



**UWWTASP**  
tele-antimicrobial stewardship program

January 29, 2019

## Agenda

- Recap and Recharge January –  
-Pro-tips from a non-microbiologist
- Case Discussions
- Open Discussion



# Pro-tips from a non-microbiologist

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# Does my patient have an infection?

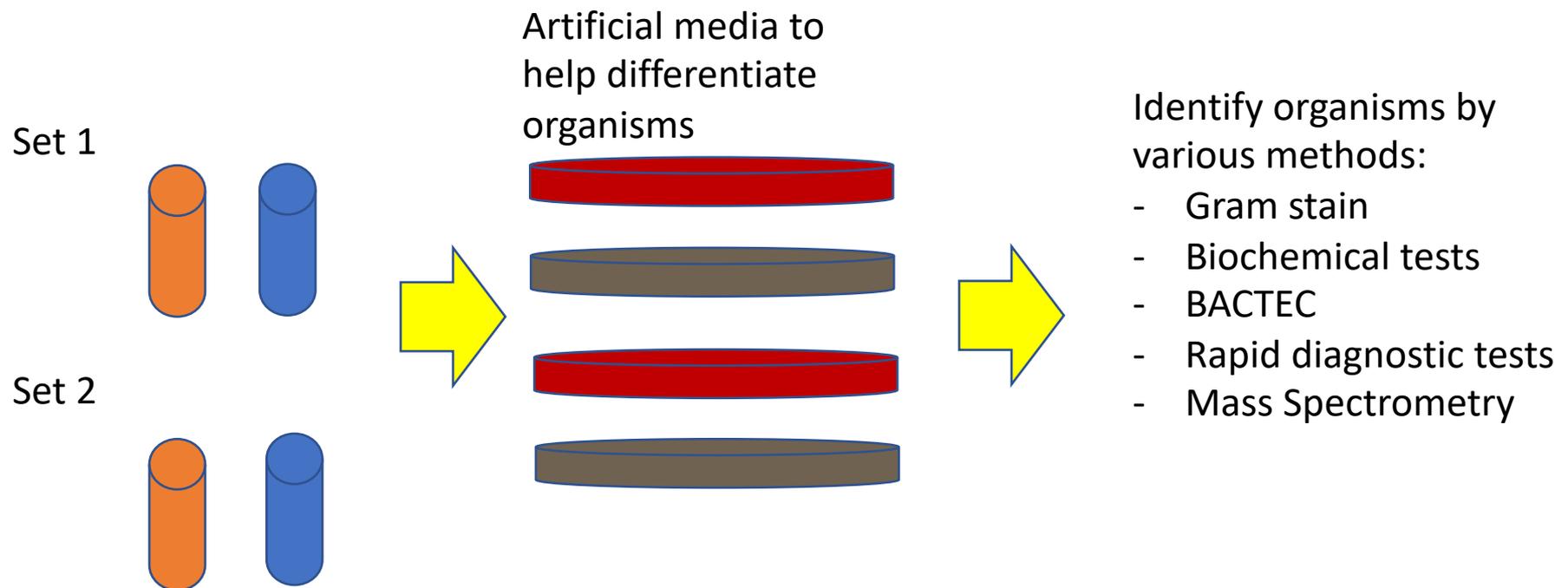
- Is my patient's illness caused by a microbe?
- If so, what is it?
- What is the susceptibility profile of the organism so therapy can be targeted?



# Obtaining blood cultures in suspected infection

Adults: 2-4 blood culture sets per septic episode

- 20-30mL of blood per culture set injected into 2 bottles



# Colonization vs infection?

Common skin flora: *Staphylococcus* spp (coagulase-negative staph), *Streptococcus* spp, *Corynebacterium* spp and *Propionibacterium* spp, *Bacillus* spp

Each set tests blood samples in an aerobic + anaerobic bottle

<u>Set 1</u>	<u>Set 2</u>	<u>Result</u>
 	 	True
 	 	True
 	 	True
 	 	Negative
 	 	Negative
 	 	True
 	 	Negative

Legend

-  Positive bottle
-  Negative bottle
-  Not tested



# Case

64 y/o F who is in her normal state of health.

She reports eating out and had an episode of diarrhea followed by chills and subjective fever.

Abd exam is benign but continues to have high fevers and chills. She is not neutropenic.

She is admitted to the UWMC for dehydration and IV antibiotics.

Pt is started on IV levofloxacin



# Blood culture: Lactose Fermenting GNR *E.coli*

What do you think it will be sensitive to?

Everybody pull out your antibiogram?



# Audience response

What is the Levofloxacin *E.coli* susceptibility at your institution?

- a. <70%
- b. 71-80%
- c. 81 -90%
- d. 90-100%
- e. No information available



# Blood culture: *E.Coli*

Drug	Interpretation	MIC value
Ceftriaxone	S	0.25
Cefazolin	S	0.5
Levofloxacin	R	8
Ertapenem	S	0.25
Gentamicin	S	2.0
Tobramycin	S	0.5
Piperacillin/tazobactam	S	4.0
Meropenem	S	0.5

- ✓ Use Interpretation column first to determine which antibiotic will be appropriate.
- ✓ If you don't see the antibiotic, don't assume susceptibility!



# Audience response

Does your institution report Minimum inhibitory concentrations (MICs) on the culture results?

- a. Yes
- b. No
- c. Sometimes
- d. I don't know



# Evaluation of Antimicrobial Activity

Methodologies for assessing antimicrobial activity

in vitro:

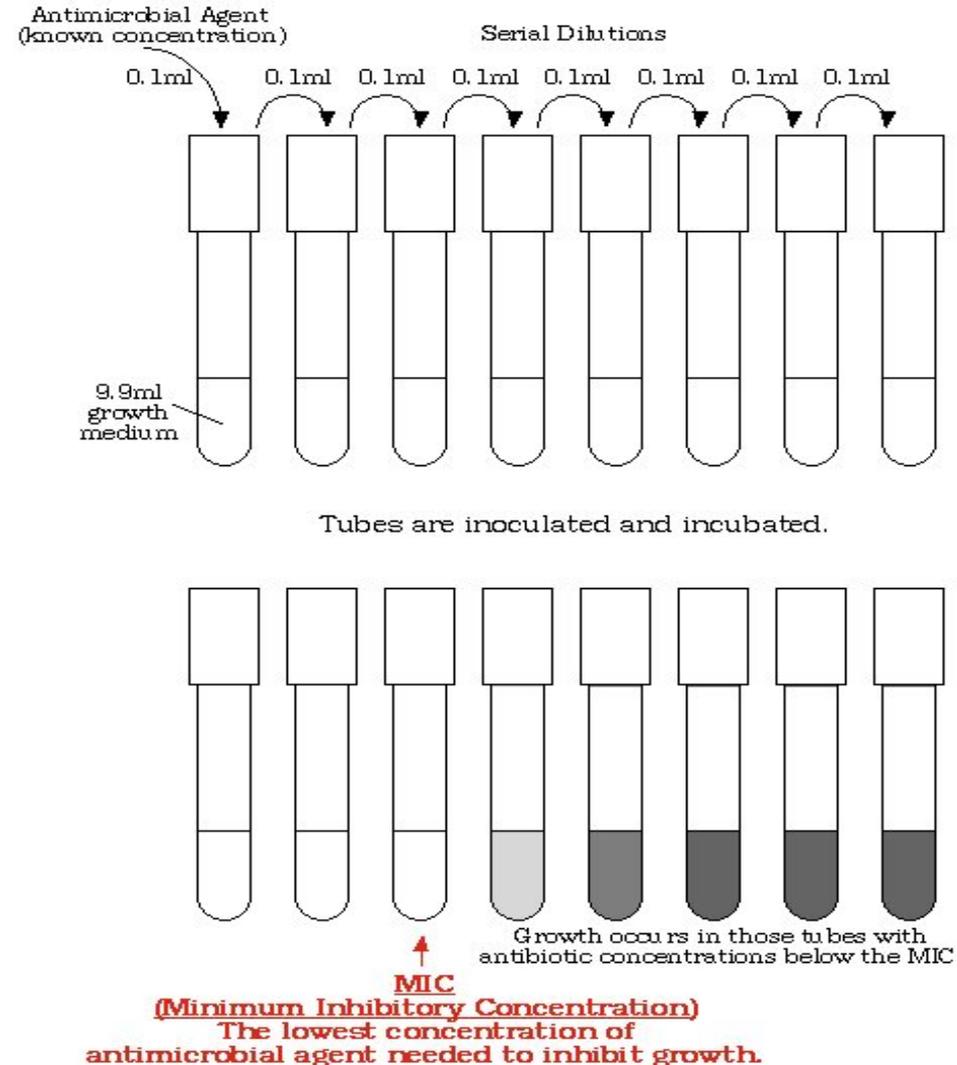
- Qualitative: disc

diffusion (Kirby-Bauer)

- Quantitative:

- broth dilution
- agar dilution
- E-test

## Determination of the MIC: Tube Dilution Assay



# Evaluation of Antimicrobial Activity

## Intrinsic resistance

Resistance to an antimicrobial is a characteristic of the microbial species (almost all isolates of that species are resistant, non-transferable)

eg. Vancomycin/GNR, Aminoglycosides/Anaerobes

Good source: CLSI document (Appendix B)

<http://em100.edaptivedocs.net/Login.aspx>

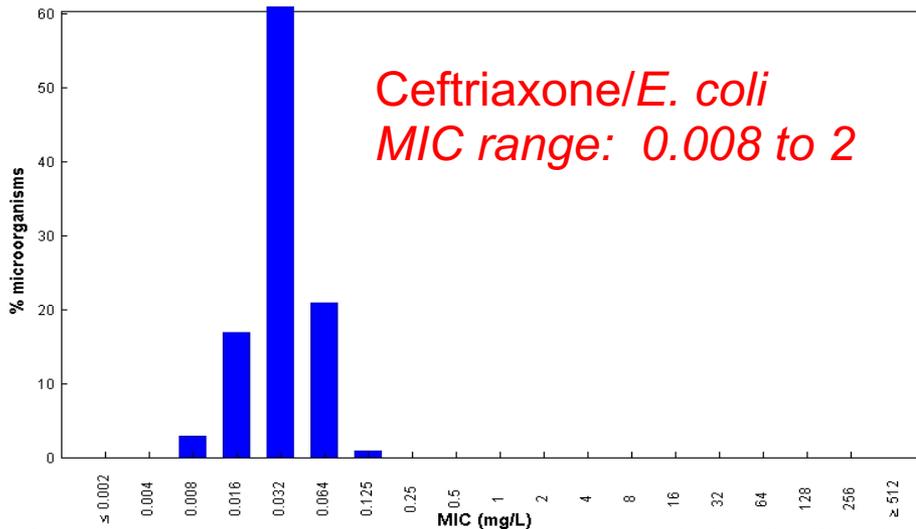


# MIC ranges

- **EACH** organism and **EACH** antimicrobial have a specific MIC range

Ceftriaxone / *Escherichia coli*  
EUCAST MIC Distribution - Reference Database 2010-09-30

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance

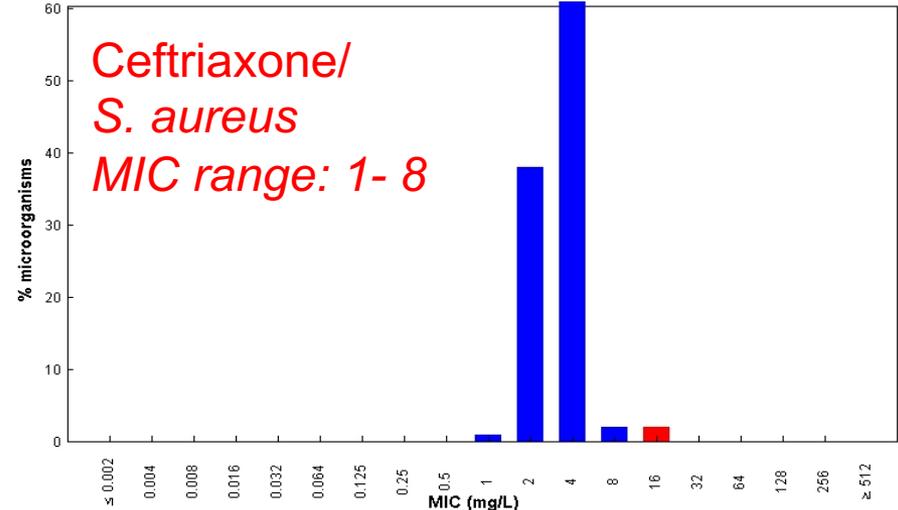


*Ceftriaxone/E. coli*  
MIC range: 0.008 to 2

MIC  
Epidemiological cut-off: WT ≤ 0.125 mg/L  
846 observations (3 data sources)  
Clinical breakpoints: S ≤ 1 mg/L, R > 2 mg/L

Ceftriaxone / *Staphylococcus aureus*  
EUCAST MIC Distribution - Reference Database 2010-09-30

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance



*Ceftriaxone/S. aureus*  
MIC range: 1- 8

MIC  
Epidemiological cut-off: WT ≤ 8 mg/L  
395 observations (4 data sources)  
Clinical breakpoints: S ≤ - mg/L, R > - mg/L

- MIC ranges are based on the pharmacokinetic information of the drug and microbiology surveillance studies



# What is a breakpoint?

- The term “breakpoint” can mean a variety of things in the literature:
  - MIC that distinguishes organisms from those with acquired or selected resistance mechanisms (microbiological breakpoint)
  - MIC that distinguishes high likelihood of treatment success vs. failure (clinical breakpoint)
  - Data generated in animal models and extrapolated to humans, Monte-Carlo simulation, etc. (PK/PD breakpoints)



# Interpretative Criteria

- In addition to S, I & R, there are two other interpretations:
- “ S-DD” = “Susceptible Dose dependent”
  - Ceftaroline MIC 2-4mcg/ml -*S.aureus*
  - Daptomycin MIC 2-4 mcg/ml– *Enterococcus*
  - Cefepime MIC 4-8mcg/ml – Enterobacteriaceae



# What does S-DD mean?

- “S-DD” – Susceptible Dose-dependent
  - *C.albicans* MIC = 4 mcg/ml
  - *C.glabrata* MIC  $\leq$  32 mcg/ml
- "Susceptibility is dependent on achieving the maximal possible blood level."

	Serum Peak (mcg/m)	Serum Trough (mcg/ml)
Fluc 400mg	20-30	12
Fluc 800mg	40-60	24



# MICs for *S. pneumoniae*

Breakpoints (mcg/ml)	Non-CNS	CNS	CSF conc (mcg/ml)
Cefepime	≤ 1	≤ 0.5	5.7 +/- 7.3
Ceftriaxone	≤ 1	≤ 0.5	4.5 +/- 3.5
Penicillin (IV)	≤ 2	≤ 0.06	0.41
Penicillin (PO)	≤ 0.06	NA	NA

## 4+ STREPTOCOCCUS PNEUMONIAE

	Etest Interp	Etest MIC (mcg/mL)	KB Interp
Ceftriaxone (meningitis)	S	0.125	
Ceftriaxone (nonmeningitis)	S	0.125	
Clindamycin			S
Erythromycin			S
Levofloxacin			S
Moxifloxacin			S
Penicillin (meningitis)	R	0.064	
Penicillin (nonmeningitis)	S	0.064	
Tetracycline			S
Trimeth_Sulfamethoxazole			S
Vancomycin			S



# Case: when MICs may be useful

Tobramycin vs. Gentamicin:

- Serum concentrations are similar (peak 8-10 mcg/ml)
- Potency depends on concentration above the MIC (Concentration-dependent)
- The breakpoint is similar (MIC = 4)

Tobramycin is a better option!

Drug	Interpretation	MIC value
Ceftriaxone	S	0.25
Cefazolin	S	0.5
Levofloxacin	R	8
Ertapenem	S	0.25
Gentamicin	S	2.0
Tobramycin	S	0.5
Meropenem	S	0.5



# Differences between carbapenems

## Ertapenem:

Covers enteric gram-negative organisms (*E.coli*, *Klebsiella*)

-doesn't cover *Pseudomonas*

-CNS penetration is unknown

-Highly protein bound

-Breakpoint MIC:  $\leq 0.5$

## Meropenem:

- Covers *Pseudomonas*

-CNS penetration known

-Breakpoint MIC:  $\leq 1$

Drug	Interpretation	MIC value
Ceftriaxone	S	0.25
Cefazolin	S	0.5
Levofloxacin	R	8
Ertapenem	S	0.25
Gentamicin	S	2.0
Tobramycin	S	0.5
Meropenem	S	0.5



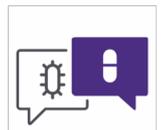
# Case summary

Levofloxacin is inappropriate

Because it is a bloodstream infection:

- All S antibiotics are appropriate
- Still consider dosing and toxicities as you would previously
  - Gentamicin/ Tobramycin not good options due to toxicity
  - Cefazolin is too frequent for outpatient
  - Avoid unnecessary Carbapenem exposure
  - Recommend Ceftriaxone

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# Summary

- Make friends with the Lab!
- MIC ranges reflect serum concentrations, but focus on source of infection.
- MICs are most useful for MDR infections or closed site infections.

