



## Some basic tenets:



- Think about the site of infection, the possible bugs and the host when choosing a regimen
- More is not always better many complications of antibiotic therapy
- · Consider the toxicities, check for drug-drug interactions,
- Ok to go broad overnight when patients are sick
- · Ok to pare down once stabilized and diagnosed
- Use your resources:
  - Partners Handbook → Clinical Topics → Infectious Disease (includes BWH Empiric Antibiotic Guidelines by Condition)
  - <u>www.uptodate.com</u>
  - https://www.hopkinsguides.com/hopkins/index/Johns Hopkins ABX Guide/All Topics/A
  - www.sanfordguide.com
- · If you have questions page ID



JP is a 48yo woman with h	/o L hip replac	em	ont ad		
TOVARE AND I DID DAID BIOU	od cultures dra	wn	ət adr	Imiti	ted with
levers and E nip pain. Dio			at aun	1133	1011.
STAPHYLOCOCCUS, COAGULASE NEGATIVE FROM AEROBIC 'FAN' MEDIUM	(BACT/ALERT)	Staphylococcus epidermidis (ZZ00) PRELIMINARY KB PANEL		Stap epide V	nylococcus rmidis (ZZ01) /ITEK MIC
	Comment	SEE	No Interpretation <sup>1</sup>		
	Comment	SEE	No		
	Comment	NOTES	Interpretation <sup>2</sup>		
	Chloramphenicol	25	Susceptible		
	Ciprofloxacin			<=0.5	Susceptible
	Clindamycin	25	Susceptible	<=0.12	Susceptible
	Daptomycin			0.25	Susceptible
	Erythromycin	30	Susceptible	<=0.25	Susceptible
	Gentamicin	23	Susceptible	<=0.5	Susceptible
A good indication for	Inducibile Clindamycin Resistance				Negative
on a a mulain	Levofloxacin	25	Susceptible	<=0.12	Susceptible
vancomycin	Linezolid	30	Susceptible	1	Susceptible
	Minocycline			<=0.5	Susceptible
	Moxifloxacin			<=0.25	Susceptible
	Oxacillin/cephalosporins	20	Resistant	>=0.5	Resistant
	Penicillin G	20	Resistant	>=0.5	Resistant
	Rifampin	31	Susceptible	<=0.5	Susceptible
	Tetracycline	25	Susceptible	2	Susceptible
	Tigecycline			0.25	Susceptible
	Trimethoprim/sulfamethoxazole	25	Susceptible No	<=10	Susceptible
	Vancomycin	10	Interpretation	1	Succeptible

## Vancomycin – basics

- Inhibits cell wall synthesis of gram-positive bacteria
- Large hydrophilic molecule NOT absorbed orally (PO does not achieve blood levels), and IV does not penetrate intestinal lumen
- Toxicities:
  - Red man syndrome
  - · local pain/phlebitis at injection sites
  - Leukopenia, thrombocytopenia, fever
  - Nephrotoxicity
  - Ototoxicity
  - Rarely, linear IgA dermatosis
    - bullous lesions



Vancomycin –dosing	See					
<ul> <li>Weight-based dosing</li> <li>(15-20mg/kg IV q8-12h)</li> </ul>	000					
<ul> <li>Depends on weight, age, CrCl, and indication (can use a loading dose)</li> </ul>						
<ul> <li>TITRATING UP TO HIGHER TROUGH LEVELS ONLY DATA-SUPPORTED IF TREATING KNOWN STAPH AUREUS INFECTION, BUT ALSO USEFUL FOR MONITORING FOR TOXICITY</li> </ul>						
<ul> <li>Goal trough level:</li> <li>10-20 if giving empirically or for "routine infection in normal host"</li> <li>15-20 for "complicated infections"</li> </ul>						
<ul> <li>Careful not to overdose, especially with elderly patients and/or borderline</li> </ul>						
renal function	CrCl	Each Dose	Interval			
Ceiling dose of 2gm per dose	> 45	15-20mg/kg	Q8-12h			
<ul> <li>Ceiling total daily dose ~ 6gm</li> </ul>	30-45	15-20mg/kg	Q24h			
<ul> <li>Vancomycin AUC monitoring is coming/here</li> </ul>	< 30	15-20mg/kg	Q48h			
,	HD	15-20mg/kg	Post-HD			

C. difficile antigen/toxin assay Collected: 7/20/2018 10:02 AM Status: Final result Visible to patient: Yes (Patient Gateway) N
Specimen Information: Stool, Stool
Ref Range & Units 7/20/18 10:02 AM
C. DIFFICILE ANTIGEN Positive C. DIFFICILE TOXIN Negative (*)

E.



- KW is a 32yo man with opiate use disorder admitted with fever and low back pain. MRI spine shows L3-4 discitis/osteomyelitis with adjacent epidural phlegmon with cord compression. Blood cultures are pending.
- Initial antibiotics?

#### vancomycin + ceftriaxone

			N / F		
od cultures =	= Stabr	n aureu	IS - IVII	$\exists SA$	
	- Olupi				
Culture & Susceptibility					
STAPHYLOCOCCUS AURFUS					
Antibiotic	Sensitivity	Result	Method	Status	
Ceftaroline	Susceptible	0.75	ETEST	Final	
Vancomycin	Susceptible	1.5	ETEST	Final	
Comm	IENT: If treatment is indicated, the BWF	H Infectious Disease Team recommend	s caution when using Vancomycin	to treat	
	Staphylococcus Aureus with a Ve	Staphylococcus Aureus with a Vancomycin MIC of 1.5mog/ml to 2.0mog/ml. Please consider a BWH Infectious Disease			
	recommendations				
Comments STAPHYLOCOCCUS AUR	EUS				
3+ STAPHYLOCOCCUS	AUREUS				
STAPHYLOCOCCUS AUREUS					
Antibiotic	Sensitivity	Result	Method	Status	
Clindemusia	Resistant	2-0	VITEK MIC	Final	
Clindamycin	Resistant	>=0	VITEK MIC	Final	
Erythromycin	Resistant	>=0	VITEK MIC	Final	
Gentamicin	Susceptible	<=0.5	VITEK MIC	Final	
Inducibile Clindamycin Resistance	Negative		VITEK MIC	Final	
Levotioxacin	Resistant	>=8	VITEK MIC	Final	
Linezolid	Susceptible	4	VITEK MIC	Final	
Minocycline	Susceptible	1	VITEK MIC	Final	
Moxifloxacin	Resistant	>=8	VITEK MIC	Final	
Oxacillin/cephalosporins	Resistant	>=4	VITEK MIC	Final	
Penicillin G	Resistant	>=0.5	VITEK MIC	Final	
Quinupristin/Dalfopristin	Susceptible	0.5	VITEK MIC	Final	
Rifampin	Susceptible	<=0.5	VITEK MIC	Final	
Tetracycline	Intermediate	8	VITEK MIC	Final	
Trimethoprim/sulfamethoxazole	Susceptible	<=10	VITEK MIC	Final	
	Succeptible	2	VITEK MIC	Final	
Vancomycin	Susceptible	-			

## Case 2

- KW is a 32yo man with opiate use disorder admitted with fever and low back pain. MRI spine shows L3-4 discitis/osteomyelitis with adjacent epidural phlegmon with cord compression. Blood cultures w MRSA.
- Treated with IV vancomycin, further blood cultures negative, undergoes operative debridement of epidural area, does well on IV vancomycin.



## B-lactams still better for Staph if susceptible

- Penicillin
  - If PCN-susceptible, still drug of choice for Staph!
- Cefazolin
  - Dosed Q8h for normal renal function
  - Equivalent to Naf/Oxa for most MSSA infections, with fewer toxicities
- Nafcillin
  - Q4h dosing, high salt/water load, risk of AIN
- Oxacillin
  - Q4h dosing, high salt/water load, risk of hepatitis

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#### **Alternate ending!**

- Real life!
- Does poorly on IV vancomycin due to:
  - Intolerance, toxicity
  - Treatment failure with ongoing bacteremia
  - Unable to discharge from hospital with PICC due to safety concerns
- What are the other options????





## Ceftaroline



- A B-lactam that treats MRSA?!?!?!?
  - FDA approved for community acquired pneumonia, including MRSA (no good data on Pseudomonas)
  - In practice more and more often used for tough MRSA cases from many infection site (if not responding to vancomycin/daptomycin, or if difficulty tolerating these)
  - Dose is 600mg IV q12h routine or q8h for MRSA
- Safety
  - Weekly CBC w diff (cytopenias very common), BUN/Cr, LFTs
  - Similar toxicity profile as most IV cephalosporins, apart from increased risk of cytopenias



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Newer Agents	The NEW ENGLAND JOURNAL of MEDICINE				
	ESTABLISHED IN 1812	JUNE 5, 2014	VOL. 370 NO. 23		
ORIGINAL ARTICLE	Once Weekly Dalbayanc	in versus Daily C	onventional Therapy		
Single-Dose Oritavancin in the Treatment	for Skin Infection				
of Acute Bacterial Skin Infections	Helen W. Boucher, M.D., Mark Wilcox, M.D., George H. Talbot, M.D., Sailaja Puttagur				
G. Ralph Corey, M.D., Heidi Kabler, M.D., Purvi Mehra, M.D., Sandeep Gupta, M.D., J. Scott Overcash, M.D., Ashwin Porwal, M.D., Philip Giordano, M.D., Christopher Lucasti, M.D., Antonio Perez, M.D., Samantha Good, Ph.D., Hai Jiang, Ph.D., Greg Moeck, Ph.D., and William O'Riordan, M.D., for the SOLO I Investigators*	Arina F. Das,	Ph.D., and Michael W. Dunne,	M.D.		
<ul> <li>Oritavancin/Dalbavan</li> </ul>	cin				
<ul> <li>Newer once weekly infu and soft tissue infection</li> </ul>	sion therapies approve , also active vs VRE	d and marketed	for MRSA skin		
<ul> <li>Many sites using predou outpatient, therapy for c</li> </ul>	ninantly for earlier trans omplicated infections w	sition to outpatie hen PICC not a	ent, or entirely n option		
ID guidance recomment	ded, use still rare, some	e risks (treatmer	nt failure)		

# Oral drugs for Strep + Staph aureus

- For Strep:
  - Penicillin, Amoxicillin, Amoxicillin-clavulanate, cephalexin, cefadroxil
- For MSSA (if PCN-resistant):
  - Amoxicillin-clavulanate, cephalexin, cefadroxil, dicloxacillin
- For MRSA (if susceptible):
  - Bactrim, Levofloxacin, Moxifloxacin, Doxycycline, Clindamycin
  - DO NOT USE RIFAMPIN WITHOUT ID GUIDANCE



## Trimethoprim-Sulfamethoxazole

BACTRIM D

- Many uses!
  - Most common = UTI, Staph aureus skin/soft tissue infections
- · Dose by the trimethoprim component
- PO formulations:
  - SS tablet = SMX/TMP 400mg/80mg
  - DS tablet = SMX/TMP 800mg/160mg
- Toxicities: GI, rash (mild → Stevens Johnson), serum sickness, aseptic meningitis, bone marrow suppression, hepatitis, methemoglobinemia (with severe G6PD deficiency)
- Renal: pseudo elevation in serum Cr, reversible hyperkalemia, real nephrotoxicity (interstitial nephritis)







## Thanks, and good luck...

