MDRO

IDENTIFYING AND REDUCING TRANSMISSION OF MULTI-DRUG RESISTANCE ORGANISMS IN LONG TERM CARE

ICCNM Foundation

AGENDA

- *Identify current CDC Targeted MDROs*
- *Describe several mechanisms of resistance in organisms*
- *Discuss lab report interpretation and variations*
- *Articulate the risks of MDRO transmission*

DEFINITIONS (CDC)

- Tier 1
- Tier 2

- **Novel MDRO**: An organism with a resistance mechanism that has never or very rarely been identified in the United States.
- **Targeted MDRO**: An organism resistant to most or all available antimicrobials and with the potential to spread widely. Current examples of targeted MDROs for much of the United States include:
  - **Focus MDRO**: The subset of targeted MDROs that the area public health jurisdiction has identified as the focus of their MDRO Prevention Plan.

CDC TIERS

Tier 1	Tier 2	Tier 3	Tier 4
▪ Novel (or very rarely) identified in the US	▪ No current treatment option ▪ Often associated with healthcare ▪ May not be in your region yet, but identified in the US	▪ Advanced spread in the region but not yet endemic ▪ Focus on Prevention	▪ Endemic in the region ▪ Trying to stop spread to community or other regions

MDRO Containment Strategy | HAIs | CDC

INTERIM GUIDANCE FOR A PUBLIC HEALTH RESPONSE TO CONTAIN NOVEL OR TARGETED MULTIDRUG-RESISTANT ORGANISMS (MDROS)

Table 2: Summary of CDC Recommendations to Assess Transmission of Novel or Targeted Multidrug-Resistant Organisms (MDROs)

Healthcare Facility Description	Recommendations to Assess Transmission
Healthcare facilities[1] where a patient with an MDRO was treated	
• Individual with targeted multidrug-resistant organism is currently present at the healthcare facility • Individual with targeted multidrug-resistant organism is not currently present in the healthcare facility, but has been treated at the healthcare facility within prior 30 days	1. Perform a laboratory lookback encompassing at least 6 months prior to the index case to identify any potential missed cases.[2] 2. Screen roommates3 and conduct broader screening as recommended for relevant response tier. 3. If transmission is suspected or confirmed: A. Perform consecutive point prevalence surveys until transmission is controlled. B. Consider implementing admission screening.[4] 4. Conduct prospective laboratory surveillance for 3 months (a) following identification of the index case (if no transmission identified) or (b) after transmission controlled to monitor for additional cases.

Table 1: Summary of Response Recommendations for MDRO Containment by Tier

Description	Tier 1 Resistance mechanisms never or very rarely identified in the United States; pan-resistant organisms with the potential for wider spread in a region	Tier 2 Mechanisms and organisms not regularly found in a region	Tier 3 Mechanisms and organisms regularly found in a region but not endemic
Healthcare Investigation[1]			
Review the patient's healthcare exposures prior to and after the positive culture	Always	Always	Always
Contact Investigation[1]			
Screening of healthcare roommates	Always	Always	Always
Broader screening of healthcare contacts[2]	Always[3]	Sometimes[4]	Sometimes
Prospective lab surveillance[5]	Always	Always	Always
Retrospective lab surveillance[6]	Always	Always	Sometimes
Household contact screening	Sometimes	Rarely	Rarely
Environmental sampling	Sometimes	Rarely	Rarely
Healthcare personnel screening	Sometimes	Rarely	Rarely
Evaluate potential spread to healthcare facilities that regularly share patients with the index healthcare facility[7]	Sometimes	Sometimes	Rarely
Infection Control Measures			
Prompt notification of healthcare providers and patient and implementation of appropriate transmission-based precautions	Always	Always	Always
Clear communication of patient status with transferring facilities	Always	Always	Always
On-site infection control assessment with observations of practice, such as Epidemiology and Laboratory Capacity (ELC) Infection Control Assessment and Response (ICAR)	Always	Always	Sometimes

[1] For Tier 1 and 2 organisms/mechanisms, healthcare exposures and healthcare contacts over the preceding 30 days should be investigated unless information is available about the time the organism was most likely acquired. This includes any healthcare facility where the patient had an overnight stay during that time period. In some investigations, outpatient facilities and emergency departments might also be included. For Tier 3 organisms, investigation of healthcare exposures and healthcare contacts is generally limited to the current and sometimes prior admission.

[2] This may include targeted screening of contacts at highest risk for acquisition and/or unit point prevalence surveys.

[3] If the MDRO is a novel organism for which data on the frequency and modes of transmission are not known, or if the index patient was not on Contact Precautions during their entire stay in a healthcare facility, then additional screening (beyond roommates) is recommended. Broader screening, including patients on the same ward as the index patient and/or patients that shared healthcare personnel, might be particularly important for detecting novel MDROs when data on the frequency and modes of transmission are lacking.

OTHER MDRO DEFINITIONS

- ASM
- WHO
  - Critical, High, Medium
- CDC
  - Urgent, Serious, Concerning
- APIC
- ECDC
- States

- New Mexico- CDC definitions currently

CDC URGENT, SERIOUS, CONCERNING, WATCH LIST

URGENT

- Carbapenem-resistant *Acinetobacter*
- *Candida auris (C. auris)*
- *Clostridioides difficile (C. difficile)*
- Carbapenem-resistant *Enterobacteriaceae* (CRE)
- Drug-resistant *Neisseria gonorrhoeae*

SERIOUS

- Drug-resistant (DR) *Campylobacter*
- DR *Candida*
- (ESBL)-producing *Enterobacteriaceae*
- Vancomycin-resistant *Enterococci* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa (P. aeruginosa)*
- DR nontyphoidal *Salmonella*
- DR *Salmonella* serotype Typhi
- DR *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- DR *Streptococcus pneumoniae (S. pneumoniae)*
- DR Tuberculosis (TB)

CDC URGENT, SERIOUS, CONCERNING, WATCH LIST

CONCERNING

- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

WATCH LIST

- Azole-resistant *Aspergillus fumigatus*
- Drug-resistant *Mycoplasma genitalium*
- Drug-resistant *Bordetella pertussis (B. pertussis)*

HOW TO GET ON THE THREAT LIST

- Clinical impact
- Economic impact (when available)
- Incidence
- 10-year projection of incidence (new infections over the next 10 years)
- Transmissibility (how easily a germ spreads or causes infections)
- Availability of effective antibiotics
- Barriers to prevention

RESISTANCE TYPES

NATURAL – INTRINSIC RESISTANCE

- Present in the species always

or

- Occurs after exposed to the antimicrobial agent each time
  - Many Gram-Negative species

Table 2.

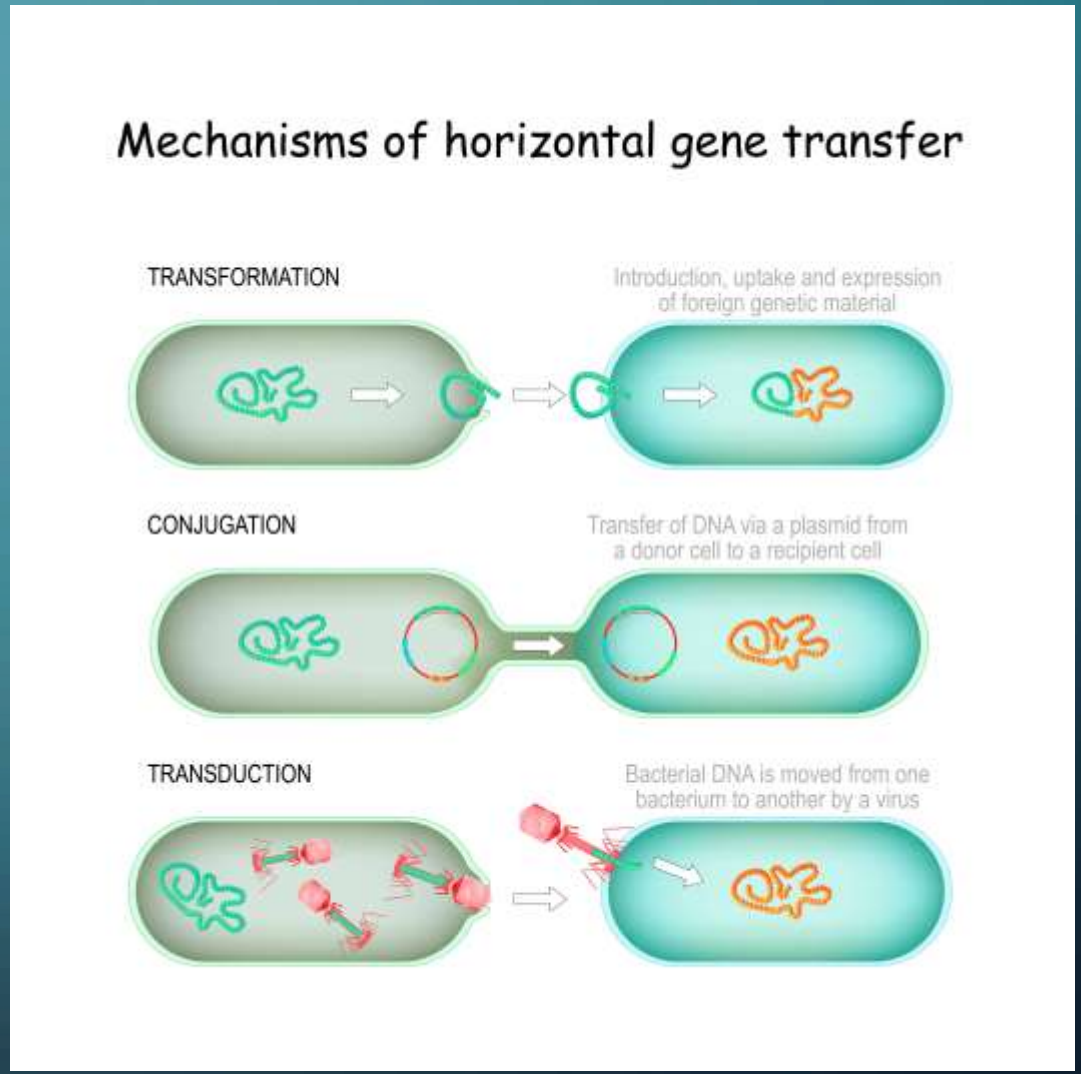
Examples of bacteria with intrinsic resistance.

Bacteroides (anaerobes)	aminoglycosides, many β-lactams, quinolones
All gram positives	aztreonam
Enterococci	aminoglycosides, cephalosporins, lincosamides
Listeria monocytogenes	cephalosporins
All gram negatives	glycopeptides, lipopeptides
Escherichia coli	macrolides
Klebsiella spp.	ampicillin
Serratia marcescens	macrolides
Pseudomonas aeruginosa	sulfonamides, ampicillin, 1st and 2nd generation cephalosporins tetracycline
Stenotrophomonas maltophilia	aminoglycosides, β-lactams, carbapenems, quinolones
Acinetobacter spp.	ampicillin, glycopeptides

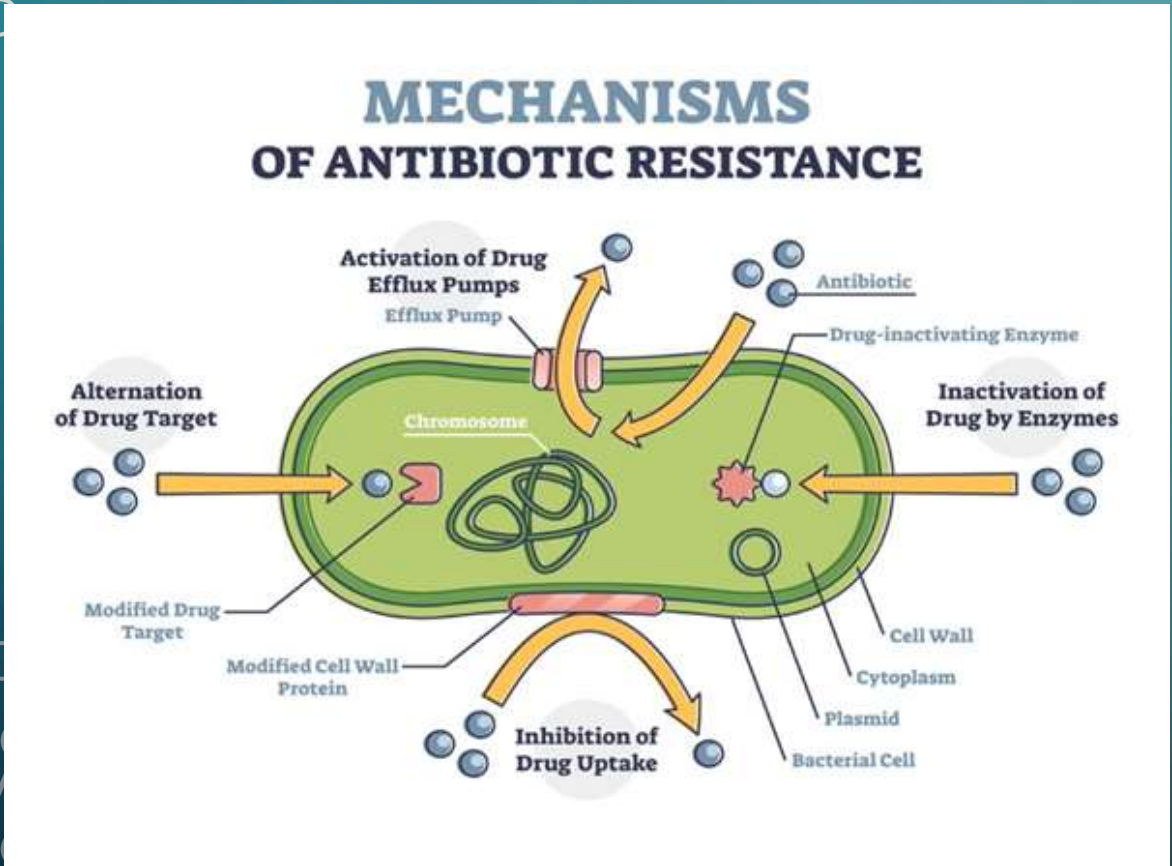
RESISTANCE TYPES

ACQUIRED RESISTANCE

- Horizontal or Vertical Gene Transfer
- Acquiring gene material from other organisms, environment, and mutations
- Same or different organisms



RESISTANCE -MECHANISMS



- Limit drug uptake
- Inactivate the drug with enzymes
- Modify the drug
- Pumping the drug out

THE ACRONYMS

- ESBL Enterobacterales Break down certain antibiotics (Penicillin and cephalosporins)
- CRO Carbapenem resistant organisms
  - CRE Carbapenem-resistant *Enterobacterales*
- CP-CRO
  - Make enzyme that destroys carbapenem antibiotics and can transfer that ability to other bacteria
- CP-CRAB
  - OXA-23-like, OXA-24/40-like, OXA-58-like
  - KPC, IMP, NDM, VIM, OXA-48-like (less common)
- CRPA
  - Carbapenem-resistant *Pseudomonas aeruginosa* (multiple genes that produce the enzyme)

UNDERSTAND THE LAB REPORT

Test	Result	Date Approved
Organism Identification	**Organism(s) isolated:**	12/13/2021
Gram Negative Bacteria	Escherichia coli	12/13/2021

Note:

REFERENCE (NORMAL) RANGE: N/A

INTERPRETIVE CRITERIA:

Organism(s) isolated: Gram negative bacterial colonies isolated and Identified by the following: colony growth characteristics, colony morphology, microscopic morphology, MALDI TOF and/or biochemical reactions, and/or 16S sequencing.

No growth: No bacterial colonies detected, non-viable.

Not isolated: No Gram negative bacterial colonies detected.

Indeterminate/contaminant: unable to detect the presence or absence of gram negative bacteria due to overgrowth of other bacteria and /or fungus.

Carbapenemase Production	**Positive**	12/9/2021
Phenotypic method used	mCIM method	12/9/2021

Note:

REFERENCE (NORMAL) RANGE: Negative

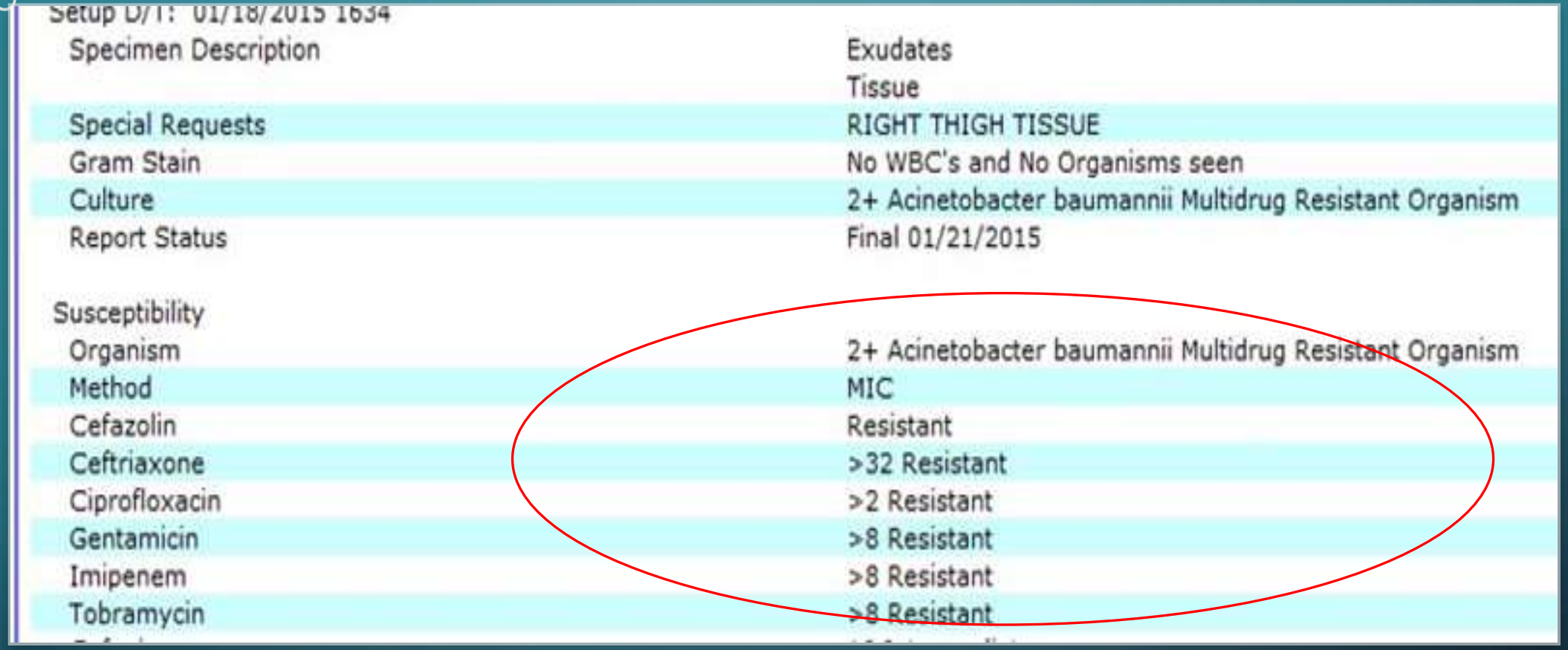
INTERPRETIVE CRITERIA:

Negative: The isolate tested does not produce a carbapenemase.

Positive: The isolate tested produces a carbapenemase, which inactivated carbapenem.

Indeterminate: The presence or absence of a carbapenemase cannot be confirmed.

Note: Test results can be used to support infection prevention measures . Test results should not be a substitute for diagnostic procedures or used to guide clinical decisions.



Setup D/T: 01/18/2015 1634

Specimen Description	Exudates Tissue
Special Requests	RIGHT THIGH TISSUE
Gram Stain	No WBC's and No Organisms seen
Culture	2+ Acinetobacter baumannii Multidrug Resistant Organism
Report Status	Final 01/21/2015

Susceptibility

Organism	2+ Acinetobacter baumannii Multidrug Resistant Organism
Method	MIC
Cefazolin	Resistant
Ceftriaxone	>32 Resistant
Ciprofloxacin	>2 Resistant
Gentamicin	>8 Resistant
Imipenem	>8 Resistant
Tobramycin	>8 Resistant

LAB REPORT

LAB REPORT

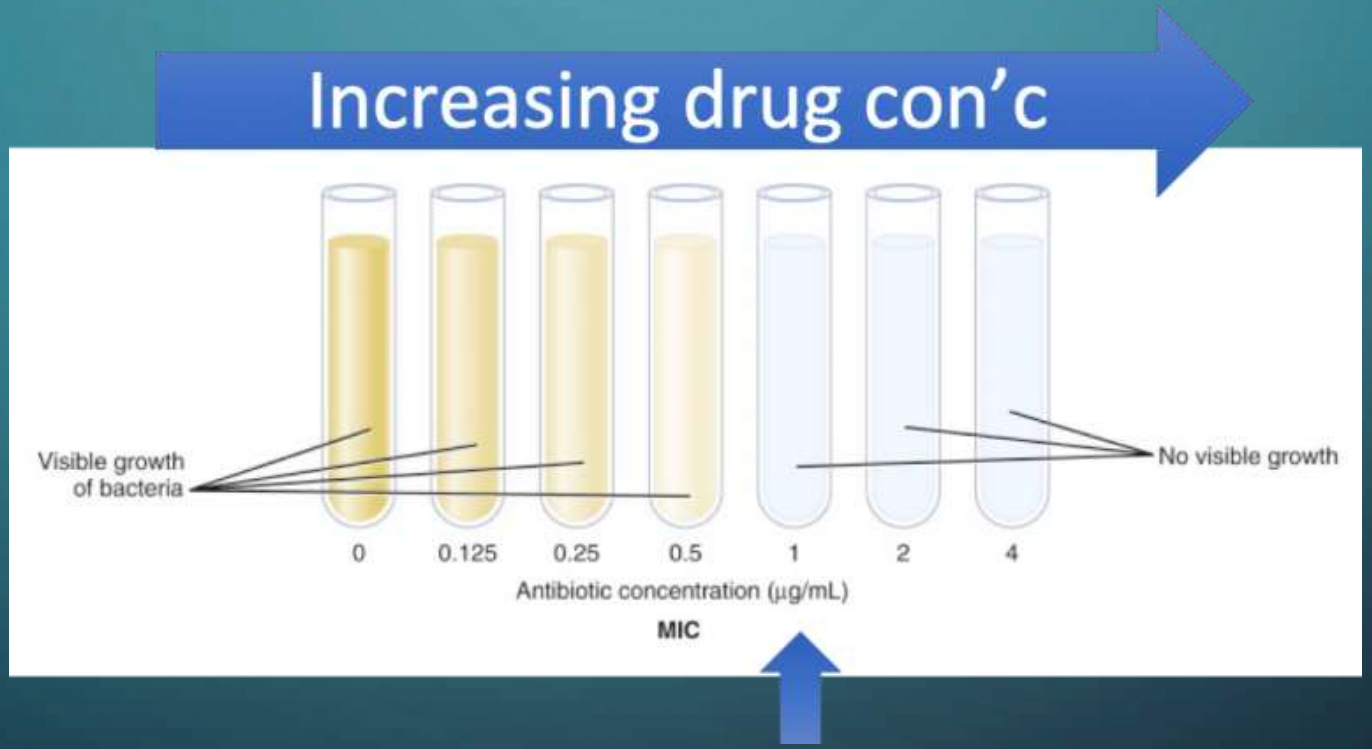
PROCEDURE:	Culture Respiratory with Gram Stain	ACCESSION:	MB-20-0031370
SOURCE:	Bron Alveolar Lavage	BODY SITE:	
COLLECTED DATE/TIME:	5/13/2020 11:26 CDT	RECEIVED DATE/TIME:	5/13/2020 11:34 CDT
START DATE/TIME:	5/13/2020 11:35 CDT	FREE TEXT SOURCE:	r lung

FINAL REPORTS
Final Report
Verified Date/Time/Personnel: 5/16/2020 09:46 CDT Jones ,Julia
1+ Carbapenem Resistant Acinetobacter baumannii

LAB REPORT

Culture Report		Date: 03/06/2020
Result:	**Pseudomonas aeruginosa**	
mCIM		Date: 03/06/2020
Result:	**Carbapenemase Detected**	
Antimicrobial Susceptibility		Date: 03/06/2020
Amikacin MIC:	**>32**	
Amikacin Interpretation:	**RESISTANT**	
Aztreonam MIC:	**16**	
Aztreonam Interpretation:	**INTERMEDIATE**	
Piperacillin/Tazobactam MIC:	**64/4**	
Piperacillin/Tazobactam Interpretation:	**INTERMEDIATE**	
Gentamicin MIC:	**8**	
Gentamicin Interpretation:	**INTERMEDIATE**	
Cefepime MIC:	**>16**	
Cefepime Interpretation:	**RESISTANT**	
Tobramycin MIC:	**>8**	
Tobramycin Interpretation:	**RESISTANT**	
Levofloxacin MIC:	**>8**	
Levofloxacin Interpretation:	**RESISTANT**	
Ciprofloxacin MIC:	**>2**	
Ciprofloxacin Interpretation:	**RESISTANT**	
Meropenem MIC:	**>8**	
Meropenem Interpretation:	**RESISTANT**	
Imipenem MIC:	**>8**	
Imipenem Interpretation:	**RESISTANT**	
Colistin MIC:	**2**	
Colistin Interpretation:	**INTERMEDIATE**	
Ceftazidime MIC:	**>16**	
Ceftazidime Interpretation:	**RESISTANT**	

MIC
MINIMUM INHIBITORY CONCENTRATION



MIC - CONTINUED

for drug selection and dosing questions.

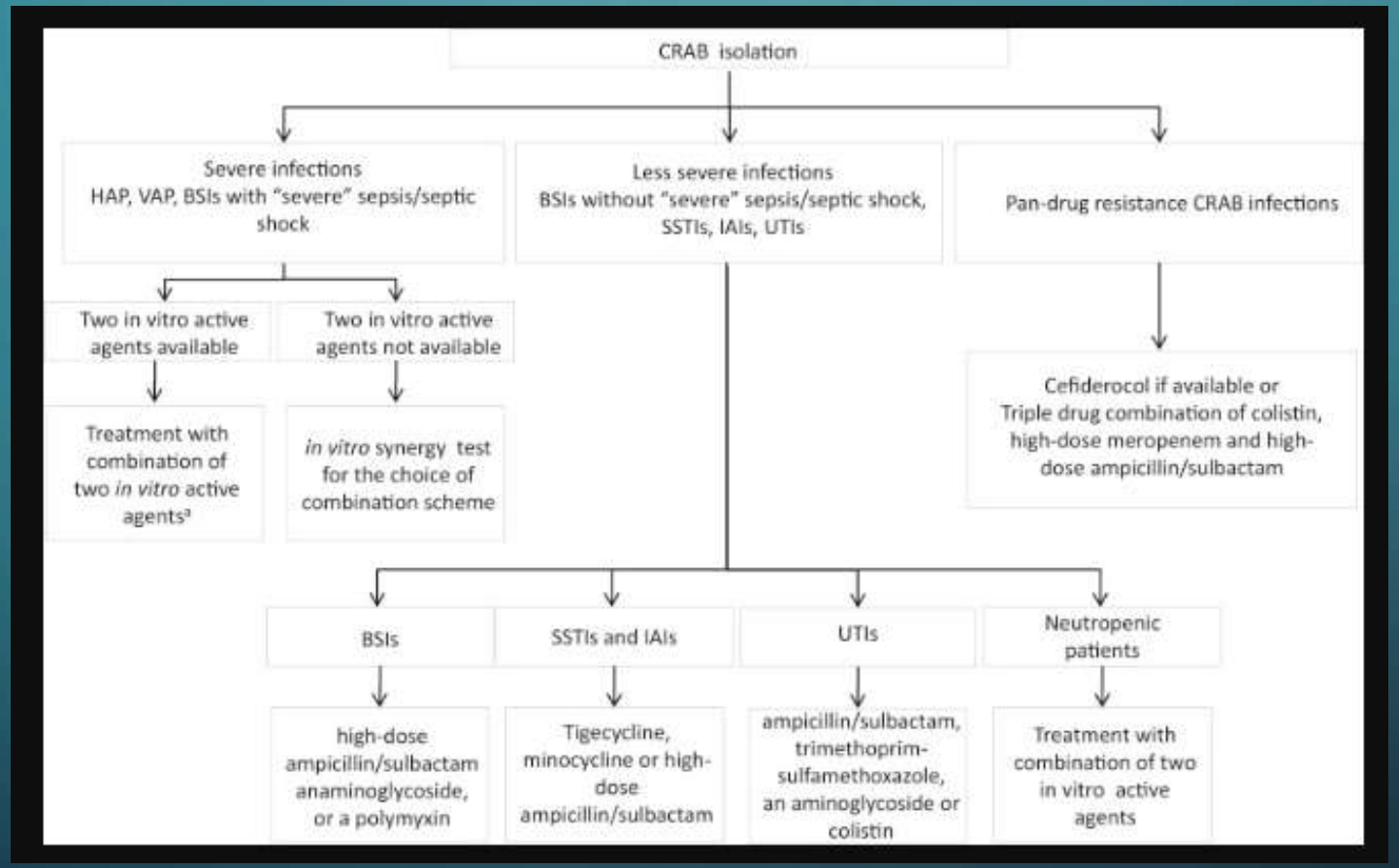
Table 1: 2014 MIC Interpretive Standards for *Enterobacteriaceae (includes E.coli, Klebsiella, Enterobacter, Citrobacter, Serratia and Proteus spp)*

Antimicrobial Agent	**MIC Interpretive Criteria (µg/mL)** *Enterobacteriaceae*		
	S	**I**	**R**
Ampicillin	≤ 8	16	≥ 32
Ampicillin-sulbactam	≤ 8/4	16/8	≥ 32/16
Aztreonam	≤ 4	8	≥ 16
Cefazolin (blood)	≤ 2	4	≥ 8
Cefazolin** (uncomplicated UTI only)	≤ 16		≥ 32
Cefepime*	≤ 2	4-8*	≥ 16
Cefotetan	≤ 16	32	≥ 64
Ceftaroline	≤ 0.5	1	≥ 2
Ceftazidime	≤ 4	8	≥ 16
Ceftriaxone	≤ 1	2	≥ 4
Cefpodoxime	≤ 2	4	≥ 8
Ciprofloxacin	≤ 1	2	≥ 4
Ertapenem	≤ 0.5	1	≥ 2
Fosfomycin	≤ 64	128	≥256
Gentamicin	≤ 4	8	≥ 16
Imipenem	≤ 1	2	≥ 4
Levofloxacin	≤ 2	4	≥ 8
Meropenem	≤ 1	2	≥ 4
Piperacillin-tazobactam	≤ 16/4	32/4 – 64/4	≥ 128/4
Trimethoprim-sulfamethoxazole	≤ 2/38	---	≥ 4/76

*Susceptibile dose-dependent – see chart below

**Cefazolin can predict results for cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime axetil, cephalexin and loracarbef for uncomplicated UTIs due to E.coli, K.pneumoniae, and P.mirabilis. Cefpodoxime, cefinidir, and cefuroxime axetil may be tested individually because some isolated may be susceptible to these agents while testing resistant to cefazolin.

GET AN EXPERT INVOLVED IN TREATMENT



Carbapenem-resistant Acinetobacter baumannii: in pursuit of an effective treatment
E.-T. Piperaki 1 , L.S. Tzouvelekis 1 , V. Miriagou 2 , G.L. Daikos 3, 2019

ANTIBIOTIC RESOURCES

- Cefdinir
- Cefditoren
- Cefepime
- Cefotaxime
- Cefotetan
- Cefoxitin
- Cefpodoxime
- Cefprozil
- Ceftazidime
- Ceftibuten
- Ceftriaxone
- Cefuroxime
- Cephalexin

Fluoroquinolones

- Ciprofloxacin

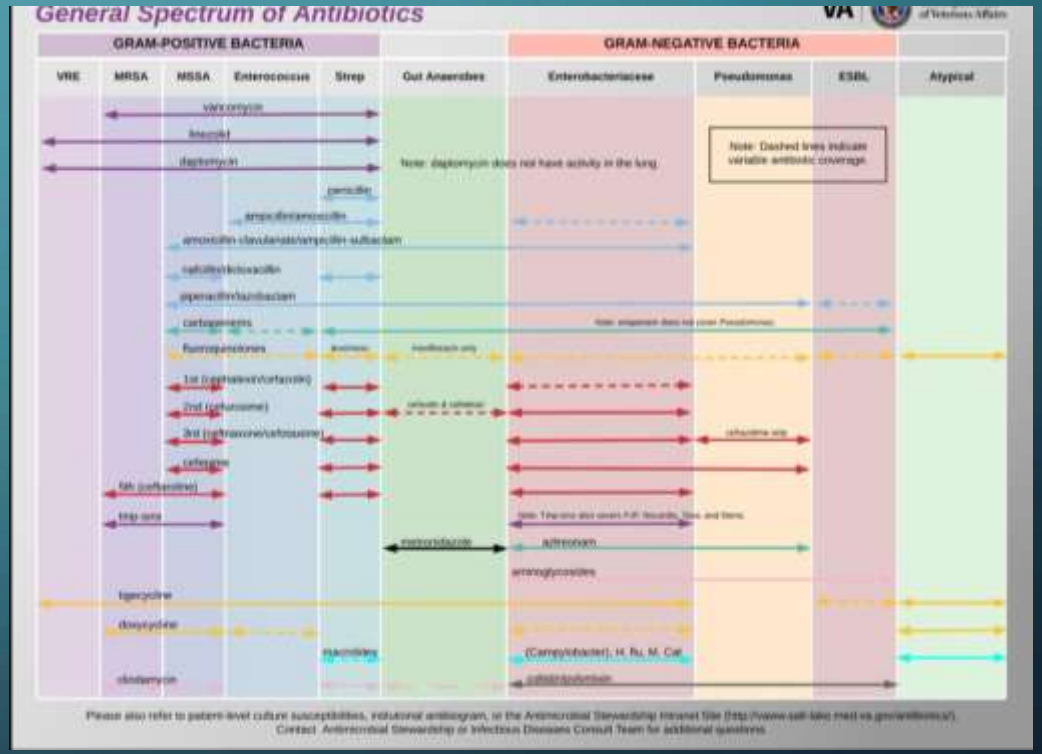
- Oxacillin

Sulfonamides

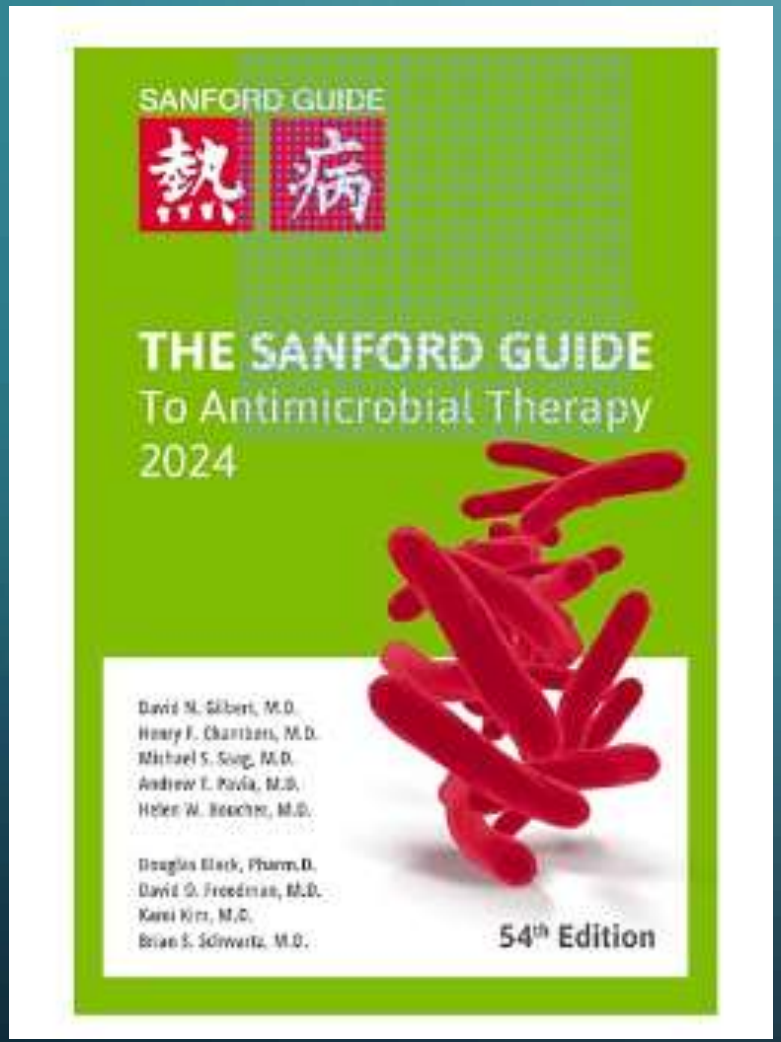
- Sulfamethoxazole
- Sulfadiazine
- Sulfasalazine
- Sulfisoxazole
- Trimethoprim/ sulfamethoxazole

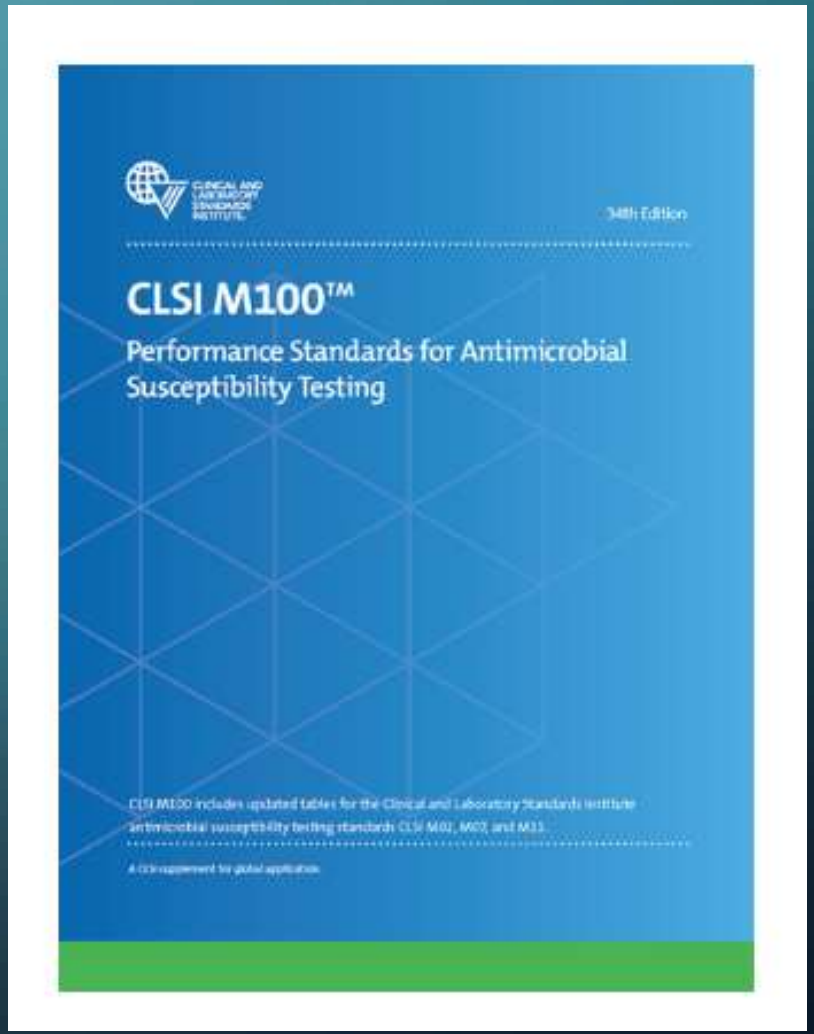
Tetracyclines

- Demeclocycline
- Doxycycline
- Minocycline
- Tetracycline



NO EXPERT? CONSULT RESOURCES





THE PROBLEM

What is the problem?	• 35K deaths from AR each year, 2.8M cases
Who has this problem?	• All of us and all spectrums across healthcare and the globe
Why has the problem occurred?	• Misuse of antimicrobials, (animals, humans, plants), Organism resiliency, Lack of IP practices, underused vaccines, STDs
How can I help stop the problem?	?

REFERENCES

- Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. AIMS Microbiol. 2018 Jun 26;4(3):482-501. doi: 10.3934/microbiol.2018.3.482. PMID: 31294229; PMCID: PMC6604941. **An overview of the antimicrobial resistance mechanisms of bacteria - PMC (nih.gov)**
- Antibiotic Resistance Threats in the United States, 2019 (cdc.gov)
- 2019 Antibiotic Resistance Threats Report | Antimicrobial Resistance | CDC
- MDRO Containment Strategy | HAIs | CDC
- Sexually Transmitted Disease Surveillance 2022: Gonococcal Isolate Surveillance Project Site-Specific Profiles Division of STD Prevention April 2024 Version 9.4 SAS System Output (cdc.gov)
- Module 9.5: Determining Antibiotic Sensitivity or Susceptibility After Isolation of the Pathogen – Clinical Veterinary Diagnostic Laboratory (umn.edu)