THE PATHCARE NEWS

THE ABC'S OF MICS:

THE VALUE OF MIC RESULTS IN ANTIBIOTIC TREATMENT DECISIONS

As we continue further into the multidrug resistant era, it becomes necessary to develop a deeper understanding of how to perform and interpret antimicrobial susceptibility testing. The clinical microbiology laboratory provides valuable susceptibility data that can guide the selection of antibiotic regimens for patients with infections. When a specific microorganism is cultured, identification of the organism and antibiotic susceptibility testing (AST) is performed. In terms of direct relevance to the management of infectious diseases, AST is arguably the single, most important activity carried out in the microbiology laboratory.

What is an MIC?

The Minimum Inhibitory Concentration (MIC) is an *in vitro* test that determines the lowest concentration of an antibiotic required to inhibit the growth of a specific bacterial strain. A low MIC value (e.g., <0.12 µg/mL) indicates that the bacteria are highly susceptible to the antibiotic. In contrast, a high MIC value (e.g., >32 µg/mL) suggests that the bacterial strain is resistant, and even high—or potentially toxic—doses of the antibiotic may be ineffective in inhibiting bacterial growth and infection. Generally, the higher the MIC, the more resistant the bacterial strain depending on the antibiotic being tested.

Why is MIC important for patient care?

MIC's assist in the selection of antimicrobials to which bacteria or yeast are susceptible and are therefore likely to effectively treat the infection.

How is MIC reported and what do the values mean?

For each bacterial group or fungal species, international standardized cutoff values, referred to as clinical breakpoints, are established for individual agents. These breakpoints facilitate the interpretation of MIC values. This, in turn, enables the laboratory to provide clinically relevant information to guide treatment.

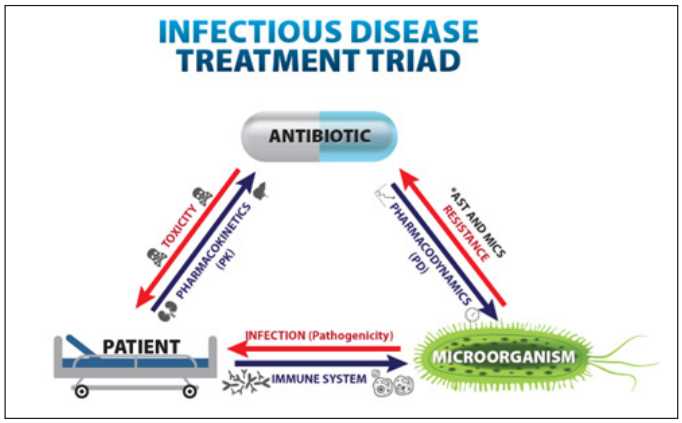
AST reports which include MIC results or breakpoints, will have a numerical value and an interpretive category:

- **S** (Susceptible): there is a high likelihood of therapeutic success using standard dosing regimens
- **I** (Intermediate) or **SDD** (Susceptible Dose Dependant): there is a high likelihood of therapeutic success when exposure to the agent is increased by utilizing a higher dosing regimen or by the agent's physiological concentration at the site of infection
- **R** (Resistant): there is a high likelihood of therapeutic failure even when there is increased exposure (i.e. higher dosing regimen)

While MIC measures the antimicrobial's *in vitro* effectiveness against a microbial strain, it does not fully predict *in vivo* efficacy (i.e., effectiveness in the patient). It is thus important to also consider the drug's pharmacokinetic/pharmacodynamic (PK/PD) properties when selecting an appropriate antibiotic.

Pathogenetic Triad:

1. Figure 1 illustrates the complex interplay between the antibiotic, the patient, and the infecting organism in infectious diseases.



AST and MIC interpretation:

The use of antimicrobials with MIC values that fall within the susceptible category during the treatment of an infection may improve therapeutic efficacy. However, several factors must be considered, including the clinical indication, site of infection, patient characteristics, comorbidities, and the PK/PD properties of the antimicrobial agent.

It is important to note that MIC values are dependent on the specific antibiotic tested as well as the organism for which susceptibility testing is being performed. Importantly, a low MIC value for one antibiotic is not necessarily comparable to a low MIC value for another.

For example, an *E. coli* isolate with a ciprofloxacin MIC of ≤0.25 µg/mL (susceptible) and an amoxicillin-clavulanate MIC of ≤4 µg/mL (susceptible) does not imply that ciprofloxacin is the preferred agent. For respiratory tract infections, amoxicillin-clavulanate is generally preferred as it is a first-line agent with a favourable safety profile. In contrast, for complicated urinary tract infections (UTIs), ciprofloxacin may be preferred due to its excellent urinary tract concentrations and prostatic tissue penetration.

Regarding urinary isolates, the MIC for trimethoprim-sulfamethoxazole may appear high at first glance. However, the reported MIC of 20 µg/mL reflects a combination of 1 µg/mL trimethoprim and 19 µg/mL sulfamethoxazole. For *E. coli*, the susceptibility breakpoint for this combination is ≤40 µg/mL (2 µg/mL trimethoprim and 38 µg/mL sulfamethoxazole). Although resistance to trimethoprim-sulfamethoxazole is common, when susceptibility is confirmed, it remains a good option for targeted treatment of infections like UTIs due to its excellent urinary concentration.

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	E.coli
PENICILLINS	
AMOXYCILLIN-CLAVULANATE	I 16
AMPICILLIN/AMOXYCILLIN	R >=32
PIPERACILLIN-TAZOBACTAM	S <=4
CEPHALOSPORINS	
CEFTAZIDIME	S <=1
CEFUROXIME/CEFPROZIL	I 8
CEFEPIME	S <=1
CEFOTAXIME/CEFTRIAXONE	S <=1
CARBAPENEMS	
DORIPENEM	S
ERTAPENEM	S <=0.5
IMIPENEM	S <=0.25
MEROPENEM	S <=0.25
QUINOLONES	
CIPROFLOXACIN	R >=4
AMINOGLYCOSIDES	
AMIKACIN	S 4
GENTAMICIN	S <=1
TOBRAMYCIN	S <=1
FOSFOMYCIN	
FOSFOMYCIN	S
NITROFURANS	
NITROFURANTOIN	S
SULFA/TRIMETHOPRIM	S <=20

MICs help when antibiotic options are limited:

In critically ill patients in the ICU setting, where the risk of infection with multidrug-resistant organisms (MDROs) is high, it may be necessary to compare the MICs of different agents within the same antimicrobial class to determine the most optimal treatment. For example, in a patient infected with carbapenem-resistant *Klebsiella pneumoniae*, where treatment options are limited, group 2 carbapenems (imipenem, meropenem, and doripenem) may have MICs that fall within the susceptible to intermediate range. In such cases, the carbapenem with the lowest MIC may be considered, often in combination with another active agent from a different class. Additionally, strategies such as dose escalation, prolonged infusion, and increased dosing frequency may be employed to optimise clinical outcomes.

AST and MIC are a valuable antimicrobial stewardship tool:

- AST and MIC reporting helps to guide safe and effective antimicrobial use.
- The 4 Ds of optimal antimicrobial therapy are "the right **D**rug, right **D**ose, **D**e-escalated to pathogen-directed therapy and the right **D**uration of therapy".
- An agent with a narrower spectrum of activity is less likely to select for colonization with MDROs compared to broad-spectrum agents.
- When a broad-spectrum antimicrobial agent is initiated for empiric antibiotic cover, it should be given for the shortest possible duration and de-escalated to the most appropriate directed agent according to PK-PD principles coupled with the culture and susceptibility report.

REFERENCES:

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