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Duke Antimicrobial Stewardship and Evaluation Team

MIC Drop: A One-Stop-Shop Review of Minimum Inhibitory Concentrations (MICS)

Frequently Asked Questions:

1. Should I just select the antibiotic with the lowest MIC?

No! The lowest MIC is not always the best agent to use. Each antibiotic's MIC must be compared to the breakpoint of that organism/drug combination and **an MIC for one antibiotic CANNOT be directly compared to an MIC for another antibiotic**. Consideration should be made for the site of infection, host-specific factors, and the pharmacodynamic target of each antibiotic, in addition to the MIC and breakpoint, when designing optimal antibiotic therapy regimens.

2. What is the clinical significance of a vancomycin MIC = 2 in *Staphylococcus aureus* infections?

S. aureus isolates are considered susceptible to vancomycin when the MIC ≤2. Prolonged exposure to vancomycin, infection with certain strains, or uncontrolled sources of infection can result in bacterial cell wall thickening which can lead to elevated MICs and increased resistance. It is important to note, that this "MIC creep" phenomenon can also be due to variability in susceptibility testing methods.

The clinical significance of this remains unclear. A multicenter cohort study evaluating patient outcomes with *S. aureus* bacteremia found that patients with higher MICs to vancomycin had increased mortality irrespective of the antibiotic received. It is speculated that vancomycin MIC may be an unidentified marker of host or organism factors that influence treatment outcomes.

Bottom line: vancomycin elevated MICs to *S. aureus* may be associated with poor outcomes, but data is mixed and multifactorial. At this time if it remains susceptible, it should still be considered a 1st line agent and continued in patients who are clinically improving.

Note: This phenomenon is not applicable to coagulase negative staphylococci which have a susceptibility breakpoint of ≤4 to vancomycin.

What is an MIC?

- A Minimum Inhibitory Concentration (MIC) is the lowest concentration of an antibacterial agent expressed in μg/mL which, under strictly controlled in vitro conditions, completely prevents visible growth of the test strain of an organism (Figure 1)

Why do MICs matter to me?

- Adequate drug exposure is critical to ensuring positive patient outcomes
- Drug exposure is directly impacted by the MIC
    - As the MIC rises, drug exposure decreases
- Antibiotic resistance can be induced from inadequate drug exposure
    - Appropriate dosing of antimicrobials is key!

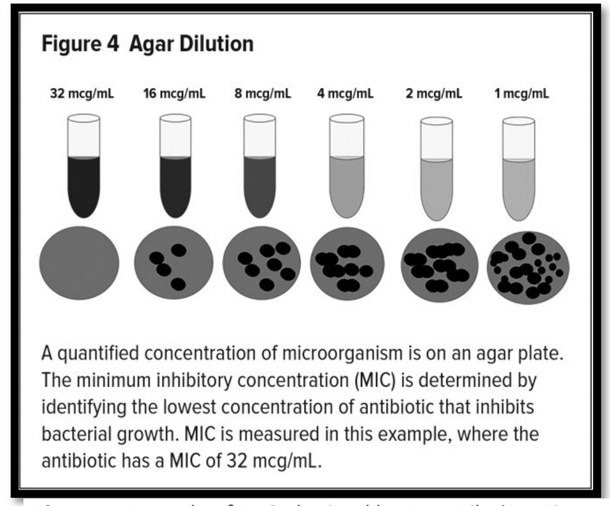


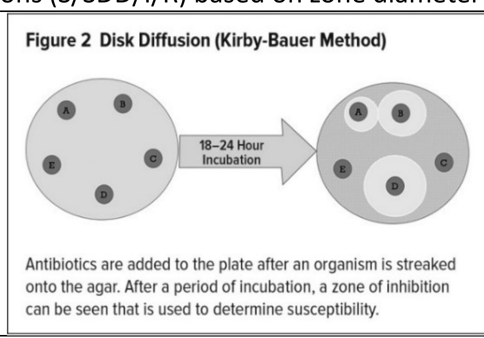
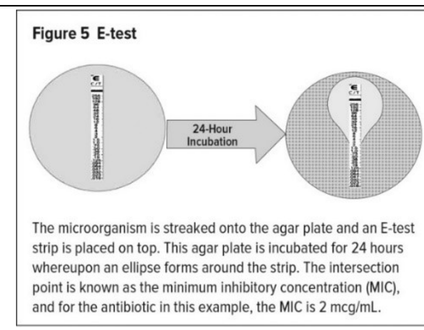
Figure 1: Example of MIC obtained by Agar Dilution. Figure from Giuliano C, et al. A Guide to Bacterial Culture Identification and Results Interpretation. *P T* 2019;44(4):192-200.

How are MICs determined?

1. Most of the MIC results we see in Epic come from automated testing methods
2. Some bug/drug combinations require manual MIC testing methods (Table 1)

Note: MIC variability can occur between susceptibility techniques

Table 1: Comparison of Manual Testing Methodologies

Kirby Bauer/Disk Diffusion	E-test
No numerical MIC value is reported, only interpretations (S/SDD/I/R) based on zone diameter of inhibition	Numerical MIC value and interpretation provided
	

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How do I interpret MIC breakpoints?

BREAKPOINT		WHAT IT MEANS FOR THERAPY	ACTION
Susceptible	☑	Standard dosing highly likely to succeed.	Proceed with standard therapy.
Susceptible Dose Dependent (SDD)	📈	Higher or more frequent dosing needed for success.	Increase dose or dosing frequency.
Intermediate	⚠	MIC ≥ the level of antibiotic than can ordinarily be achieved; clinical response is less likely	Use only if drug concentrates highly in body fluid (e.g., urine).
Resistant	✕	High likelihood of failure, even with increased drug exposure.	Select an alternative agent.

How are breakpoints set?

- Antimicrobial susceptibility standards are currently set by the FDA. The FDA typically refers to standards set by the Clinical and Laboratory Standards Institute (CLSI).
    - The CLSI uses microbiologic data, pharmacokinetic and pharmacodynamic data, and clinical studies to establish breakpoints.
    - Breakpoints may change over time as additional information becomes available.
- The Clinical and Laboratory Standards Institute M100 is available online as a free resource and offers the most up-to-date information on breakpoints.

Questions? Contact ASET!

Figure 3: CLSI M100 ED 33: 2023 Zone Diameter and MIC Breakpoints for Enterobacterales (e.g., *E. coli)* and Ampicillin[6]

Breakpoints for Kirby Bauer/Disk Diffusion

Breakpoints for E-tests and Automated Testing

Check comments for recommended dosing regimens and surrogate drugs (e.g., using ampicillin to predict amoxicillin)

Antimicrobial Agent	Disk Content	nearest whole mm				μg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
PENICILLINS										
Ampicillin	10 μg	≥ 17	-	14-16^	≤ 13	≤ 8	-	16^	≥ 32	(7) Results of ampicillin testing can be used to predict results for amoxicillin. (8) Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h. (9) Breakpoints when oral ampicillin is used **only** for therapy of **salmonellosis, shigellosis, or** uncomplicated UTIs due to *E. coli* **and** *P. mirabilis* are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or an amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h. See general comment (3).

References:

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