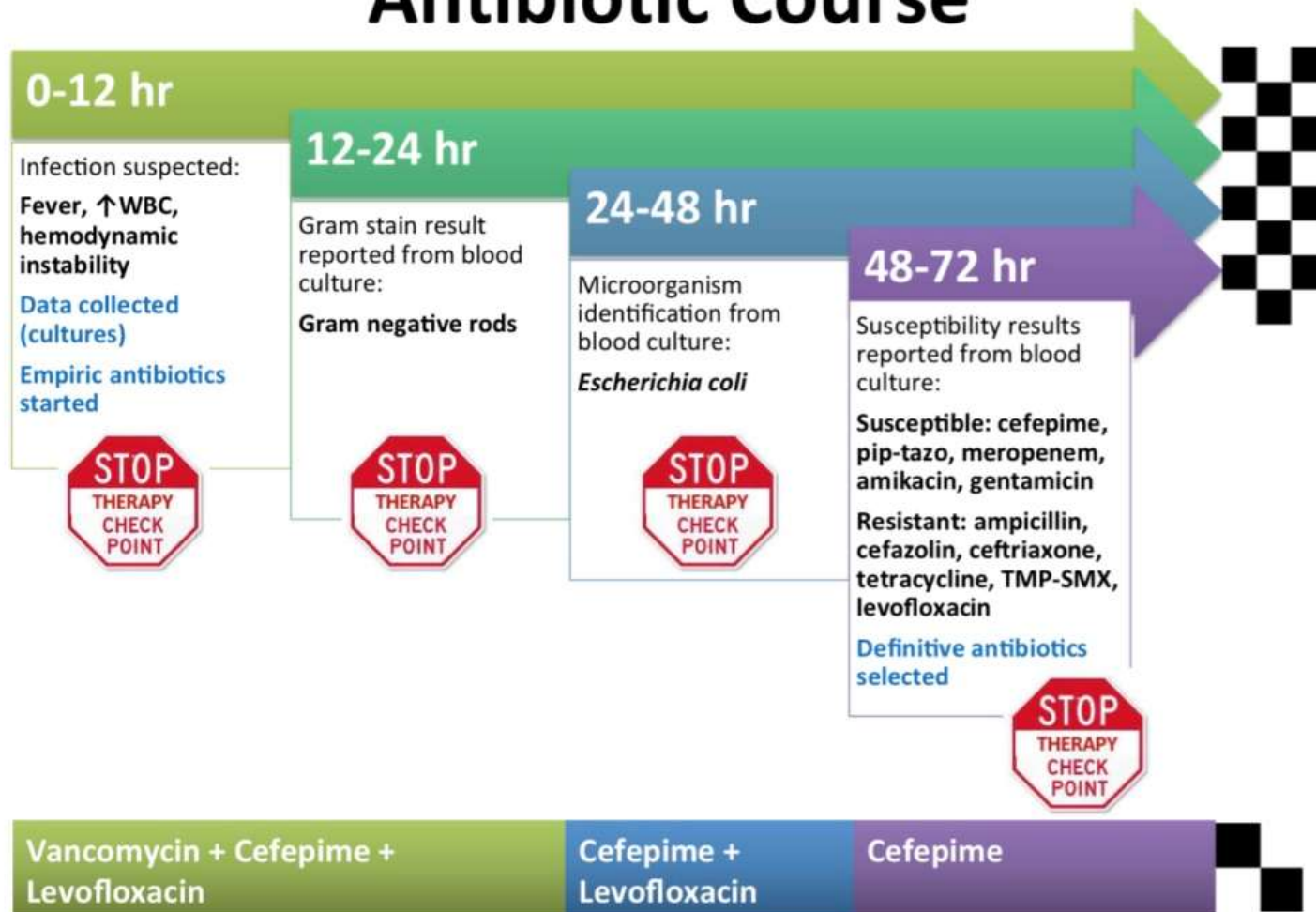
# Where to find information?

- Up To Date
  - Quick resource
  - Very opinionated
  - References not great
- Lexi-Comp
  - Most widely used reference for drugs including dosing
  - Basically package insert dosing
  - Not necessarily those used in practice
  - Refer to guidelines when can
- Local policies and order sets are very helpful in many circumstances

# Diagnostic Tests to Know

- Urinary antigens for CAP
  - *S. pneumoniae*
  - *L. pneumophila*
  - Most helpful if positive
  - Not affected by antibiotics like cultures
- Procalcitonin
  - Specific for bacterial infection
  - Cutoffs ***in general*** indicating no bacterial infection (serum)
    - CAP (< 0.25 ng/mL)
    - Sepsis (< 0.5 ng/mL)
  - Most helpful for discontinuing ABX, not withholding them
  - Renal dysfunction can falsely elevate
- Make sure tests are available onsite vs. send out
  - Delay in results if send out

# Antibiotic Course



Courtesy of  
 Justo J,  
 PharmD,  
 MS, BCPS,  
 AQ-ID

# Rapid Diagnostics

- Revolution occurring in microbiology labs
- Results in hours vs. days
- Many infectious syndromes available for testing
  - GI
  - LRTI
  - Upper Respiratory
  - Bacteremia
  - Meningitis
- Screening tests as well (MRSA nares/*C. difficile*)
- Many platforms available commercially
- Slowly working to outpatient setting as well

# Rapid Diagnostics

- Work with local lab/stewardship team to discern if available and how information is processed/communicated
- Most platforms do not give susceptibilities, only ID
- Many clinicians unaware of what technology is present
  - Failure of education
- Rapid is only “rapid” if information gets to prescriber
  - Someone has to disseminate result to team
  - Facilities vary in who communicates information
    - Nursing vs. Stewardship pharmacists

Foster RA et al. *Infect Control Hosp Epidemiol.* 2017;38:863-66.

Porter AM et al. *Antimicrob Agents Chemother.* 2018;63:e01575-18.



# Rapid Diagnostic Tests: Options

- Polymerase Chain Reaction (PCR)
  - Xpert *C. difficile*
- Multiplex PCR
  - Biofire FilmArray (Blood/Sputum/Meninges/GI): **1 hour**
- Nanoparticle Probe Technology
  - Verigene (Blood): **2.5 hours**
- Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)
- Multiplex FISH
  - Accelerate (Gives antimicrobial susceptibilities in 7 hours)
- Peptide Nucleic Acid Fluorescent in Situ Hybridization
  - PNA-Fish/PNA QuickFISH

Bauer KA et al. Clin Infect Dis.  
2014;59:S134-45.

# Rapid Molecular Tests: Bloodstream Infections

Organism: Gram Positive	PCR	Multiplex PCR*	Nanoparticle Probe	PNA FISH	MALDI-TOF
<i>Staphylococcus aureus</i>	mecA	mecA/C/MREJ	mecA	X	X
Coagulase-negative <i>Staphylococcus</i> spp.	X	mecA/C/MREJ	mecA	X	X
<i>Streptococcus</i> spp.	X	X	X		X
<i>Enterococcus</i> spp.	X	vanA/B	vanA/vanB	X	X
<i>Listeria</i>		X	X		X
<i>Bacillus</i> spp.		X			X
<i>Corynebacterium</i> spp.		X			X
<i>Cutibacterium acnes</i>		X			X
<i>Lactobacillus</i> spp.		X			X
<i>Micrococcus</i> spp.		X	X		X
Organism: Fungal	PCR	Multiplex PCR*	Nanoparticle Probe	PNA FISH	MALDI-TOF
<i>Candida</i> spp.		X		X	X
<i>Cryptococcus</i> spp.		X			X
<i>Fusarium</i> spp.		X			X
<i>Rhodotorula</i> spp.		X			X

# Rapid Molecular Tests: Bloodstream Infections

Organism: Gram Negative	PCR	Multiplex PCR*	Nanoparticle Probe	PNA FISH	MALDI-TOF
<i>Acinetobacter</i> spp.		CTX-M, KPC, IMP, VIM, Oxa-48, NDM, mcr-1	CTX-M, KPC, IMP, VIM, Oxa, NDM		X
<i>Bacteroides fragilis</i>		X			X
<i>Enterobacteriales</i>		CTX-M, KPC, IMP, VIM, Oxa-48, NDM, mcr-1	CTX-M, KPC, IMP, VIM, Oxa, NDM	X	X
<i>Fusobacterium</i> spp.		X			X
<i>Haemophilus influenzae</i>	X	X			X
<i>Neisseria meningitidis</i>	X	X			X
<i>Pseudomonas aeruginosa</i>		CTX-M, KPC, IMP, VIM, Oxa, NDM	CTX-M, KPC, IMP, VIM, Oxa, NDM	X	X
<i>Stenotrophomonas maltophilia</i>		CTX-M			X

# Notable Antimicrobials with Pearls

# Vancomycin in 2022

- Over 60 years since introduction
- Approved based on open label data by FDA in 1958 on 15 patients
- “Drug of Choice” for serious MRSA infections in hospital
  - ~90% of use is empiric
- **Inferior** to beta-lactams for **MSSA** infections
  - Nafcillin or Cefazolin with cefazolin preferred in most patients
- Increased failure rates in MRSA isolates within the susceptible range (MIC  $\leq$  2mg/L)

Stryjewski ME et al. Clin Infect Dis 2007;44:190-6.

Chang FY et al. Medicine 2003; 82: 333-9.

Hidayat LK et al. Arch Intern Med 2006; 166:2138-44.

# Vancomycin

- Most use is inappropriate
  - Less than 10% of patients remain on vancomycin by day 3 of therapy
- Use reasonable if high risk for MRSA infection
  - Exception: Meningitis to cover ceftriaxone-resistant *S. pneumoniae*
- When does vancomycin make sense empirically?
  - High amounts of MRSA in patient ward/ICU (> 10-20% rates)
  - Previous colonization (CAP guidelines)
  - Prior **intravenous** antibiotic use within 90 days (HAP/VAP guidelines)
  - Recent influenza like illness
  - New infection in hospitalized patient (2 days or more in house)
  - Septic shock as part of clinical presentation
  - Treatment of acute bacterial skin/skin structure infection (ABSSSI)
    - In particular abscesses where MRSA very likely pathogen

Kalil AC et al. *Clin Infect Dis*. 2016;63:e61-111.

Metlay JP et al. *Am J Respir Crit Care Med*. 200;e45-e67.

# Vancomycin: Pitfalls and Perils

- Serum drug monitoring is becoming more painful
  - Area under the curve (AUC) based dosing vs. trough based dosing
  - May require 2 levels
  - Pharmacists typically manage dosing
- Nephrotoxicity has increased in last 10-15 years
  - Higher troughs for invasive MRSA infections (15-20 mcg/mL)
  - Probably additive when combined with piperacillin/tazobactam (Zosyn)
- Don't forget about Red Man's Syndrome
  - Pruritic, erythematous rash of face, neck, upper torso
  - Not allergic reaction
  - Management: Slow infusion +/- antihistamines
  - Tends to be more prominent in younger patients
- Patients can be vancomycin allergic (check profile)

# Vancomycin: When to use alternative MRSA agents?

- Linezolid (Zyvox)
  - Excellent choice for MRSA pneumonia
  - **PO dosage form**
  - More affordable as generic
  - Monitor platelets
  - Avoid > 2 weeks of therapy
  - Monitor with SSRIs
- Daptomycin (Cubicin)
  - MRSA bacteremia/endocarditis
  - IV only
  - Good option for outpatient antimicrobial therapy (OPAT)
  - Monitor CPKs and muscle symptoms
  - NOT for Pneumonia
    - Lung surfactant inactivates
- Ceftaroline (Teflaro)
  - MRSA pneumonia AND bacteremia
  - Most expensive non-vancomycin MRSA agent in hospital
- Dalbavancin (Dalvance)
  - Long-acting agent to facilitate discharge
- Costs of most newer agents are causing re-evaluation of their use vs. vancomycin



# How to stop vancomycin?

- Reassess patient risk factors once dust settles
- Nares MRSA screening
  - Rapid turnaround at most facilities
  - Tremendous negative predictive value (~95-99%)
    - Immunocompromised as well
  - Best data in pneumonia
  - Other sites of infection approximate 90-95% negative predictive value
    - Wound
    - Intrabdominal
    - Blood
    - Renal

Perreault SK et al. *Infect Control Hosp Epidemiol.* 2021;42:853-856.  
Mergenhagen KA et al. *Clin Infect Dis.* 2020;71:1142-1148.

# Cefazolin (Ancef) is your friend

- Great coverage vs. streptococcal species and MSSA
- Extremely well tolerated
- Shares no side chains with penicillins or cephalosporins
  - Can be given to most patients with mild-moderate allergies
- Great option for ABSSSI if no abscess (e.g. cellulitis) or MSSA abscess
- Can easily change to PO cephalexin upon discharge
- Dosing: 2gm IV q8h for most patients
  - Adjust if renal dysfunction
  - In patients  $\geq$  120kg, can consider 3gm

# Ceftriaxone (Rocephin)

- 3<sup>rd</sup> generation cephalosporin
- Excellent coverage vs. many GPC and GNR
  - Holes in Coverage: MRSA, Pseudomonas species, and GI anaerobic coverage
- Used frequently for a number of infections
  - UTI
  - STI
  - CAP
- Can be given IV or IM
- Dose
  - Typically 1gm or 2gm daily
    - 2gm IV daily superior for ICU patients
- High *C. difficile* risk compared to other agents
- No renal adjustment unless cirrhosis as well

Ackerman A, et al. *Antimicrob Agents Chemother.* 2020;64:e00066-20.

# Carbapenems

- Meropenem
  - Extremely broad agent typically reserved
  - Drug of choice for ESBL-producing *E. coli* or *K. pneumoniae* bloodstream infections
  - Dosing: 1g IV q8h or 500mg IV q6h
  - May accumulate causing seizures (watch kidney function)
- Ertapenem
  - No activity vs. APE
    - Acinetobacter, Pseudomonas, Enterococcus species
  - Dosing: 1g IV once daily
  - Ideal for OPAT
- Neither agent available orally

# Fluoroquinolones in 2022

- CNS
  - Hallucinations
  - Seizures
- GI
  - N/V/D
  - *C. difficile* infection
- CV
  - QTc prolongation
  - Aortic Dissection or rupture (rare)
- Peripheral Nervous System
  - Neuropathy
- Musculoskeletal system
  - Tendonitis
  - Tendon rupture
    - Elderly
    - Systemic corticosteroids
  - Arthropathy
    - Avoid in most children
  - Myasthenia gravis
    - Contraindicated

# Fluoroquinolones- Then why are they used?

- Excellent bioavailability
  - Useful for numerous infections, even Gram-negative bacteremia
    - *E. coli* pyelonephritis
- Tissue penetration excellent
  - Hence the side effect profile
- Only oral therapy with *Pseudomonas aeruginosa* coverage
- No serum drug monitoring required

# Fluoroquinolone Options

- Ciprofloxacin

- UTIs ✓
- Nosocomial pneumonia ✓
- Community-acquired pneumonia  
⊠
  - Lacks coverage vs. *S. pneumoniae*
- Pseudomonas coverage ✓
- Dosed BID
  - Adjust in renal dysfunction: QD

- Levofloxacin

- UTIs ✓
- Nosocomial pneumonia ✓
- Community-acquired pneumonia-  
monotherapy ✓
  - Unless admitted to ICU
- Pseudomonas coverage ✓
- Atypical coverage ✓
- Dosed once daily
  - Adjust in renal dysfunction: Q48h

# Moxifloxacin (Avelox)

- Minimally used
- Nearly completely hepatically metabolized
  - Not useful for UTIs
- Useful for CAP as monotherapy outpatient
- No *Pseudomonas aeruginosa* coverage
- Dosing: 400mg once daily (IV or PO)
- Useful for some STDs
  - Mycoplasma urealyticum due to levo/cipro resistance



# Ways to Facilitate Discharge

# IV to PO Conversions are In!

- Many IV antibiotic recommendations are based on tradition not evidence
- A growing number of disease states can be effectively and safely treated with oral antibiotics
  - Gram-negative bacteremia from UTI/pyelonephritis
  - Osteomyelitis
  - Many others
- Core Antimicrobial Stewardship Activity
- Bacteria don't respond better to IV antibiotics

CDC. Core Elements of Hospital Antibiotic Stewardship Programs. 2019.

# Benefits of Oral Therapy

- Patient
  - Lower costs
  - Increased patient satisfaction and quality of life
  - Decreased risk of IV catheter-related infections
  - Decreased length of hospitalization
- Institution
  - Lower costs
  - Increased patient satisfaction and quality of life
  - Decreased risk of IV catheter-related infections
  - Decreased length of hospitalization

Chastain DB et al. ID Update in 2020.  
powerpak.com. (In Press)

# Risks of Parenteral Antibiotic Therapy

- Infection, Infection, Infection
- Clotting Sequelae
- Pain
- Pump malfunctions
  - Resulting in incorrect infusions

Sax Paul. NEJM Journal Watch Blog. May 16<sup>th</sup>, 2013.

# Agents with Comparable Serum/Tissue Concentrations

- TMP/SMX (Bactrim or Septra)
- Azithromycin
  - Absorption only 38% but those macrophages!
- Metronidazole
  - Why is this drug TID...?
- Doxy or Minocycline
- Clindamycin
  - Why is oral dose lower than IV?
- Linezolid (Zyvox)
- Fluoroquinolones
  - Don't forget about chelation interactions
    - Magnesium
    - Calcium
    - Zinc
    - Iron
    - MVIs
    - Tube feeds
- Fluconazole

# Specific Pearls for these agents...

- Clindamycin
  - Excellent streptococcal activity and regional MRSA activity
  - Caution with pill esophagitis (PO)
  - Frequent dosing
  - Pediatric safety and effectiveness
  - Adjunct for necrotizing fasciitis
    - Decreases toxin production through ribosomal inhibition
- Metronidazole
  - Incredible anaerobic activity with decades of use
  - Metallic taste can be annoying
  - Long-term usage associated with peripheral neuropathy

# Specific Pearls for these agents continued

- Doxycycline
  - Phototoxicity is real
  - Pill esophagitis can be problematic
- TMP/SMX
  - DS tablets are HUGE
  - Liquid dosage form available
    - Careful with higher dose calculations (10-20 mg/kg/day of TMP component)
- Linezolid (Zyvox)
  - Caution with serotonergic drug interactions
  - Bone marrow suppression increases  $\geq 14$  days of therapy

# Dalbavancin (Dalvance)

- Long-acting lipoglycopeptide for ABSSSI
  - Oritavancin (Orbactiv or Kymrsa) also an option
- Safe in vancomycin allergic patients
- Half-life: 8.5 days (204 hours)
- Dosing: 1500mg IV X 1 dose (30 minute infusion)
- Can prevent admission to hospital from ED
- Can shorten length of stay (LOS)
  - Jones et al: Shortened LOS 4 days
- Fantastic option for persons who inject drugs (PWID)



# Fosfomycin

- Oral, little known agent for cystitis
  - Avoid in serious UTI including pyelonephritis
- Dissolve powder in water which is consumed
- Excellent coverage vs. MDR Gram-negative infections
  - VRE as well
- 3g one time dose or dose q48-72 hours in more complicated UTI
- Watch cost if sending home on therapy
  - Prior authorization often required

# Penicillin Allergy

# Background

- Penicillin allergy is one of the most frequently reported drug allergies
  - Approximately 10% of patients report hypersensitivity
  - Results in limited treatment options, increased healthcare costs, and increased resistance with the use of broad-spectrum agents
- Up to 90% of patients reporting hypersensitivity do not truly have a penicillin allergy
- Many patients therefore do not receive optimal therapy for infecting pathogen

*Ann Allergy Asthma Immunol.* 2010; 105:259-273.; *Mayo Clinic Proc.* Mar 2005; 80(3):405-410.; *Ann of Allergy, Asthma, and Immunology.* 2007; 98: 355-359.

# Implications of PCN “Allergy”

- Increased adverse effects
- Increased hospital stays
  - Approximately one-half day longer
  - 30,000 hospital days/65 million in expenditures
- Development of MDR infections
  - 23.4% increase in CDI
  - 14.1% more MRSA
  - 30.1% increased VRE

MacFadden DR et al. Clin Infect Dis.  
2016;63:904-10.

Macy E et al. J Allergy Clin Immunol  
2014;133:790-6.

# Clinical Indications where Beta-lactams are best

- Surgical Prophylaxis
- Methicillin-susceptible *Staphylococcus aureus*
  - Superior to vancomycin for MSSA bacteremia
- Severe Pseudomonas infections
  - Often backbone at many institutions
- Group A streptococcal infections
  - Including invasive necrotizing infections
- Several STIs
  - Syphilis, PID, Gonococcal infections

Blumenthal KG et al. Clin Infect Dis. 2015;61:741-9.

# Penicillin Allergy Assessment and Skin Testing (PAAST)

- Many facets all with benefit
- PAAST has many potential options depending on resources
  - Allergy record confirmation
  - Detailed allergy interview with EHR biopsy
    - Many times not documented in EHR
  - Side Chain Assessment for Cephalosporins
  - Graded Challenge
  - Direct Oral Challenge
  - Desensitization
  - Penicillin Skin Testing

# Cross- Reactivity Assessment

- Penicillin cross-reactivity lower in recent assessments
  - Cephalosporins (< 2%)
  - Carbapenems (<1%)
- May obviate need for direct penicillin challenge/skin testing
- Side chains key tool in determining risk
- Shared R1 and R2 side chains good predictor

Jones BM et al. *Current Treatment Options Infect Dis.* 2019. In Press online.

Romano A et al. *J Allergy Clin Immunol.* 2018;6:1662-72.

Romano A et al. *NEJM.* 2006;354:2835-7.

## Beta-lactam Antibiotic Cross-Allergy Chart

Beta-lactams	AMOXICILLIN*	AMPICILLIN	CLOXACILLIN	PENICILLIN	PIPERACILLIN*	CEFADROXIL	CEFAZOLIN	CEPHALEXIN	CEFOXITIN	CEFPROZIL	CEFUROXIME	CEFIXIME	CEFOTAXIME	CEFTAZIDIME	CEFTRIAXONE	CEFEPIME	ERTAPENEM	IMIPENEM	MEROPENEM
AMOXICILLIN*	█	X <sup>1</sup>	X <sup>5</sup>	X <sup>4</sup>	X <sup>3</sup>	X <sup>1</sup>	✓	X <sup>1</sup>	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
AMPICILLIN	X <sup>1</sup>	█	X <sup>5</sup>	X <sup>4</sup>	X <sup>3</sup>	X <sup>2</sup>	✓	X <sup>2</sup>	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CLOXACILLIN	X <sup>5</sup>	X <sup>5</sup>	█	X <sup>5</sup>	X <sup>5</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PENICILLIN	X <sup>4</sup>	X <sup>4</sup>	X <sup>5</sup>	█	X <sup>5</sup>	✓	✓	✓	X <sup>3</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PIPERACILLIN*	X <sup>3</sup>	X <sup>3</sup>	X <sup>5</sup>	X <sup>5</sup>	█	X <sup>3</sup>	✓	X <sup>3</sup>	✓	X <sup>3</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFADROXIL	X <sup>1</sup>	X <sup>2</sup>	✓	✓	X <sup>3</sup>	█	✓	X <sup>1</sup>	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFAZOLIN	✓	✓	✓	✓	✓	✓	█	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEPHALEXIN	X <sup>1</sup>	X <sup>2</sup>	✓	✓	X <sup>3</sup>	X <sup>1</sup>	✓	█	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFOXITIN	✓	✓	✓	X <sup>3</sup>	✓	✓	✓	✓	█	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓
CEFPROZIL	X <sup>2</sup>	X <sup>2</sup>	✓	✓	X <sup>3</sup>	X <sup>2</sup>	✓	X <sup>2</sup>	✓	█	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFUROXIME	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>2</sup>	✓	█	X <sup>3</sup>	X <sup>1</sup>	X <sup>3</sup>	X <sup>1</sup>	X <sup>2</sup>	✓	✓	✓
CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>3</sup>	█	█	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	✓	✓	✓
CEFOTAXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>1</sup>	X <sup>3</sup>	█	█	X <sup>3</sup>	X <sup>1</sup>	X <sup>1</sup>	✓	✓	✓
CEFTAZIDIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	█	█	X <sup>3</sup>	X <sup>3</sup>	✓	✓	✓
CEFTRIAXONE	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>1</sup>	X <sup>3</sup>	X <sup>1</sup>	X <sup>3</sup>	█	█	X <sup>1</sup>	✓	✓	✓
CEFEPIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>2</sup>	X <sup>3</sup>	X <sup>1</sup>	X <sup>3</sup>	X <sup>1</sup>	█	█	✓	✓	✓
ERTAPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	█	X <sup>5</sup>	X <sup>5</sup>
IMIPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>5</sup>	█	X <sup>5</sup>
MEROPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>5</sup>	X <sup>5</sup>	█

\* Also applies to beta-lactamase inhibitor combinations (amoxicillin-clavulanate and piperacillin-tazobactam)

### AVOID ALL beta-lactam antibiotics if:

- ICU admission related to allergy
- Delayed beta-lactam antibiotic allergy causing:
  - interstitial nephritis
  - hepatitis
  - hemolytic anemia
- Delayed severe skin allergic reactions:
  - Stevens-Johnson syndrome
  - toxic epidermal necrolysis
  - exfoliative dermatitis
  - acute generalized exanthematous pustulosis (AGEP)
  - drug reaction with eosinophilia and systemic symptoms (DRESS)

### LEGEND:

Penicillins	
1st Generation Cephalosporins	
2nd Generation Cephalosporins	
3rd Generation Cephalosporins	
4th Generation Cephalosporins	
Carbapenems	
✓	Different structure. CONSIDERED SAFE TO PRESCRIBE
Reaction likely based on side chain:	
X <sup>1</sup>	Same side chain - clinical evidence of cross reaction. DO NOT PRESCRIBE
X <sup>2</sup>	Same side chain - Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE
X <sup>3</sup>	Similar side chain - Potential for cross reaction. DO NOT PRESCRIBE
Reaction likely based on Beta-lactam ring:	
X <sup>4</sup>	Clinical evidence of cross reaction. DO NOT PRESCRIBE
X <sup>5</sup>	Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE



# Antibiotic Allergy Assessment Tool

- What is name of antibiotic that allergy is from?
- Details of reaction?
- How many years ago did reaction happen?
  - More than 10 years ago?
- How long post 1<sup>st</sup> dose did reaction occur?
- How was this reaction managed?
- Were you hospitalized?
- Other antibiotics received since?

Devchand M. et al. *J Allergy Clin Immunol Pract.* 2019;7:1063-65.e5.

# Warfarin (Coumadin) and Antimicrobials

- Any antibiotic has potential to affect warfarin and ultimately INR
- Beta-lactams in general less effect
  - Nafcillin can ↓ INR significantly
- Most antimicrobials increase INR and increase risk for bleeding
- Worst offenders that ↑ INR (Avoid if possible)
  - TMP/SMX
  - FQs
  - Fluconazole
    - One dose okay for vaginal candidiasis
  - Clarithromycin
    - Rarely used except in *H. pylori* regimens

# Clinical Syndromes: CAP Options

- CAP (non-ICU)
  - Ceftriaxone 2gm IV once daily PLUS azithromycin 500mg IV once daily
  - Max of 5 days azithromycin for 99% of patients due to long half-life
  - Severe penicillin allergy
    - Levofloxacin 750mg once daily
    - Moxifloxacin 400mg once daily
- CAP (ICU)
  - Ceftriaxone 2gm IV once daily PLUS azithromycin 500mg IV once daily OR
  - Ceftriaxone 2gm IV once daily PLUS levofloxacin 750mg IV once daily
- Doxycycline can be substituted for azithromycin when QTc an issue
- Discharge regimen: Amox/clav OR cefdinir OR cefpodoxime +/- azithromycin
  - Cefdinir (Omnicef) can be chelated like FQs or Doxy
- Many can get 5 days total of therapy!

# Take Home Points

- There are often many good antibiotic choices for given patient
- Decision based on patient and pathogen/syndrome factors
- Local antibiogram important to have on hand for empiric prescribing
- Diagnostics are rapidly improving to quicken optimal prescribing
- Penicillin allergies are often incorrect and can be corrected
- Antimicrobial stewardship team ready to help

# Questions?

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