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Agenda

- Didactic: *Interpreting Susceptibility Data*
- Case Discussions
- Open Discussion

Interpreting Susceptibility Data

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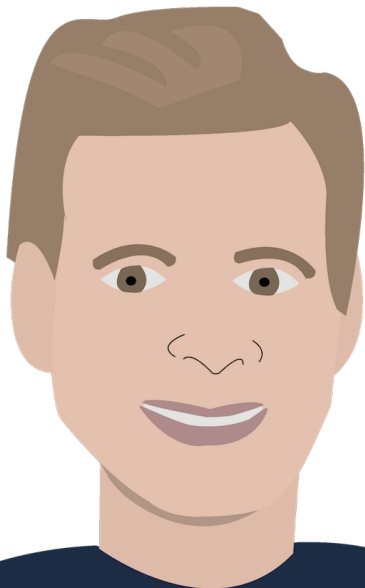
The University of Washington School of Medicine

October 3, 2017



Disclosures

- No financial conflicts of interest
- Everything we discuss is QI, thus protected from legal discovery under WA State Code



Paul Pottinger MD



Question...

“When we see a bacterial isolate with “intermediate” sensitivity, should we treat it as being “resistant?”

- A. Yep
- B. Nope
- C. I’m not sure...

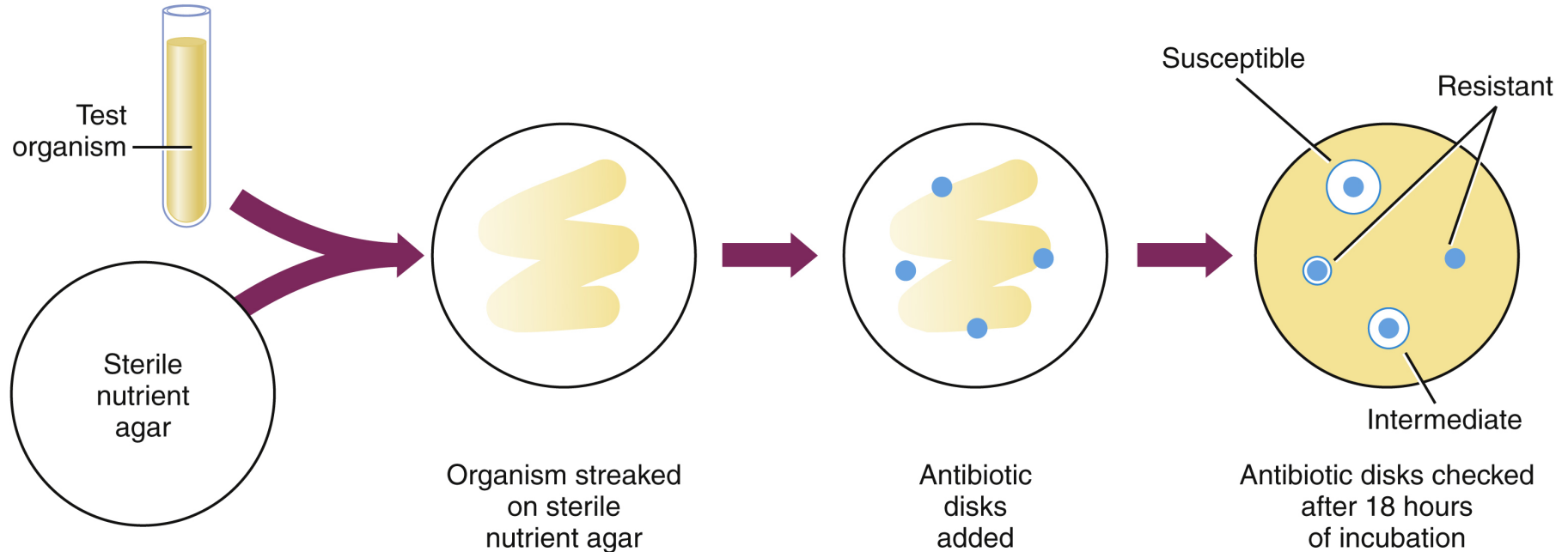
Antimicrobial Susceptibility Testing

- Qualitative (disk diffusion)
 - ✓ Susceptible, intermediate, resistant
- Quantitative (macro- or microdilution, E-test)
 - ✓ Minimal inhibitory concentration (MIC) is the lowest concentration of a given antimicrobial that prevents growth of the test organism
- Attempt to correlate *in vitro* growth inhibition with a clinical response to a specific antibiotic
 - ✓ Clinical Laboratory Standards Institute (CLSI) testing guidelines for each bug-drug combination
- ALL IGNORE HOST FACTORS & SPECIFIC CLINICAL SITUATIONS!



Disk Diffusion (Qualitative)

- “Kirby-Bauer-Turck” method.



Disk Diffusion (Qualitative)

- “Kirby-Bauer-Turck” method.
- Antimicrobial impregnated disks placed on agar plate inoculated with standard concentration of microorganism.
- Measure zone of inhibition in millimeters.
- Zones are interpreted as sensitive, intermediate, or resistant based on CLSI criteria.
- Criteria vary by drug and bug.

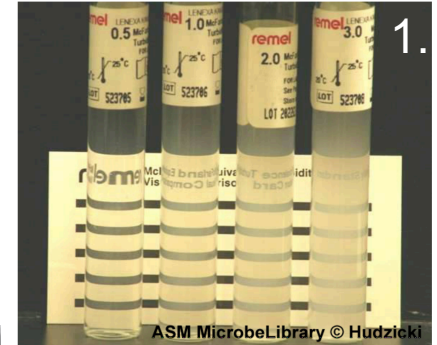
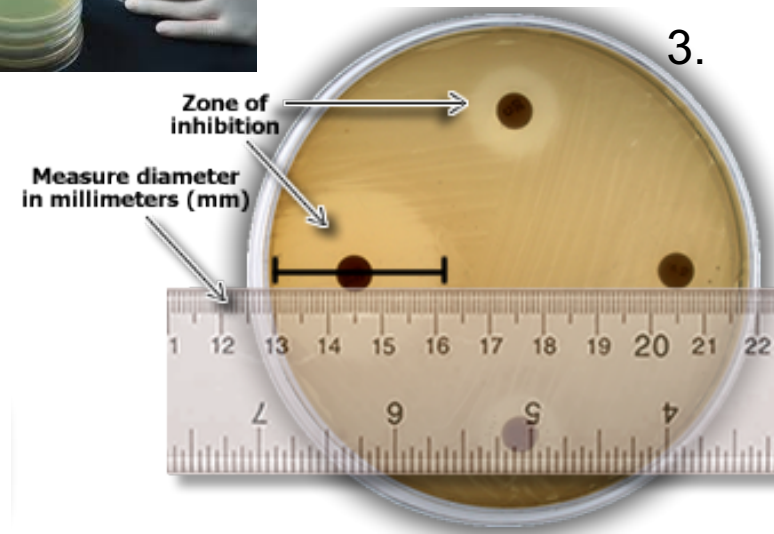


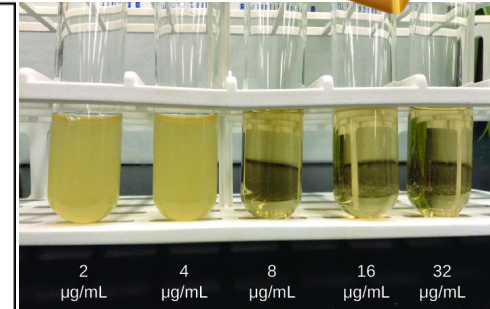
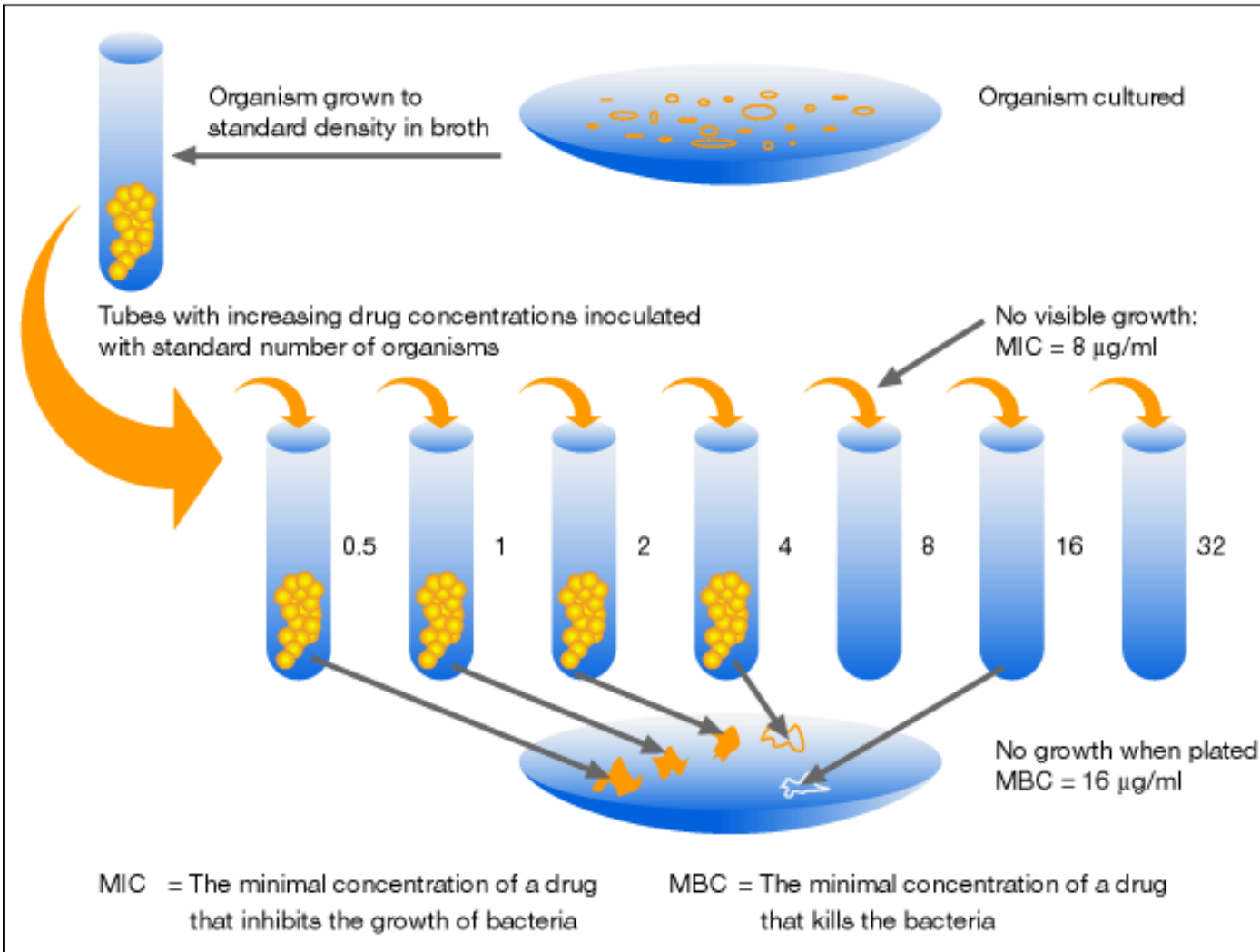
FIG. 1. McFarland standards (left to right) 0.5, 1.0, 2.0, 3.0, positioned in front of a Wickerham card. McFarland standards are used to prepare bacterial suspensions to a specified turbidity. In the Kirby-Bauer disk diffusion susceptibility test protocol, the bacterial suspension of the organism to be tested should be equivalent to the 0.5 McFarland standard.



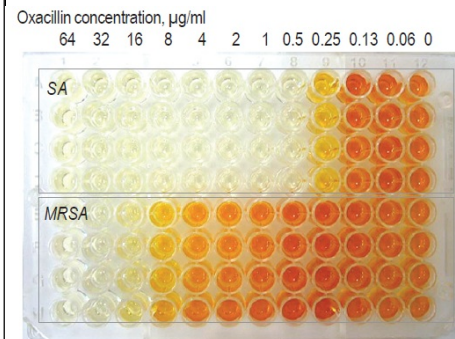
Broth Dilution (Quantitative)



Determination of MIC (here: broth dilution test)



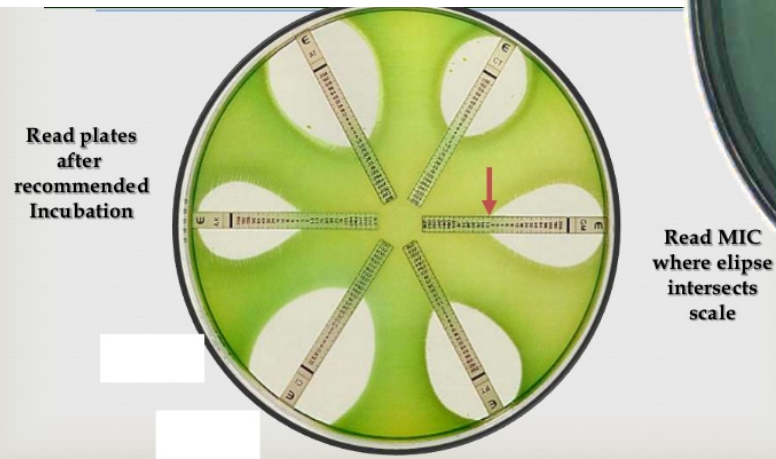
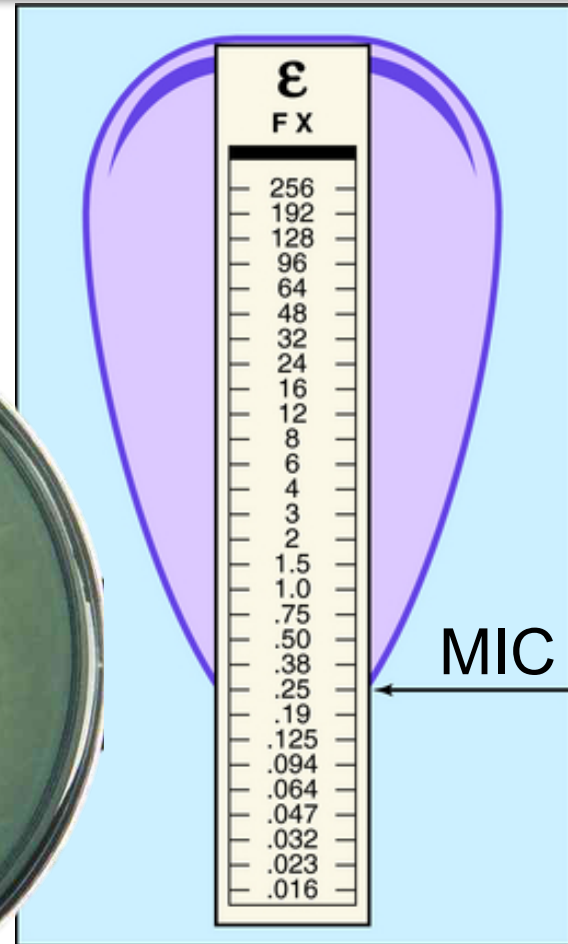
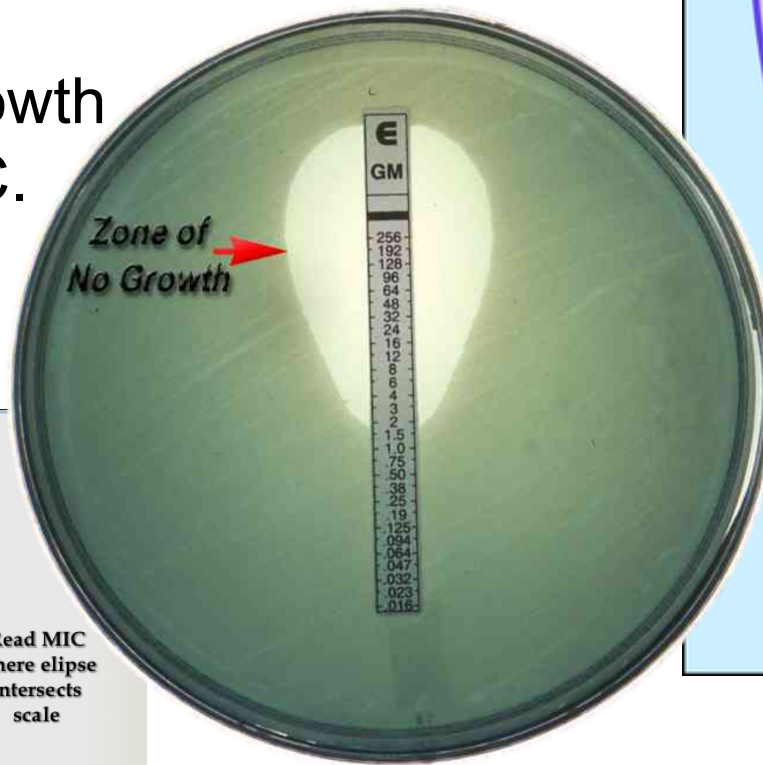
Macrobroth



Microbroth

E-test (Quantitative)

- Drug permeates strip in a gradient, less drug towards the top.
- Intersection of growth on strip is the MIC.



Quantitative Susceptibility Testing

- MIC = Minimum Inhibitory Concentration
 - ✓ A lower MIC means smaller amounts of drug are necessary to inhibit growth. That's good!
 - ✓ But... Lowest MIC does not necessarily mean that is the most effective drug *in vivo*
 - ✓ PK/PD properties of drug?
 - ✓ Drug toxicity... interactions... collateral damage... cost?

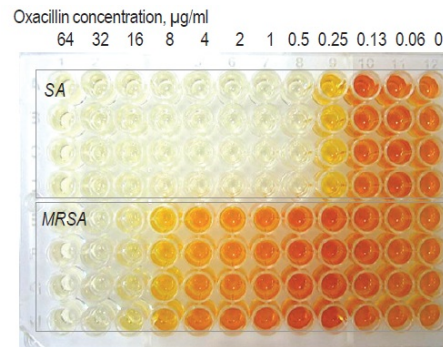
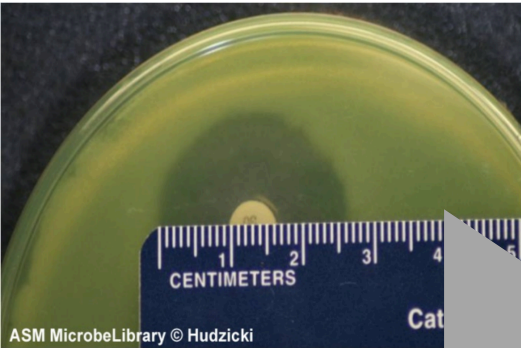


Quantitative Susceptibility Testing

- MIC = Minimum Inhibitory Concentration
 - ✓ Expect variability of one dilution from run to run... in some cases, MICs predictably different in one assay than another (eg MRSA vanco MIC higher in E-test than microbroth).



Intermediate... Beyond “S” or “R”



Pre-Defined
Interpretive
Breakpoints

2+ KLEBSIELLA PNEUMONIAE

	Microtiter MIC Interp	Microtiter MIC Value
Amikacin	S	≤16
Ampicillin	R	>16
Ampicillin/Sulbactam	R	>16
Aztreonam	R	>8
Cefazolin	R	>16
Cefepime	R	>16
Cefotetan	I	32
Ceftazidime	R	>16
Ceftriaxone	R	>2
Ciprofloxacin	R	>2
Ertapenem	R	>1
Gentamicin	R	>8
Levofloxacin	R	>4
Meropenem	S	≤1
Piperacillin/Tazobactam	R	>64
Tigecycline	--	0.5
Tobramycin	R	>8
Trimeth_Sulfamethoxazole	R	>4

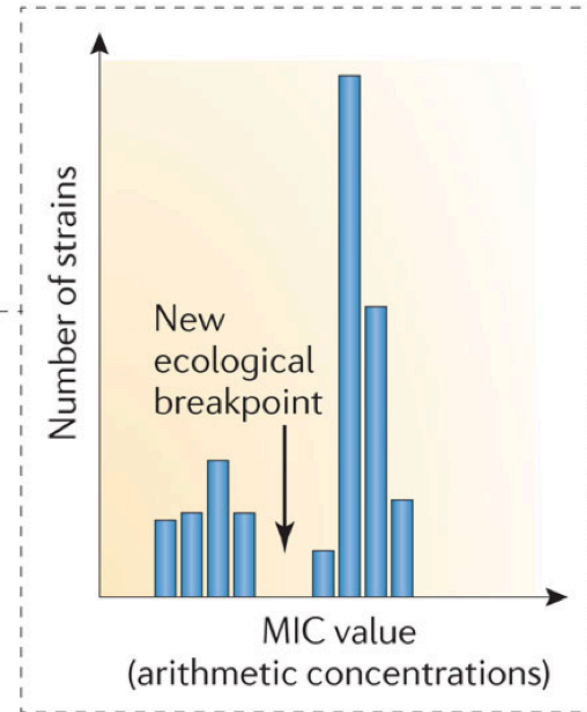
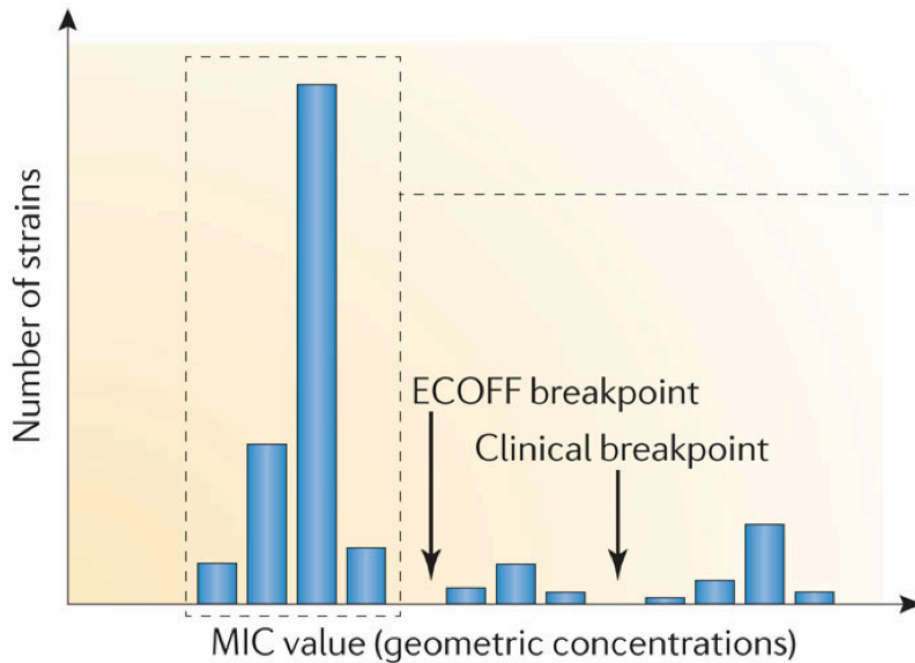
Interpretive Breakpoints

- The Limits of S/I/R
 - ✓ “S” drugs usually work... if the host can mount a good immune response, and source is drained.
 - ✓ “R” drugs sometimes work too... if body site concentrates the drug!
- So... who decides “S” or “R” anyhow?



Interpretive Breakpoints

Clinical Labs Standards Institute
(Formerly NCCLS)



Interpretive Breakpoints

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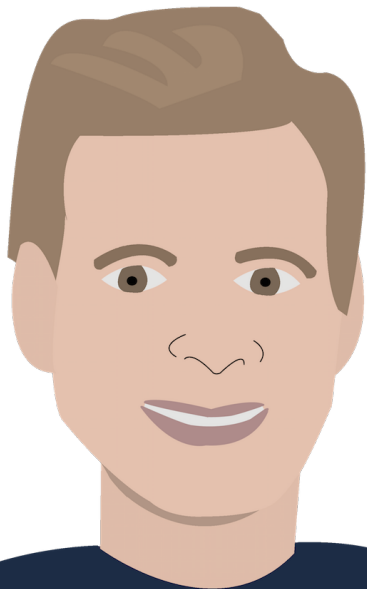


- ✓ Well-Intentioned
- ✓ Multi-Disciplinary
- ✓ Standard distribution examined... but decision for “susceptible” ultimately arbitrary.
- ✓ Pharma at the table... good and problematic

“Intermediate” may represent gradual MIC creep... or political controversy.

Conclusions

“When we see a bacterial isolate with “intermediate” sensitivity, should we treat it as being “resistant?”



Paul Pottinger MD

Conclusions

It totally depends!

- ✓ Drug concentration in body compartment?
- ✓ Synergy with other drugs?
- ✓ Do you have a better option?

This is the art of ID Medicine! If considering using an “I” drug, reasonable to consult ID.