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MHSAL Guidelines for the Prevention and Control of Antimicrobial Resistant Organisms (AROs) - Response to Questions

Dr. Andrew Walkty

Medical Microbiologist, Diagnostic Services Manitoba (DSM)

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Question:
What is the difference between CRE and CPO?

Definitions

- Carbapenem-resistant organism (CRO):
  - Gram-negative bacilli that test non-susceptible (as defined by CLSI) to one or more carbapenem antimicrobials
  - Includes Enterobacteriaceae and non-Enterobacteriaceae (e.g., *Acinetobacter*, *Pseudomonas aeruginosa*)
  - May or may not be due to a carbapenemase
- Carbapenemase-producing organism (CPO):
  - Gram-negative bacteria that produce a carbapenemase enzyme. The term CPO includes Enterobacteriaceae that produce a carbapenemase (CPE), as well as other carbapenemase-producing non-Enterobacteriaceae such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Most CPO isolates demonstrate phenotypic resistance to carbapenems.

Definitions

- Carbapenem-resistant Enterobacteriaceae (CRE):
  - Gram-negative bacteria in the family Enterobacteriaceae that that test non-susceptible (as defined by CLSI) to one or more carbapenem antimicrobials.
  - NB. Phenotypic resistance to carbapenems may result from the production of a carbapenemase enzyme or from other mechanisms (e.g., permeability changes, efflux, etc.).
- Carbapenemase-producing Enterobacteriaceae (CPE):
  - Gram-negative bacteria in the family Enterobacteriaceae that produce a carbapenemase enzyme. Most CPE isolates demonstrate phenotypic resistance to carbapenems and would therefore also meet the definition of CRE.

Laboratory Protocol

- Phenotypic resistance to carbapenems is determined with routine susceptibility testing methods (VITEK, disk diffusion, E-test, etc…)
- For Enterobacteriaceae that demonstrate reduced carbapenem susceptibility, a phenotypic test for carbapenemase production is performed (Neo-Rapid CARB Kit – carba NP test)
  - Isolates positive for carbapenemase production get a molecular test for common carbapenemase genes

Example 1:

Selected Organism: Klebsiella pneumoniae ssp pneumoniae

Susceptibility Information	Card: AST-N208		Lot Number: 578315520	Expires: Aug 4, 2015 12:00 GMT-06:00	
	Completed: Jun 22, 2014 01:20 GMT-06:00		Status: Final	Analysis Time: 9.00 hours	
Antimicrobial	**MIC**	**Interpretation**	**Antimicrobial**	**MIC**	**Interpretation**
Ampicillin	>= 32	R	Ertapenem	>= 8	R
Amoxicillin/Clavulanic Acid	>= 32	R	Meropenem	>= 16	R
Piperacillin/Tazobactam	>= 128	R	Amikacin	>= 64	R
Cefalotin	>= 64	R	Gentamicin	>= 16	R
Cefazolin	>= 64	R	Tobramycin	>= 16	R
Cefoxitin	>= 64	R	Ciprofloxacin	>= 4	R
Cefixime	>= 4	R	Tetracycline	>= 16	R
Ceftazidime	>= 64	R	Nitrofurantoin	>= 512	R
Ceftriaxone	>= 64	R	Trimethoprim/Sulfamethoxazole	>= 320	R

+= Deduced drug *= AES modified **= User modified

Supplemental testing: carba NP test POSITIVE, PCR demonstrates the presence of NDM-1

Example 1:

- This *Klebsiella* isolate demonstrates resistance to carbapenems by routine susceptibility testing, hence, by definition it is a carbapenem-resistant Enterobacteriaceae (CRE)
- The carba NP test is positive indicating the isolate produces a carbapenemase enzyme, hence it is also a carbapenemase-producing Enterobacteriaceae (CPE)
- The enzyme here is the NDM enzyme – a metallo beta-lactamase (Ambler Class B)

Example 2.

Selected Organism: Escherichia coli

Susceptibility Information	Card: AST-N208		Lot Number: 578315520	Expires: Aug 4, 2015 12:00 GMT-06:00	
	Completed: Jun 22, 2014 06:36 GMT-06:00		Status: Final	Analysis Time: 14.25 hours	
Antimicrobial	**MIC**	**Interpretation**	**Antimicrobial**	**MIC**	**Interpretation**
Ampicillin	>= 32	R	Ertapenem	>= 8	R
Amoxicillin/Clavulanic Acid	>= 32	R	Meropenem	2	*R
Piperacillin/Tazobactam	>= 128	R	Amikacin	8	S
Cefalotin	>= 64	R	Gentamicin	>= 16	R
Cefazolin	>= 64	R	Tobramycin	>= 16	R
Cefoxitin	>= 64	R	Ciprofloxacin	>= 4	R
Cefixime	>= 4	R	Tetracycline	>= 16	R
Ceftazidime	>= 64	R	Nitrofurantoin	128	R
Ceftriaxone	>= 64	R	Trimethoprim/Sulfamethoxazole	>= 320	R

+= Deduced drug *= AES modified **= User modified

Supplemental testing: carba NP test POSITIVE, PCR demonstrates the presence of OXA-48

Example 2.

- This *E. coli* isolate demonstrates resistance to carbapenems by routine susceptibility testing, hence, by definition it is a carbapenem-resistant Enterobacteriaceae (CRE)
- The carba NP test is positive indicating the isolate produces a carbapenemase enzyme, hence it is also a carbapenemase-producing Enterobacteriaceae (CPE)
- The enzyme here is the OXA-48 enzyme – a serine beta-lactamase (Ambler Class D)

Example 3:

***Enterobacter cloacae* complex**

Ampicillin	**R**
Cephalexin	**R**
Cefazolin	**R**
Ceftriaxone	**R**
Ceftazidime	**R**
Piperacillin-tazobactam	**R**
Gentamicin	**R**
Tobramycin	**R**
TMP/SMX	**R**
Ciprofloxacin	**R**
Ertapenem	**R**
Meropenem	**S**

Supplemental testing: carba NP test NEGATIVE

Example 3:

- This *Enterobacter* isolate demonstrates resistance to carbapenems by routine susceptibility testing, hence, by definition it is a carbapenem-resistant Enterobacteriaceae (CRE)
- The carba NP test is negative, indicating the isolate does NOT produce a carbapenemase enzyme – it is NOT a CPE
- The mechanism of reduced carbapenem susceptibility here is likely AmpC hyperproduction in combination with reduced permeability

Example 4.

Selected Organism: Pseudomonas aeruginosa

Susceptibility Information	Card: AST-N208		Lot Number: 578315520	Expires: Aug 4, 2015 12:00 GMT-06:00	
	Completed: Jun 16, 2014 21:17 GMT-06:00		Status: Final	Analysis Time: 8.50 hours	
Antimicrobial	**MIC**	**Interpretation**	**Antimicrobial**	**MIC**	**Interpretation**
Ampicillin	>= 32	R	Ertapenem		
Amoxicillin/Clavulanic Acid	>= 32	R	Meropenem	>= 16	R
Piperacillin/Tazobactam	>= 128	R	Amikacin	>= 64	R
Cefalotin	>= 64	R	Gentamicin	>= 16	R
Cefazolin	>= 64	R	Tobramycin	>= 16	R
Cefoxitin	>= 64	R	Ciprofloxacin	>= 4	R
Cefixime	>= 4	R	Tetracycline	>= 16	R
Ceftazidime	>= 64	R	Nitrofurantoin	>= 512	R
Ceftriaxone	>= 64	R	Trimethoprim/Sulfamethoxazole	>= 320	R

+= Deduced drug *= AES modified **= User modified

Supplemental testing: carba NP test POSITIVE, PCR demonstrates the presence of VIM

Example 4.

- This *Pseudomonas* isolate demonstrates resistance to carbapenems by routine susceptibility testing, hence, by definition it is a carbapenem-resistant organism (CRO)
  - Not a member of the family Enterobacteriaceae, therefore NOT CRE
- The carba NP test is positive indicating the isolate produces a carbapenemase enzyme, hence it is also a carbapenemase-producing organism (CPO)
  - Not a member of the family Enterobacteriaceae, therefore NOT CPE
- The enzyme here is the VIM enzyme – a metallo beta-lactamase (Ambler Class B)
- NB. the lab does NOT routinely look for carbapenemase production in non-Enterobacteriaceae (e.g., *Pseudomonas*)