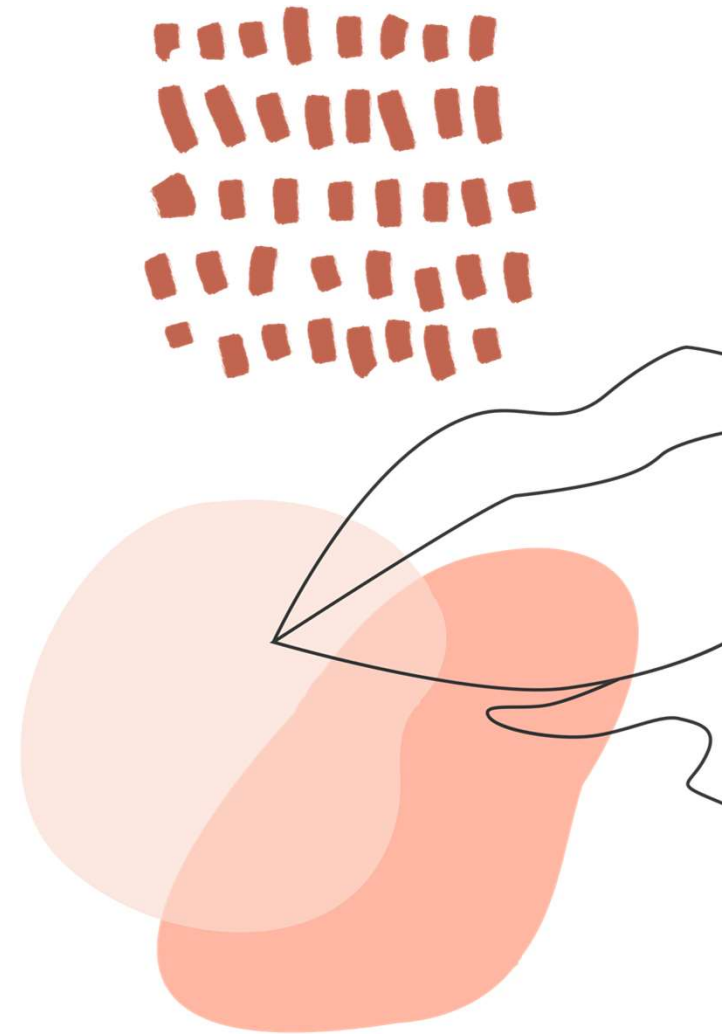


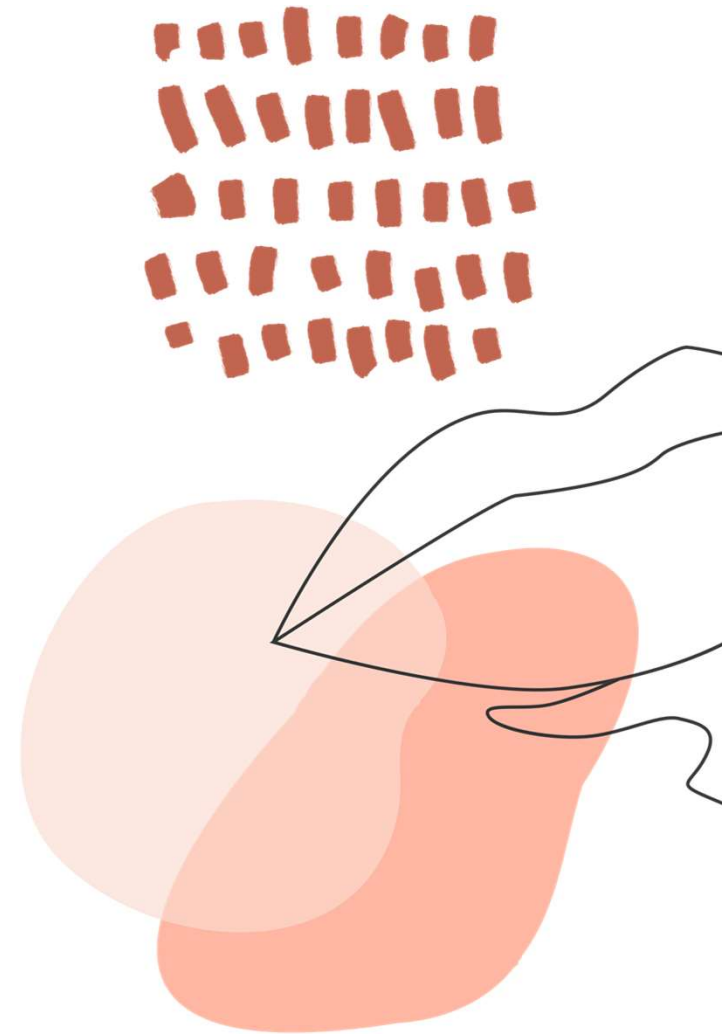
INFECTIOUS DISEASES PEARLS FOR THE “CULTURED” HOSPITALIST

RACHEL HENDRYX, PA-C



Disclosure statement


I have no relevant relationships with Ineligible companies to disclose within the past 24 months. (Note: Ineligible companies are defined as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.)





OBJECTIVES

At the conclusion of this session participants should be able to:

- Recognize hospital medicine specific ID pearls and clarify common mistakes or misunderstandings regarding obtaining and interpreting microbiology data
 - Describe specific principles when choosing an anti-infective: side-effects, interactions, doses, delivery, etc.
 - Recall ID-specific resources to reference in daily clinical use
- 

A QUICK MICROBIOLOGY REVIEW

OBTAINING GOOD CULTURES

- All cultures BEFORE antibiotics
- Blood: 2 sets, 2 separate sites, within one hour ideally
- Urine: UA always, clean catch, exchange foley, straight cath or from stoma aka at the source
- Respiratory: engage RT early
- CSF: Cell counts, cytology
- Pleural: Cell counts, cytology
- To swab or not to swab?

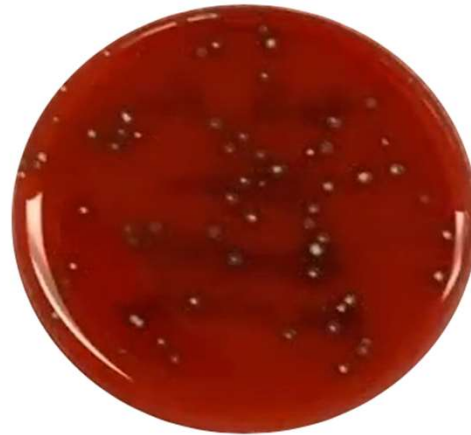
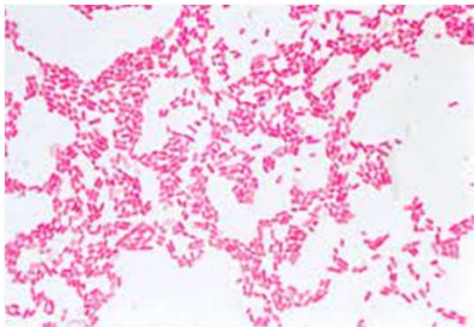
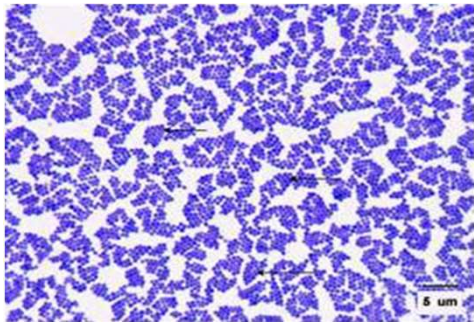
THE GRAM STAIN

- Gram stain does not equal growth on cultures
- Gram stain does not always translate to true pathogenic infection, i.e. mixed respiratory flora.
- Are there heavy PMN's?

CONTAMINANTS

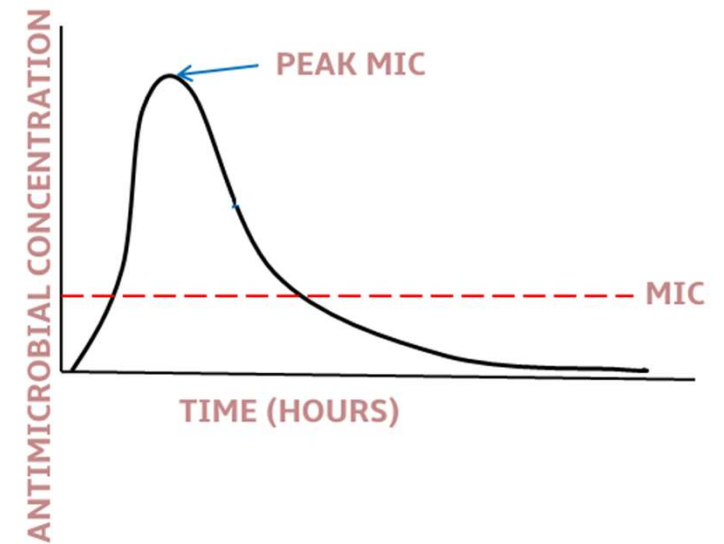
- It begins with step one: obtaining good cultures.
- Know your common skin colonizers
- Yeast in urine and respiratory cultures often colonization
- Colonization vs. contamination
- Transient bacteremias

MICRO LAB: BEHIND THE SCENES



Gram stain: A sample is looked at under a microscope after having a stain applied.

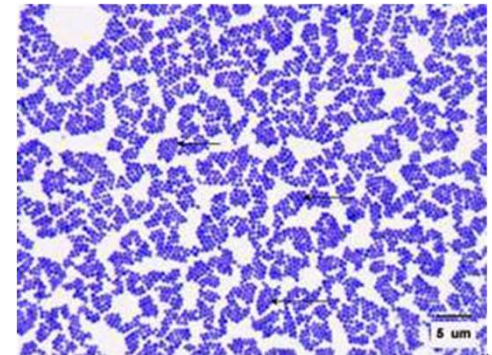
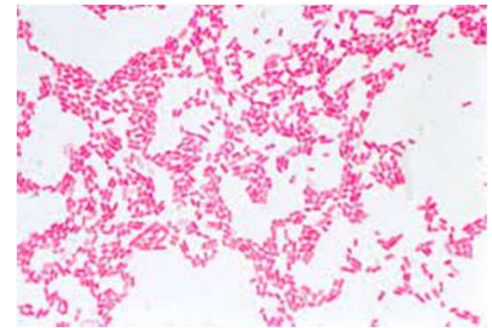
Culture: Bacteria, yeast, etc. from the sample are grown and examined to help determine the pathogen



Sensitivity: This determines which drug is best for treating the infection.

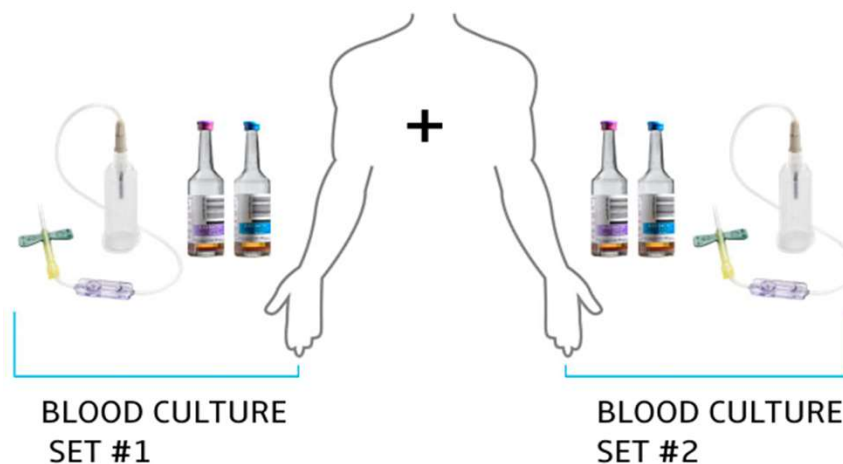
MICRO LAB: THE GRAM STAIN

- Gram stain does not always translate to growth on culture media, and likewise growth on cultures does not always equate to pathogenic infection
- Are there heavy PMN's? – increased PMN's can infer inflammatory/infectious response. Few PMN's making this less likely
 - Example: Respiratory gram stain shows few GPC's and GNR's, few PMN's. culture = mixed respiratory flora



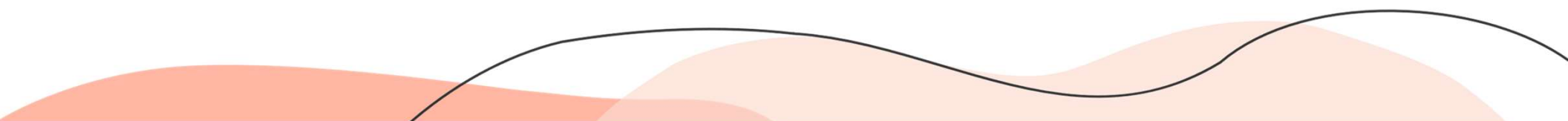
A QUICK MICROBIOLOGY REVIEW: BLOOD CULTURES

- A blood culture set is defined as two bottles, an aerobic bottle and an anaerobic bottle. Two blood culture sets (a total of 4 bottles) should be drawn
- Reminder: ALWAYS specify in EMR order to draw one set from Ports, PICC's, etc.
- Always draw before starting antibiotics
- Always order 2 sets, they need to be drawn ideally within one hour from each other and from 2 separate sites
- 2/2 sets positive = at least one bottle from each set is positive
- Don't be confused by micro reports, "2/2 bottles positive" = one set positive (institution specific)



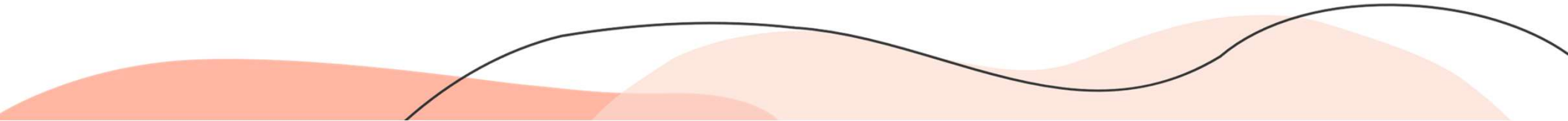
ALWAYS OBTAIN ONE SET FROM CENTRAL LINE WHERE APPLICABLE WITH SECOND SET FROM PERIPHERY.

A QUICK MICROBIOLOGY REVIEW: URINE CULTURES

- NEVER draw from old bag (nephrostomy, foley, etc.)
 - Draw from stoma, after foley exchange, after SPC exchange etc.
 - Remember to document when the foley was exchanged and if urine obtained post exchange
 - Don't forget the UA (asymptomatic bacteriuria, or bacterial growth on urine culture in setting of negative UA for instance shouldn't infer automatic infection)
- 

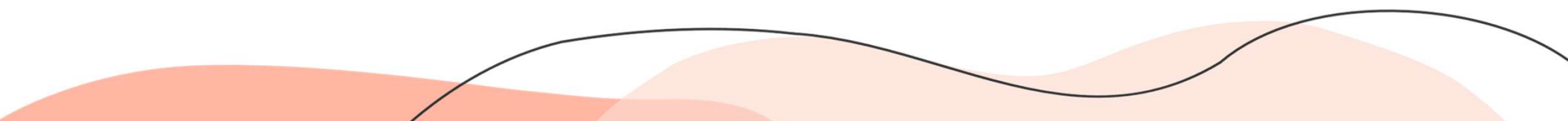
A QUICK MICROBIOLOGY REVIEW: RESPIRATORY CULTURES

- Engage RT early to avoid delays
- Hospital specific: AFB Order sets to r/o TB
- Remember: positive gram stain does not equate to positive cultures
 - Multiple isolates on gram stain commonly speciate to mixed respiratory flora
 - If micro lab notes a pseudomonas, staph aureus and few others will be denoted as such and not combined with mixed respiratory flora



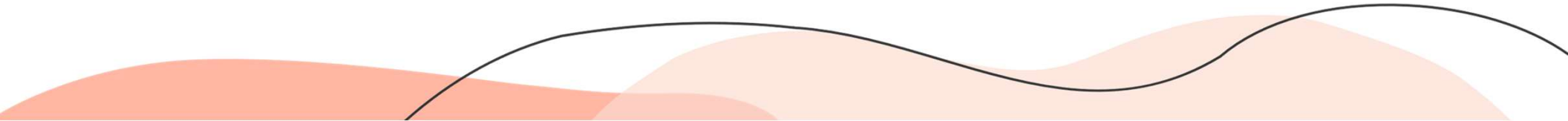
A QUICK MICROBIOLOGY REVIEW: PLEURAL, PERITONEAL, CSF ETC.

- Always draw fluid for cell counts, glucose, protein, cytology, etc and not just cultures. Often cannot rule out contamination in absence of these markers
- Doesn't hurt to save extra CSF for add-on tests pending ID consult / further recommendations
- IR CULTURES
 - Typically need anaerobic, aerobic and fungal cultures (sometimes AFB?). Don't expect IR to place the orders. It may be your responsibility as a hospitalist to make sure cultures are ordered *prior to the procedure!*
 - Another reminder NOT to draw cultures off an existing drain bag. Only reliable cultures obtained during drain placement or exchange



A QUICK MICROBIOLOGY REVIEW: CONTAMINANTS, COLONIZERS

- Distinguishing colonization from infection is an important factor in making the correct diagnosis
- Improperly obtained cultures can lead to mis-diagnoses and lengthy / expensive / invasive workups (TEE, prolonged antibiotic durations, CT scans etc.)



A QUICK MICROBIOLOGY REVIEW: CONTAMINANTS, COLONIZERS

COMMON SKIN CONTAMINANTS

- Coagulase negative staph species (CoNS)
 - exception: staph lugdunensis
- Corynebacterium species
- P. acnes
- Bacillus species (not anthracis)

COMMON URINE CONTAMINANTS

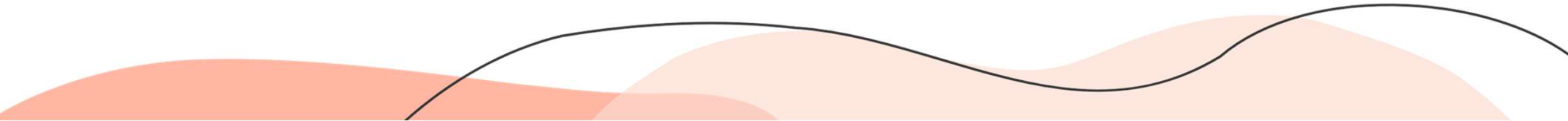
- Yeast
- Staph aureus = concerning for bacteremia / deep seeded infection
- Other skin colonizers that aren't staph aureus

COMMON RESPIRATORY CONTAMINANTS

- Yeast (typically, but not always, other markers like beta d glucan, aspergillus galactomannan also helpful)

A QUICK MICROBIOLOGY REVIEW: CONTAMINANTS, COLONIZERS

- Staph aureus in blood cultures almost never considered contaminant (risk of not treating is too high)
- Yeast in blood cultures is never a contaminant
- Joint aspirates, CSF cultures, etc. similar contaminants as skin colonizers on previous slide: again very important to get cell counts for correlation



SHOULD I SWAB IT? (PROBABLY NOT)

- Skin swabs = Contaminants / colonizers
- Okay to swab If you can unroof a lesion or drain the abscess for a fresh sample



A QUICK MICROBIOLOGY REVIEW: SUSCEPTIBILITIES, BREAKPOINTS

- A reminder MIC = minimum inhibitory concentration, or minimum medication needed to inhibit bacterial or fungal growth
- MIC(aka breakpoint, cutoff) vary from facility to facility based on local isolates and their respective sensitivities
- Not every antibiotic is tested, clinicians must infer certain types of antibiotic susceptibility based on bacterial patterns of resistance and sensitivities of other antibiotics
- Many isolates may report susceptible but be at high risk for developing resistance or already has, i.e. Amp-C inducers, if a patient is very sick or at risk of resistance keep this in mind

GSBLD CX		Gram negative rods	
Resulting Agency: AMC Lab			
Susceptibility		Escherichia coli AUTOMATED SUSCEPTIBILITY (PHOENIX)	
Amoxicillin/Clavulanic	<=4/2 ug/mL	Susceptible	
Ampicillin	>16 ug/mL	Resistant	
Ampicillin/Sulbactam	8/4 ug/mL	Susceptible	
Aztreonam	8 ug/mL	Intermediate	
Cefazolin	>16 ug/mL	Resistant	
Cefepime	4 ug/mL	Intermediate	
Cefoxitin	8 ug/mL	Susceptible	
Ceftazidime	4 ug/mL	Susceptible	
Ceftazidime/Avibactam	<=0.25/4 ug/mL	Susceptible	
Ceftriaxone	32 ug/mL	Resistant	
Ciprofloxacin	0.5 ug/mL	Intermediate	
Ertapenem	<=0.25 ug/mL	Susceptible	
Gentamicin	<=2 ug/mL	Susceptible	
Levofloxacin	<=0.5 ug/mL	Susceptible	
Meropenem	<=0.5 ug/mL	Susceptible	
Meropenem/Vaborbactam	<=2/8 ug/mL	Susceptible	
Minocycline	4 ug/mL	Susceptible	
Piperacillin/Tazobactam	<=2/4 ug/mL	Susceptible	
Tetracycline	>8 ug/mL	Resistant	
Tigecycline	<=1 ug/mL	Susceptible	
Trimethoprim/Sulfamethoxazole	<=0.5/9.5 u...	Susceptible	

MICRO LAB BEHIND THE SCENES: MIC TESTING

MIC Microbroth dilution



MIC Disks



ANTIBIOTIC (OR ANTIFUNGAL/ANTIVIRAL) SELECTION

ALLERGIES	DELIVERY	INTERACTIONS	RESISTANCE	EXPOSURES	PENETRATION /DOSE	DURATION
Childhood allergy? Cross-Reactivity Side-chains	IV vs. PO Absorption Volume status Bio-availability	Home meds	Local antibiogram Hx of resistance?	Hospital acquired Environmental Workplace Housing insecurity, etc.	CNS Bone Urine Endocarditis	Guidelines, case reviews, Up to Date etc. can be helpful

ANTIBIOTIC SELECTION: START WITH ALLERGIES

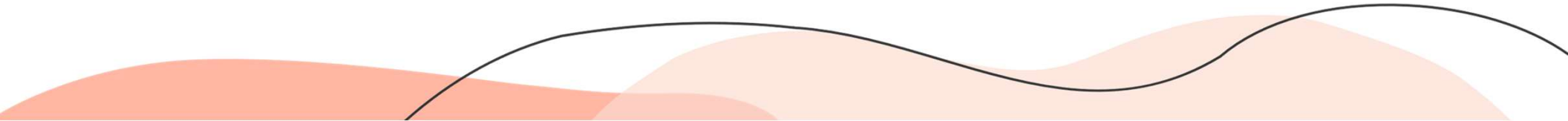
- First thing to consider when selecting an agent: (for pretty obvious reasons) but always clarify the allergy severity and timeframe
- Did you know? About 10% of all people in the United States report having a penicillin allergy, but only 1% of those people actually have an allergy. Furthermore, patients are at risk of increased adverse outcomes with abx allergy labels
- Offer allergy testing inpatient if offered at your institution or referral on discharge followed by desensitization if available
- Not all antibiotics within the same class share the same allergy profile / cross-reactivity (different side chains)

	Penicillin	Amoxicillin	Ampicillin	Cephalexin	Cefuroxime	Cefoxitin	Ceftriaxone	Cefotaxime	Cefepime	Ceftazidime
Similar side chains										
Penicillin	■					X				
Amoxicillin		■	X	X						
Ampicillin		X	■	X						
Cephalexin		X	X	■						
Cefuroxime					■	X	X	X		
Cefoxitin	X				X	■				
Ceftriaxone					X		■	X	X	X
Cefotaxime					X		X	■		X
Cefepime							X		■	
Ceftazidime							X	X		■

• chart courtesy of Meghan Jeffres pharmD

ANTIBIOTIC SELECTION: DELIVERY

- Do I need IV?
 - Critically ill patients
 - Is the patient NPO or at risk of aspiration?
 - Any concern for GI absorption ability? Short gut syndrome, hx of gastric bypass etc. (typically if the abx has rapid absorption, still okay for PO but not extended release, delayed release, etc.)
 - Do I have concerns about their volume status and unnecessary fluid burden?
 - Bio Availability
 - Many agents are equally bio-available whether IV or PO. Always prefer PO if none of the above are concerns
 - Penetration sites, IV may be necessary vs dose adjustment or both

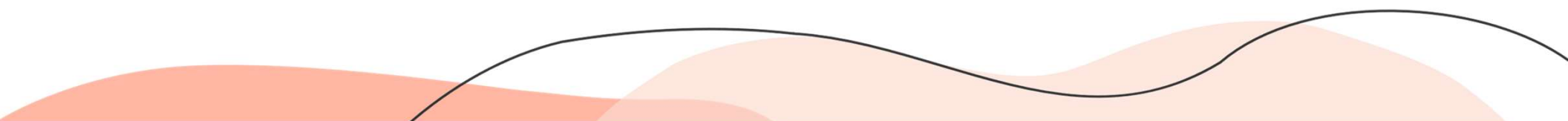


ANTIBIOTIC SELECTION: MORE ON BIO-AVAILABILITY

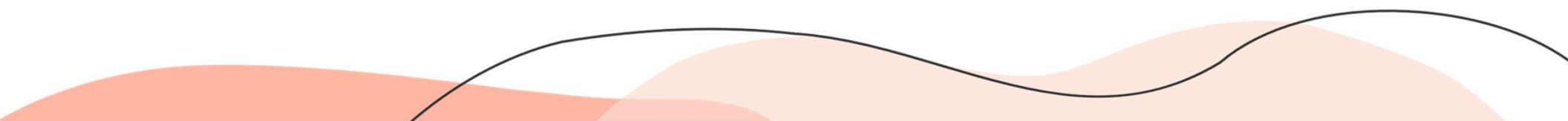
- COMMON AGENTS THAT ARE EQUALLY BIO-AVAILABLE IV VS. ORAL

ANTIBIOTICS	ANTIFUNGALS	ANTIVIRALS
<ul style="list-style-type: none">• Fluoroquinolones: Moxifloxacin, Levofloxacin, Ciprofloxacin but need to adjust dose• Metronidazole• Bactrim• Linezolid	<ul style="list-style-type: none">• Azoles: i.e. Fluconazole, Voriconazole	<ul style="list-style-type: none">• None

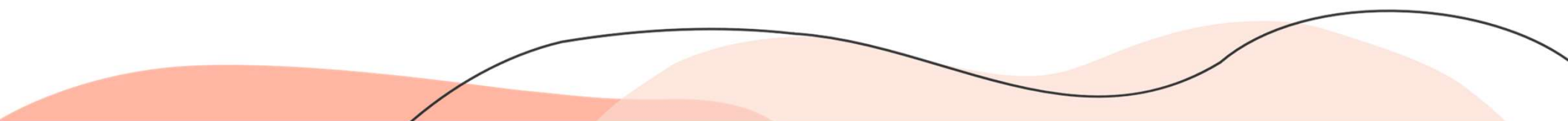
ANTIBIOTIC SELECTION: INTERACTIONS / RISK FACTORS

- Typically EMR will flag this for you but good to remember common interactions:
 - Medications that lower seizure threshold in epileptics or someone at risk for seizure (i.e. brain tumor, mass effect, etc.) (4th generation cephalosporins, carbapenems, quinolones, Unasyn)
 - Serotonin syndrome (particularly with linezolid)
 - QTc prolonging agents (fluoroquinolones, azoles, macrolides)
 - Warfarin and most antimicrobials
 - Encephalopathy: carbapenems, cefepime (reversible so don't necessarily avoid therapy with this in patients at risk for AMS, can always change therapy as needed if concerns present)
 - Vascular disease (increased risk of aortic dissection with quinolones)
 - Alcohol use (avoid metronidazole)
 - Remember antibiotics can lower efficacy of contraceptive pills
- 

ANTIBIOTIC SELECTION: EXPOSURES

- Am I treating a hospital or community acquired infection?
 - Do I need to be worried about pseudomonas or MRSA?
 - Does the patient have hx of resistance / MDR's? How long ago?
 - Local resistance – utilize your facility antibiogram
 - Environmental exposures
 - Is Listeria a concern?
 - Mycobacterial infections: save your antibiotics to reduce risk of resistance
 - Risk of invasive or atypical fungal infections? (soil / livestock exposures, patient is immunocompromised, etc.)
- 

ANTIBIOTIC SELECTION: PENETRATION / DOSE

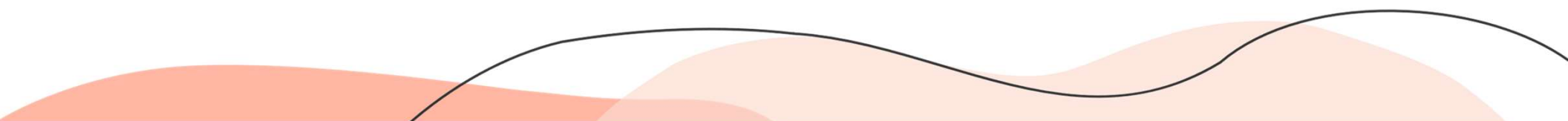
- BONE PENETRATION
 - CNS / OCULAR PENETRATION
 - URINE / RENAL PENETRATION
 - PULMONARY
- 
- The bottom of the slide features a decorative graphic consisting of several overlapping, wavy, light-orange shapes that create a sense of movement and depth.

*Image from UCH Antibioqram

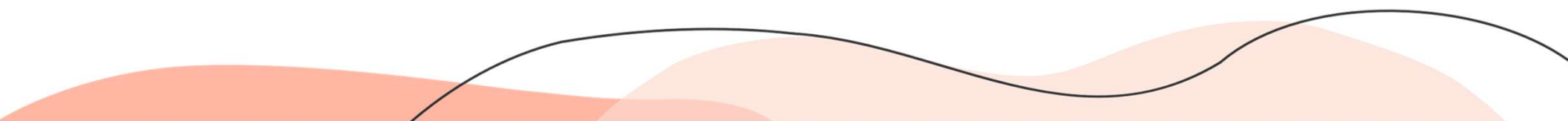
CNS, Bone, and Urinary Penetration for Select Antimicrobial Agents

Drug	CNS Uninflamed (%)	CNS Inflamed (%)	Bone	Urine
Beta-Lactams - Penicillins				
Penicillin G/V	Low	Moderate (30)	N/A	Excellent
Nafcillin	Low (1-2)	Moderate (20-30)	Moderate	Good
Ampicillin	Low (1.6)	Moderate (39)	Mod-Good	Good
Sulbactam	Low (7)	Low (10)	Mod-Good	Good
Amoxicillin	Low	Low (5.8)	Moderate	Excellent
Clavulanic Acid	Low (3.7)	Low (8.4)	Moderate	Excellent
Piperacillin / tazobactam ²	Low (3.7/10.6)	Moderate (32)	Moderate	Good
β-Lactams- Monobactam				
Aztreonam	Moderate	Moderate (13-18)	Moderate	Good
β-Lactams – Cephalosporins				
Cefazolin ²	Low	Low (9-10)	Moderate	Excellent
Cefotaxime	Low (9)	Moderate (17)	Moderate	Good
Cefoxitin ²	Low (0-9)	Good (41-50)	Moderate	Good
Ceftriaxone	Low (0.7-2)	Moderate (20-35)	Moderate	Good
Ceftazidime	Low (2-8)	Moderate (36-40)	Mod-Good	Excellent
Ceftazidime-Avibactam ²	N/A	N/A	N/A	Excellent
Cefepime	Low (8-10)	Moderate (20-34)	Good	Good
Ceftolozane-Tazobactam ²	N/A	N/A	N/A	Excellent
Ceftaroline ²	Low (3)	Moderate (15)	N/A	Good
β-Lactams – Carbapenems				
Ertapenem ²	?	Low-Moderate	Moderate	Good
Meropenem	Moderate (5-25)	Good (39-75)	Moderate	Good
Imipenem/Cilastatin	Low	Moderate (14)	Low	Good
Fluoroquinolones				
Ciprofloxacin ²	Good (24-43)	Excellent (92)	Excellent	Excellent
Moxifloxacin ^{2,3}	Good (46)	Excellent (71-94)	Excellent	Low
Levofloxacin ²	Good (71)	Excellent (>90)	Excellent	Excellent

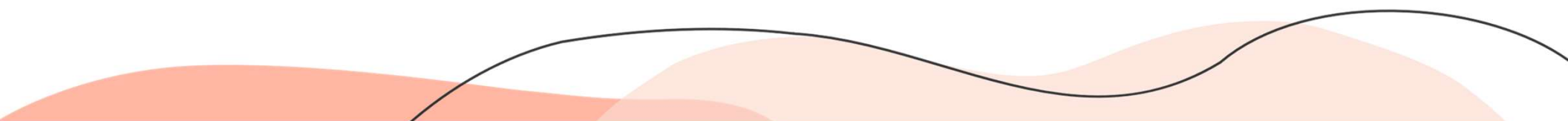
ANTIBIOTIC SELECTION: DOSE

- Similar to choosing an antibiotic with specific sites of penetration, the dose may need to be altered depending on site of infection:
 - Endocarditis, Osteomyelitis, CNS infection, renal infection vs. UTI, etc.
 - Don't forget patient's weight/age
 - Trough levels: vancomycin for instance
 - Renal function/HD/CRRT dosing, may need to frequently adjust dose based on renal function
 - Augmented renal clearance: can check cystatin C for more accurate dosing
 - MIC: some antimicrobials are dose dependent based on the MIC, ex: *c. glabrata*
- 

ANTIBIOTIC SELECTION: DURATION

- Simple guidelines do exist for common infections: pneumonia, SSTI, endocarditis, bacteremias, CNS infections. A quick UptoDate check can be helpful, case review for less documented infections.
 - Do I have source control? Typically first day of appropriate therapy is when source control is achieved, example: I&D, surgical washout, line removed, etc.
 - Many guidelines don't exist: when in doubt choose an even number (*joking-ish)
- 

ANTIBIOTIC SELECTION: NARROW AS ABLE!

- Antibiotic-resistant superbugs = a looming health threat
 - Bugs are smart! Pathogens can genetically adapt themselves through repeated exposures to antibiotics
 - Repeated use of narrow spectrum antibiotics eventually lead to super bugs requiring broad spectrum antibiotics
 - Set realistic antibiotic durations
 - Narrow your regimen as quickly as able
 - Judicious use of antibiotics: ex: asymptomatic bacteriuria vs UTI vs. colonization, etc.
- 
- The bottom of the slide features a decorative graphic consisting of several overlapping, wavy, light-orange shapes that create a sense of movement and depth, resembling a stylized horizon or a series of hills.



AS AN FYI: A FEW ID RESOURCES WE LIKE:

APPS

- John Hopkins Antimicrobial guide
- Sanford guide
- Case reviews
- IDSA practice guidelines
- CDC Provider resources

ANTIBIOGRAMS

- Don't forget your local antibiogram

PHARMACISTS

- Don't forget about antimicrobial stewardship!
 - Simple/initial/empiric antibiotic choice/dose/duration and when to narrow can be done by ID pharmacy



UCHealth AMC/BFH Antibiogram (1/1/2022-12/31/2022)

Gram Negatives: Community Acquired (Cultures obtained ≤48 hours from admission)

Organism	n	Ampicillin	Amoxicillin-Clavulanate	Cefazolin	Ceftriaxone	Ceftazidime	Cefepime	Piperacillin-tazobactam	Meropenem	Ertapenem	Levofloxacin	Amikacin	Tobramycin	Sulfamethoxazole-Trimethoprim	Nitrofurantoin ¹
<i>Escherichia</i> spp	1580	49	92	69	86	89	87	94	99	99	77	100	-	70	97
<i>Klebsiella</i> spp	338	0	90	70	90	92	91	86	99	99	90	99	-	84	54
<i>K. pneumoniae</i>	81	0	91	80	90	92	91	87	99	99	87	99	-	82	44
<i>K. oxytoca</i>	139	0	80	16	83	92	86	80	100	100	95	100	-	86	93
<i>Enterobacter</i> spp.	191	-	-	-	70	71	85	72	98	84	93	100	-	91	33
<i>Proteus</i> spp.	139	70	97	10	93	100	98	99	100	100	93	100	-	83	0
<i>Citrobacter</i> spp.	73	0	32	28	76	78	93	80	100	98	90	100	-	95	85
<i>C. freundii</i>	44	0	0	0	68	65	90	72	100	100	88	100	-	95	100
<i>P.aeruginosa</i>	225	-	-	-	-	88	76	88	88	-	76	98 ^[1]	99	-	-

- Antibiogram example:

This data is pulled from facility specific microbiology lab to assess local antimicrobial susceptibility patterns to help guide empiric therapy

Gram Negatives: Hospital Acquired (Cultures obtained >48 hours from admission)

Organism	n	Ampicillin	Amoxicillin-Clavulanate	Cefazolin	Ceftriaxone	Ceftazidime	Cefepime	Piperacillin-tazobactam	Meropenem	Ertapenem	Levofloxacin	Amikacin	Tobramycin	Sulfamethoxazole-Trimethoprim	Nitrofurantoin ¹
<i>Escherichia</i> spp	352	40	74	58	79	84	81	90	99	99	67	100	-	66	96
<i>Klebsiella</i> spp	229	0	84	62	85	87	87	81	97	96	90	99	-	83	54
<i>K. pneumoniae</i>	159	0	84	72	85	85	86	80	97	96	88	99	-	81	41
<i>K. oxytoca</i>	55	0	76	18	81	89	87	76	93	92	97	100	-	83	100
<i>Enterobacter</i> spp.	179	0	0	0	62	63	78	61	95	78	95	100	-	91	27
<i>Proteus</i> spp.	64	73	95	9	92	98	98	100	100	100	84	100	-	84	0
<i>Citrobacter</i> spp.	59	0	27	18	59	59	77	55	100	96	90	100	-	89	84
<i>C. freundii</i>	43	0	4	2	46	46	72	46	100	95	89	100	-	88	88
<i>P.aeruginosa</i>	183	-	-	-	-	89	79	87	87	-	81	100 ^[1]	97	-	-

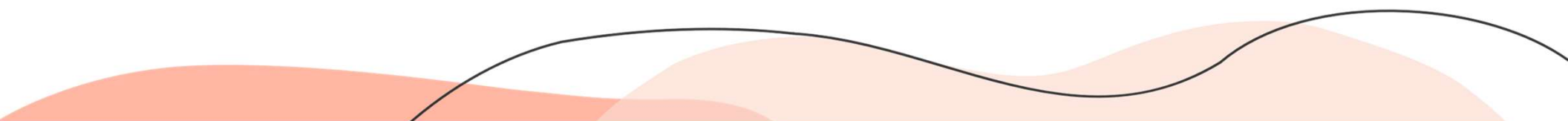
***Klebsiella (Enterobacter) aerogenes* is included with *Enterobacter* spp.

1: urinary isolates only

Practice question #1

A 37yo F with no significant PMH presents to the hospital with abdominal pain, diarrhea, fever. Your leading diagnosis is simple viral gastroenteritis however you obtain blood cultures and she has one out of two sets with Gram Positive Clusters

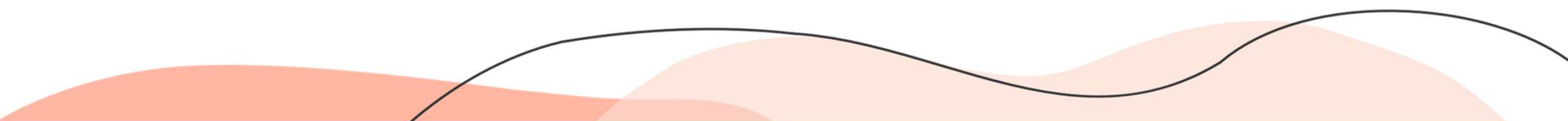
What is your initial plan?

- A. Wait until blood cultures are speciated before starting antibiotics
 - B. Defer antibiotics because this is probably a contaminant
 - C. Start IV Vancomycin
 - D. Start PO linezolid
- 

Practice question #2

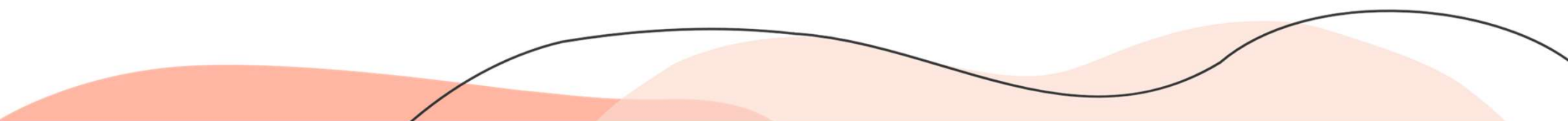
A 68yo M with PMH BPH, HTN, CAD presents to the hospital with abdominal pain with associated nausea and vomiting. The patient is s/p lap cholecystectomy two weeks prior for cholelithiasis. His vital signs are notable for a tmax of 101.8F, HR 119, 93% on room air. Labs notable for a WBC of 19, normal lactate, Cr .95, normal LFT's. A CT a/p with contrast is obtained and demonstrates a 6cm x 8.5cm abscess in the cholecystectomy bed. IR has been consulted and plans to place a drain later today and obtain cultures.

What is your initial plan?

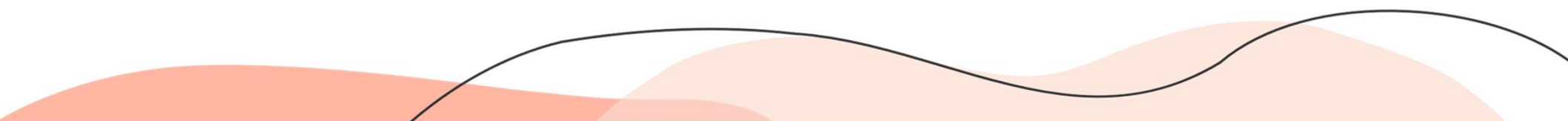
- A. Defer antibiotic therapy until IR cultures have resulted
 - B. Start IV Ceftriaxone and IV flagyl
 - C. Start IV vancomycin / IV meropenem
 - D. Start IV Piperacillin/tazobactam
 - E. Start IV Unasyn
 - F. Start PO Augmentin
- 

Practice question #3

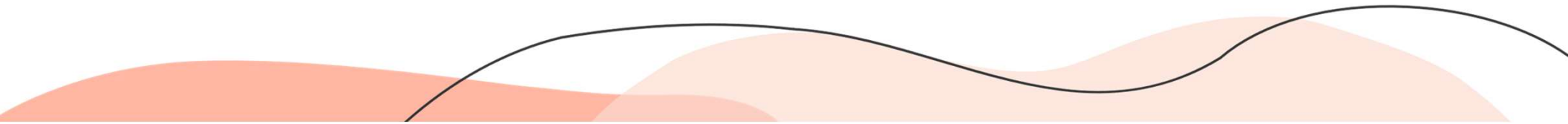
A 57 yo F with PMH of MS complicated by neurogenic bladder / chronic suprapubic catheter, recurrent UTI's presents with fevers, flank pain and foul smelling urine. You exchange her suprapubic catheter and obtain a urine culture, preliminary UA appears has +WBC, nitrites and leukocyte esterase. You find records from the last 6 months that demonstrate prior urine cultures for pan susceptible e. coli, pan susceptible pseudomonas. The gram stain of the urine demonstrates >100k Gram negative rods. What is your initial antibiotic choice?

- A. PO Levofloxacin
 - B. IV Levofloxacin
 - C. IV Cefepime
 - D. IV Ertapenem
 - E. IV meropenem
 - F. IV Ceftriaxone
- 

Summarization

- Prioritize obtaining quality specimens for delivery to the microbiology lab, will avoid unnecessary, invasive and expensive workups.
 - Consider multiple factors when choosing an anti-infective including allergies, IV vs. PO, dose, interactions, penetration, exposure history, duration. Use evidence based judgment to narrow patient's regimens in a timely and concise manner to avoid resistant super-bugs.
 - Utilize common resources to help guide your diagnoses and subsequent management.
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Questions?



References

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