

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

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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...

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*

Summary of Disease States where Short Is In

Stewardship: Shorter = Better				
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 [†]
Osteomyelitis	42	84	Equal	2
Osteo with Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2 [‡]
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
Total: 14 Diseases			64 RCTs	
<small>*1 RCT in males; **GNB bacteremia also in UTI/cIAI RCTs; †3 RCTs equal, 1 (low dose oral flucox) [‡]relapses 2° endpoint; †all patients debrided, in 1 study total bone resection (clean margins); refs at https://www.bradspellberg.com/shorter-is-better </small>				

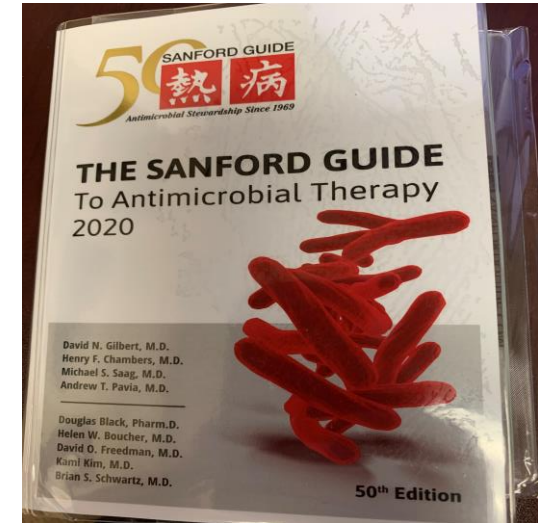
<https://twitter.com/BradSpellberg/status/1375468869100335108/photo/1>. Accessed 9/9/21.

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
 - Tables are your friend!



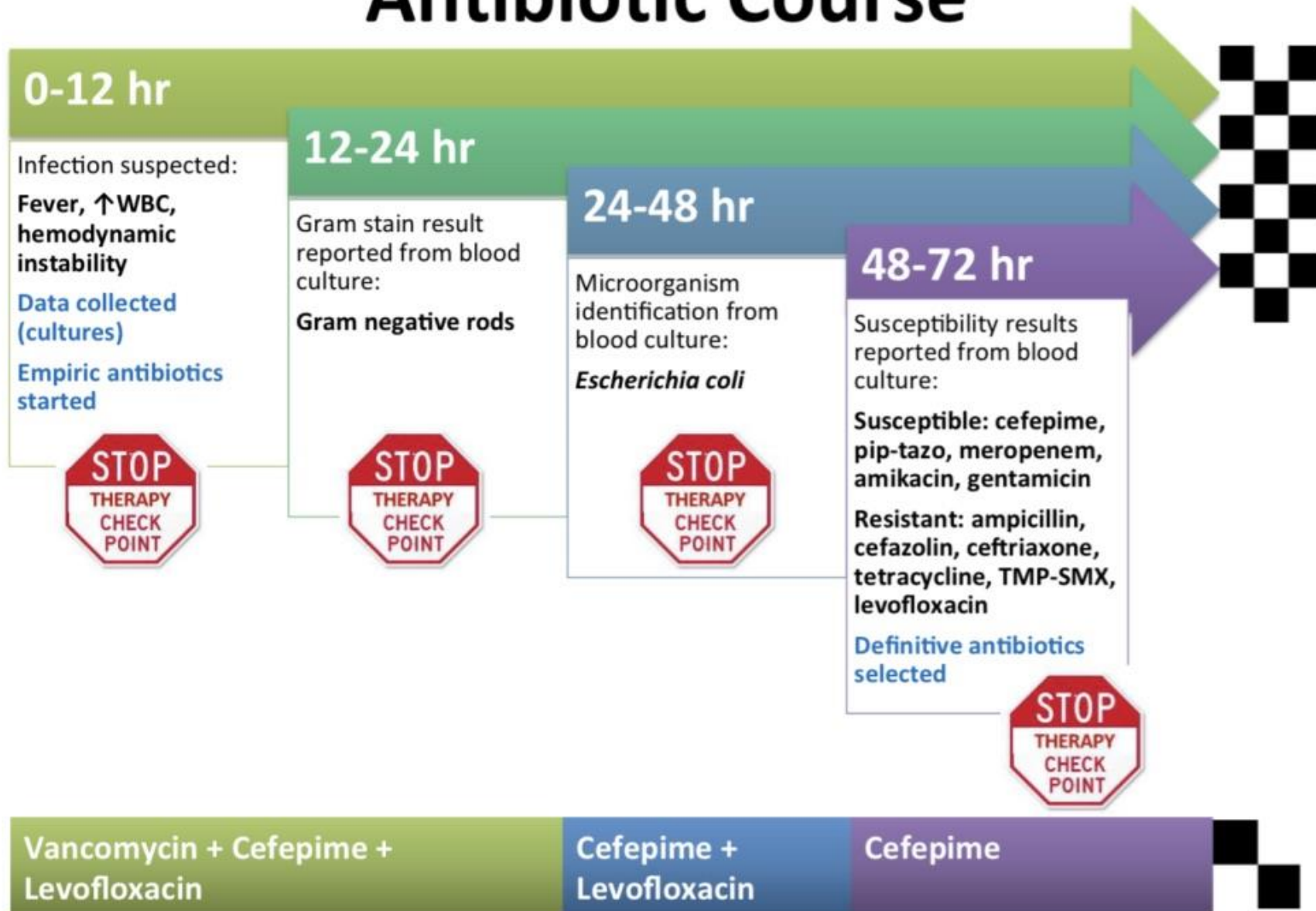
Where to find information?

- Up To Date
 - Quick resource
 - Very opinionated
 - References not great
- Lexi-Comp
 - Most widely used reference for drugs including dosing
 - Basically package insert doses
 - 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

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

- 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

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 2021

- 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*. 2009;180: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

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)

- 3rd 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 2021

- 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
- 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

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

Risks of Parenteral Antibiotic Therapy

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

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 (shuts down toxin production)
- 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
 - Watch those pesky calculations
- Linezolid (Zyvox)
 - Caution with serotonergic drug interactions
 - Bone marrow suppression increases ≥ 14 days of therapy

Dalbavancin (Dalvance)

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

Dalvance Package Insert.

Jones BM et al. *JACCP*. 2019;2:477-481.

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 ¹	X ⁵	X ⁴	X ³	X ¹	✓	X ¹	✓	X ²	✓	✓	✓	✓	✓	✓	✓	✓	✓
AMPICILLIN	X ¹	█	X ⁵	X ⁴	X ³	X ²	✓	X ²	✓	X ²	✓	✓	✓	✓	✓	✓	✓	✓	✓
CLOXACILLIN	X ⁵	X ⁵	█	X ⁵	X ⁵	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PENICILLIN	X ⁴	X ⁴	X ⁵	█	X ⁵	✓	✓	✓	X ³	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PIPERACILLIN*	X ³	X ³	X ⁵	X ⁵	█	X ³	✓	X ³	✓	X ³	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFADROXIL	X ¹	X ²	✓	✓	X ³	█	✓	X ¹	✓	X ²	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFAZOLIN	✓	✓	✓	✓	✓	█	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEPHALEXIN	X ¹	X ²	✓	✓	X ³	X ¹	█	✓	X ²	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFOXITIN	✓	✓	✓	X ³	✓	✓	✓	█	✓	X ²	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFPROZIL	X ²	X ²	✓	✓	X ³	X ²	✓	X ²	█	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFUROXIME	✓	✓	✓	✓	✓	✓	✓	✓	X ²	✓	█	X ³	X ¹	X ³	X ¹	X ²	✓	✓	✓
CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ³	█	█	X ³	X ³	X ³	X ³	✓	✓	✓
CEFOTAXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ¹	X ³	█	█	X ³	X ¹	X ¹	✓	✓	✓
CEFTAZIDIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ³	X ³	X ³	█	█	X ³	X ³	✓	✓	✓
CEFTRIAXONE	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ¹	X ³	X ¹	X ³	█	█	X ¹	✓	✓	✓
CEFEPIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ²	X ³	X ¹	X ³	X ¹	█	█	✓	✓	✓
ERTAPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	█	X ⁵	X ⁵
IMIPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ⁵	█	X ⁵
MEROPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X ⁵	X ⁵	█

* 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 ¹	Same side chain - clinical evidence of cross reaction. DO NOT PRESCRIBE
X ²	Same side chain - Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE
X ³	Similar side chain - Potential for cross reaction. DO NOT PRESCRIBE
Reaction likely based on Beta-lactam ring:	
X ⁴	Clinical evidence of cross reaction. DO NOT PRESCRIBE
X ⁵	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 1st 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 \downarrow INR significantly
- Most antimicrobials increase INR and increase risk for bleeding
- Worst offenders that \uparrow INR
 - TMP/SMX
 - FQs
 - Fluconazole
 - Clarithromycin

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 +/- azithromycin
- 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?