UWTASP tele-antimicrobial stewardship program | echo

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Antibiogramming 101 + MIC

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Project ECHO

Objective

- What is susceptibility
- How is susceptibility defined / determined
- Minimum inhibitory Concentrations (MICs)
- Putting it all together into an Antibiogram

Antibiotic Susceptibility

Laboratory test to determine activity of an antibiotic against a specific bacteria

Intrinsic Resistance	Acquired Resistance
Target bacteria is innately non-susceptible to antibiotic e.g. doesn't possess the end target of the antibiotic	Target bacteria is usually susceptible but expresses self-defense e.g. by upregulating efflux pumps or acquires a drug resistance mutation

The Minimum Inhibitory Concentration

Broth Dilution

The minimum inhibitory concentration (MIC):
The lowest concentration of a drug which prevents visible bacterial growth

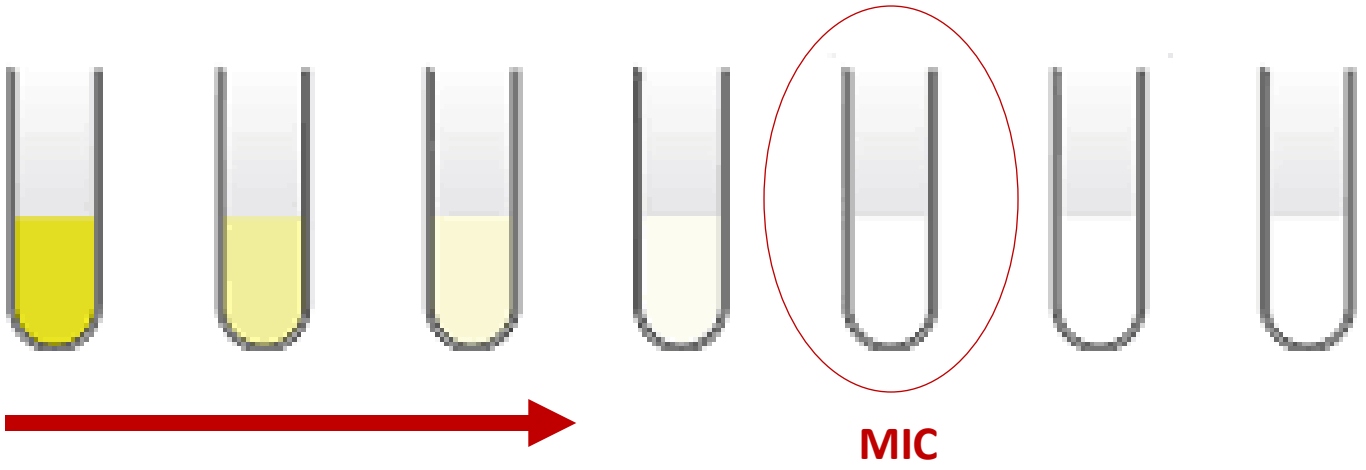


Image from: clinicalgate.com/antimicrobial-agents/ Accessed 7/23/18

Other Antibiotic Susceptibility Tests

Disk Diffusion & E-Test

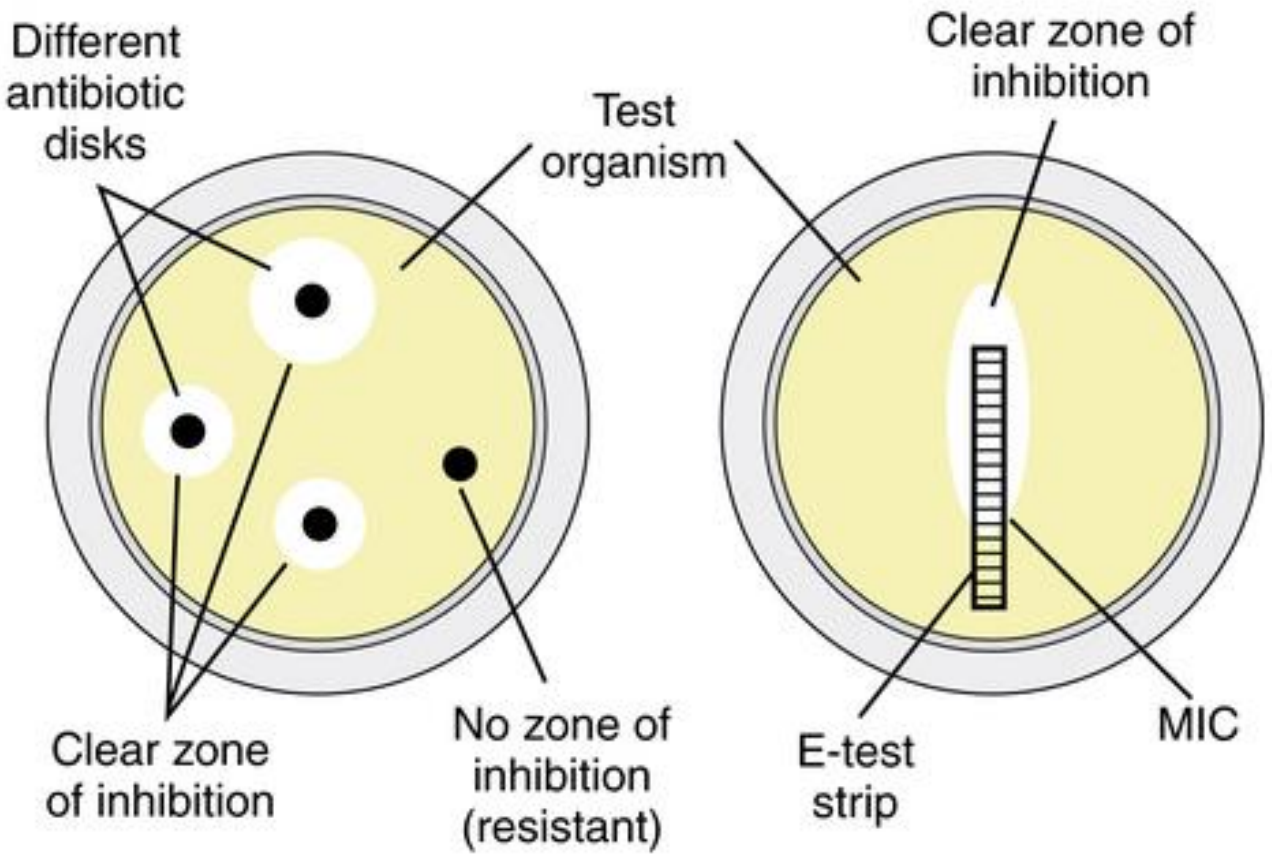
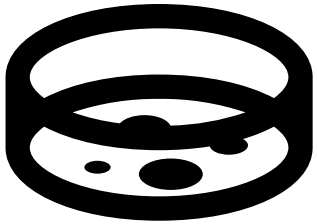


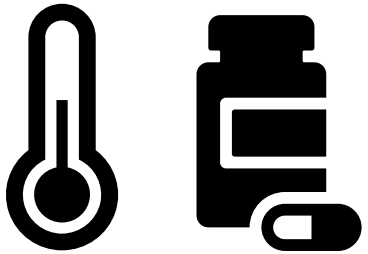
Image from: clinicalgate.com/antimicrobial-agents/ Accessed 7/23/18

MICs Vary



Population variation

Lab variation



Organism history and stress

Should you pick an antibiotic based on the lowest MIC?

- Yes
- No
- Not sure

MICs & Breakpoints

MIC is the number, Breakpoint is the interpretation (Susceptible/Intermediate/Resistant)

Susceptibility

	Staphylococcus aureus, coagulase positive			
	ETEST MIC (MCG/ML)		MICROTITER MIC (MCG/ML)-SELECT	
Clindamycin			<=0.5	**Susceptible**
Daptomycin			<=0.5	**Susceptible**
Erythromycin			>4	**Resistant**
Levofloxacin			<=0.25	**Susceptible**
Moxifloxacin			<=0.25	**Susceptible**
Oxacillin			>2	**Resistant**
Tetracycline			<=2	**Susceptible**
Trimeth_Sulfamethoxazole			<=2	**Susceptible**
Vancomycin	1.5	**Susceptible**		**Susceptible**

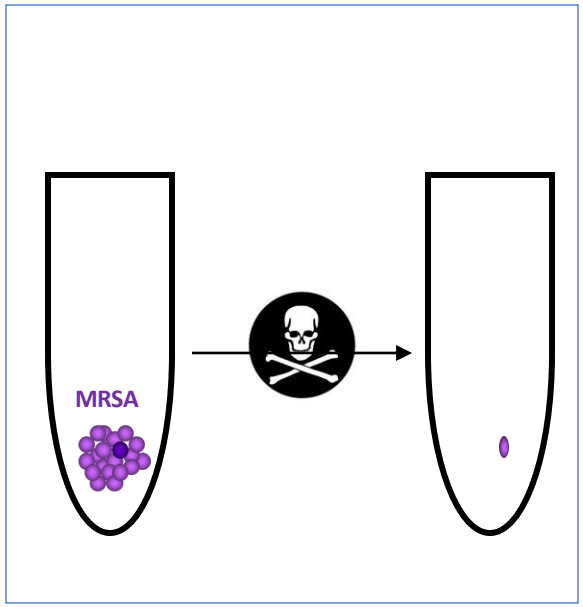
MIC ≠ Breakpoint

MIC is a number, Breakpoint is an interpretation (Susceptible/Intermediate/Resistant)

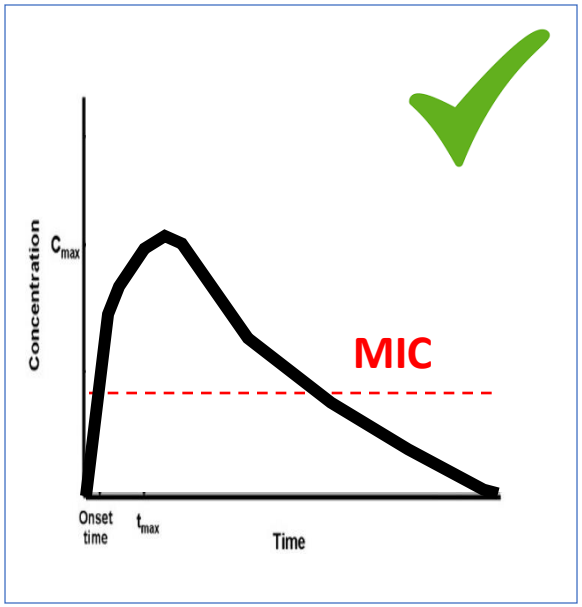
The Breakpoint:

Breakpoint setting integrates knowledge of **wild-type MICs**, assessment of antimicrobial **pharmacokinetics and pharmacodynamics**, and studies of **clinical outcomes** when the antimicrobial is used

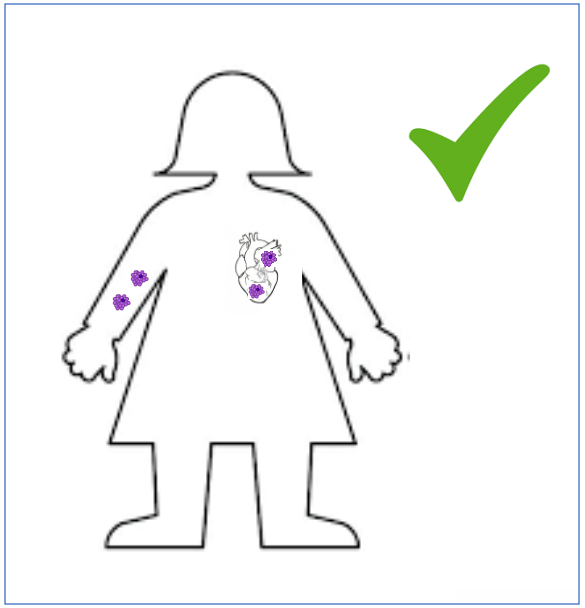
MIC



PK/PD



Clinical Outcomes



Turnidge J, Paterson DL. Setting and Revising Antibacterial Susceptibility Breakpoints. Clin Microbiol Rev 2007; 20(3):391-408.

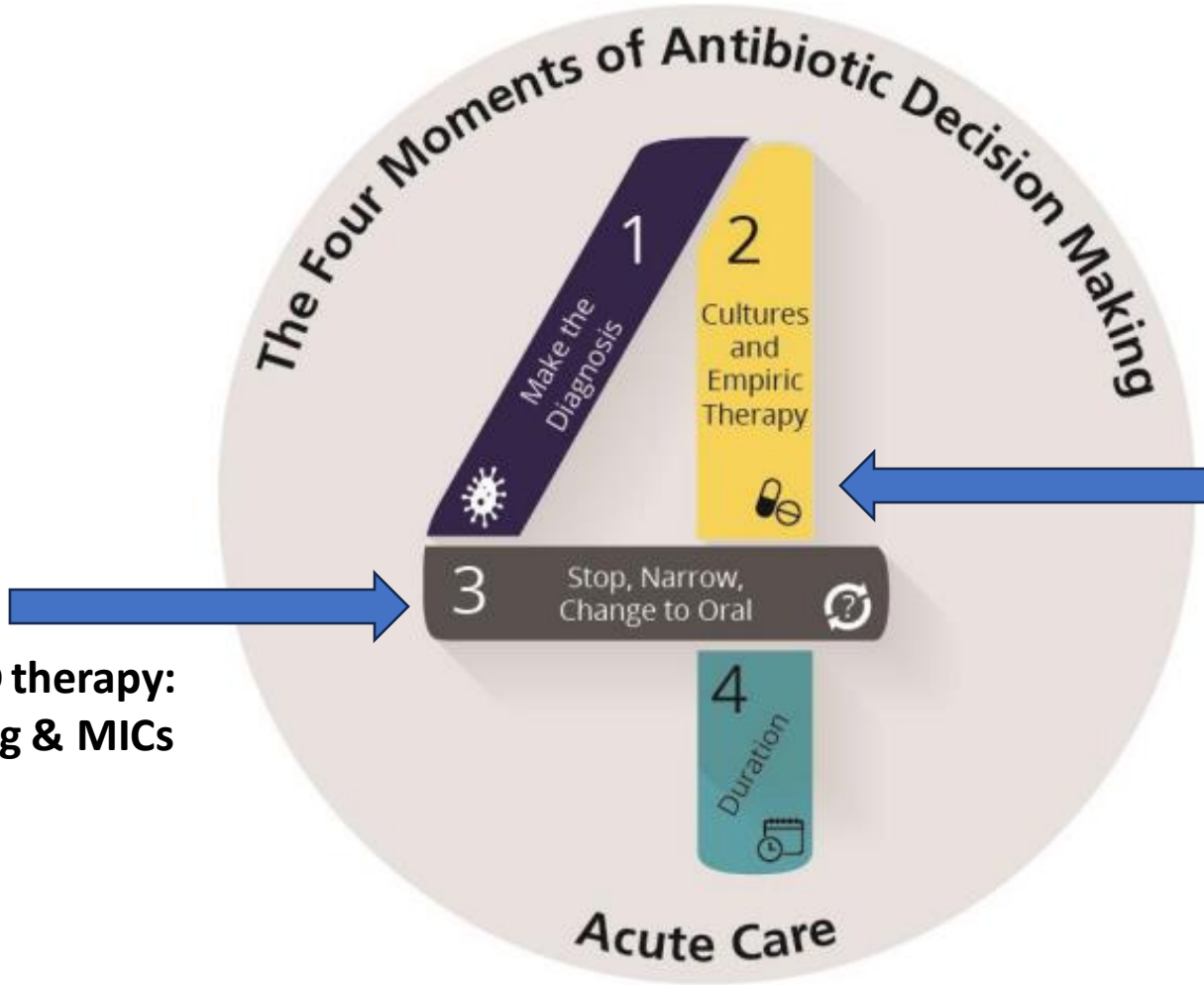
What is an Antibiogram?

A chart that collates MICs over time to describe antibiotic susceptibility trends

Organism (% susceptible)	Maximum # of isolates tested	Ceftriaxone	Clindamycin	Erythromycin	Levofloxacin	Oxacillin [a,b]	Penicillin	Tetracyline	Trimeth/sulfa	Vancomycin
Coagulase-negative *Staphylococcus*	151		62	0	24	4		82	39	100
Staphylococcus aureus	290		81	62	75	75		91	95	100
MSSA	222		85	75	93	100		94	98	100
MRSA	73		69	21	20	0		85	87	100
Staphylococcus lugdunensis [c]	20		82	12	100	100		90	100	100
Viridans group streptococci	145	93	83	34	40		63			100
Streptococcus mitis	107	92	84	24	24		55			100

Blank cells = insufficient data or drug was not tested.
MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant S. *aureus*.
[a] Cefazolin and oxacillin (or nafcillin) are preferred over other agents for treatment of MSSA bacteremia.
[b] Molecular testing for *mecA* is required for coagulase-negative *Staphylococcus* isolates to be reported as methicillin-susceptible.
[c] For organisms with less than 30 isolates, caution is advised when interpreting susceptibiilty data due to small numbers.

Practical Question:
When to use antibiogram vs. Lab testing and MICs?



EMPIRIC therapy: Antibiogram

DIRECTED therapy: Lab testing & MICs

https://ahrq.gov/antibiotic-use/acute-care/four-moments/index.html

How can I optimize Antibiogram Use?

Interpret common infections for providers

March 1, 2018

Colleagues,

Please find attached the 2017 Antibiotic Susceptibility Report. This is provided annually to evaluate for progression of bacterial resistance at UW Valley Medical Center. Overall, 2017 is similar to 2016 showing minimal increase in resistance. We encourage culture directed therapy once full susceptibilities are available. As in the past, we will share comments about the report and antibiotic treatment:

- Avoid clindamycin in Group B streptococcal infections without susceptibility data showing that it is active against the particular strain
- Cefepime is preferable to Piperacillin/tazobactam for HAP/VAP due to higher anti-Pseudomonal activity
- Ampicillin/sulbactam is NOT recommended for empiric therapy for intra-abdominal infections due to high rates of E coli resistance

How can I optimize Antibiogram Use?

Color-code it

Green is generally effective

Yellow effective in certain circumstances

Red is generally not encouraged for use

Gram Negative Isolates
Percent susceptible

Organism	No. of Isolates	Ampicillin	Ampicillin/Sulbactam	Aztreonam	Cefazolin	Ceftriaxone	Gentamicin	Levofloxacin	Nitrofurantoin	Piperacillin/tazo	Trimethoprim/Sulfa	Cefepime	Ertapenem	Meropenem	Minocycline
Acinetobacter species	36						100	97		92	97	86		100	
Citrobacter freundii	62			85		85	89	94	97	89	76		100		
Citrobacter koseri	55			96		96	100	100	93	98	98		100		
Enterobacter aerogenes	72			88		88	100	97	21	82	99		100		
Enterobacter cloacae complex	134			89		90	98	97	48	90	90		98		
Escherichia coli	3540	56	65	94	85*	91	93	79	96	96	78		100		
Klebsiella oxytoca	105		61	90	59*	93	99	97	86	90	96		100		
Klebsiella pneumoniae	562		90	98	95*	98	98	94	37	97	92		100		
Morganella morganii	64			89		95	88	73		92	61		100		
Proteus mirabilis	420	80	90	100	94*	98	85	77		100	70		100		
Providencia rettgeri	11			91		100	91	100		100	100		100		
Providencia stuartii	8			100		100	0	13		100	88		100		
Pseudomonas aerugenosa	337			87			97	77		96		94		92	
Raoultella planticola	10		90	90		90	90	100	100	100	90		100		
Serratia marcescens	54			100		100	98	100		96	100		100		
Stenotrophomonas maltophilia	41							93			95				100

* Urine isolates only

How can I optimize Antibiogram Use?

Localize your sepsis care

Organism	No. of Isolates	Ampicillin	Ampicillin/Sulbactam	Aztreonam	Cefazolin	Ceftriaxone	Gentamicin	Levofloxacin	Nitrofurantoin	Piperacillin/tazo	Trimethoprim/Sulfa	Cefepime	Ertapenem	Meropenem	Minocycline
Pseudomonas aerugenosa	337			87			97	77		96		94		92	

Would you choose levofloxacin, pip/tazo, cefepime, or meropenem for septic shock and a suspected respiratory source

When numbers lie: Antibiogram interpretation

How many isolates were tested?

Organism (% susceptible)	Maximum # of isolates tested	Amikacin	Ampicillin	Ampicillin-sulbactam	Aztreonam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Ciprofloxacin	Ertapenem	Gentamicin	Levofloxacin	Meropenem	Nitrofurantoin [a]	Pip/tazo	Tobramycin [b]	Trimeth/sulfa
Citrobacter species [c]	64	100	0		80	0	100	82	80	85	100	92	84	100	95	85	40	78
Enterobacter cloacae [c]	72	100	0	0	78	0	100	78	77	95	94	97	95	98	78	84	0	87
Escherichia coli	485	100	55	67	89	69	96	91	85	71	99	92	73	100	98	98	53	75
Klebsiella (formerly Enterobacter) aerogenes [c,d]	20		0	0	83	0	100	73	73	89	100	100	88	100	80	81		100
Klebsiella oxytoca	59	100	1	58	89	41	100	93	87	89	100	91	100	100	97	96	0	80
Klebsiella pneumoniae	138	100	0	73	87	76	94	88	84	78	98	92	86	99	93	94	22	75
Proteus mirabilis	42	100	87	95	100	2	100	100	100	92	100	92	92	100	0	100	66	90
Pseudomonas aeruginosa	134	99					92	96		86	100	96	84	94		89	97	
Serratia marcescens [c]	36		6	6	100	0	100	97	97	85	100	100	90	100	0	100		100
Stenotrophomonas maltophilia [d]	28							42					64					100

Blank cells = insufficient data or drug was not tested.

[a] Indicated in urinary tract infections only.

[b] Tobramycin is reported when Enterobacterales are resistant to gentamicin.

[c] *Citrobacter* species, *Enterobacter cloacae*, *Klebsiella aerogenes*, and *Serratia marcescens* have an inducible beta-lactamase. Resistance to penicillins and 3rd generation cephalosporins may arise on therapy.

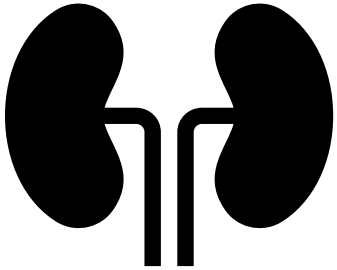
[d] For organisms with less than 30 isolates, caution is advised when interpreting susceptibility data due to small numbers.

- How many isolates were tested?
- What were the specimens? (Blood vs. Urine vs. Wound, etc)
- Who were the patients whose cultures are informing your antibiogram?

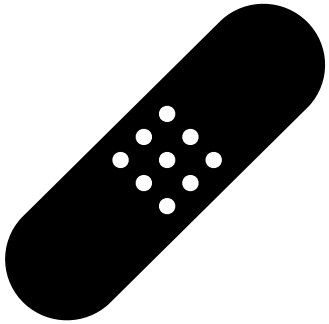
When numbers lie: Antibiogram interpretation

What were the specimens?

Blood



Urine



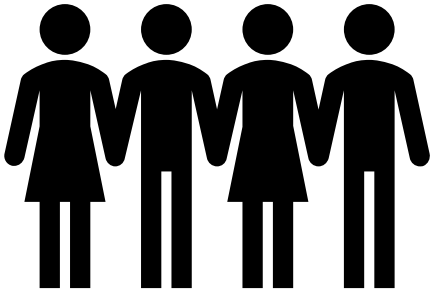
Wounds

When numbers lie: Antibiogram interpretation

Who were the patients whose cultures are informing your antibiogram?

Nursing home

Swing beds



Generally healthy individuals

Summary & Conclusions

- Antibiotic susceptibility is measured with MICs and defined by breakpoints
- Antibiograms are a graphic summarizing MICs over time
- Antibiograms can be used to build local guidelines and to select best empiric treatment before culture data are available