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**MICHIGAN
DEPARTMENT OF
COMMUNITY HEALTH**

June 25, 2015

“CRE Mechanisms and their Importance for Infection Prevention ”

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Financial Disclosures

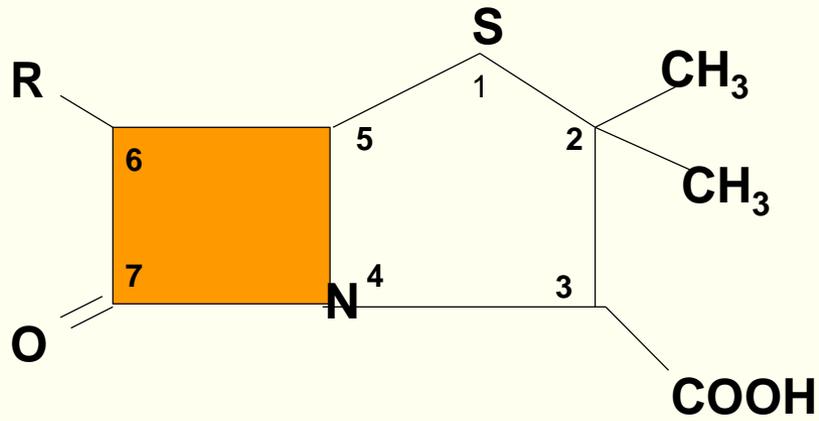
Type of Financial Interest	Name of Commercial Interest
Salaried Employee	Loyola University Medical Center
Stocks/Stock Options	None
Independent contractor/Speaker's Bureau	Accelerate Dx., Beckman Coulter, bioMerieux, BioFire, Cepheid, Hardy Diagnostics, Merck, Thermo Fisher Scientific
Consultant/Advisory Committees	BioFire, Cempra, Cepheid, GenMark, Quidel, Thermo Fisher Scientific, Theravance
Research Grants	Accelerate Dx, Becton-Dickinson, Beckman Coulter, BioFire, bioMerieux, Bruker, Cepheid,

Learning Objectives

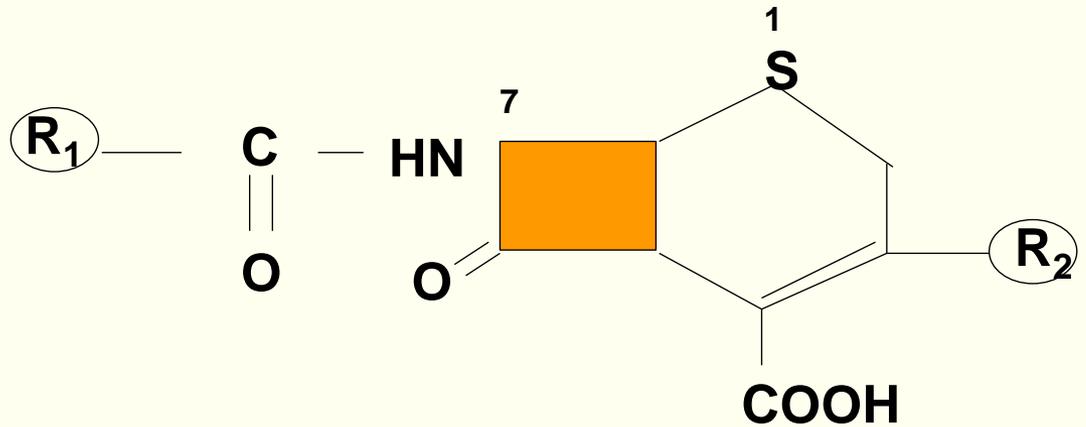
At the conclusion of this session, participants will be able to:

1. Describe the five major types of CRE
2. Review conventional and new approaches to detecting CRE
3. Explain the CSTE CRE definition proposal and its implications for labs
4. Evaluate their own laboratories readiness for detecting and reporting CRE

Penicillin nucleus



Cephalosporin nucleus



MODE OF ACTION OF BETA LACTAMS IN GRAM NEGATIVES

SUSCEPTIBLE

β-Lactam Antibiotic



Diffusion through
Outer Membrane



Diffusion through
Peptidoglycan



Penicillin Binding Proteins



Cell Death

RESISTANT

← Porin Blocks Entry

← Efflux Pump

← Beta-Lactamase
Hydolyzes Beta-Lactam

← Changes in PBP results in
Failure to Bind to β-Lactam

The β -lactam family of antibiotics

Penicillins	Cephalosporins	Cephamycins	Carbapenems	Monobactams
Benzylpenicillin	Cephalothin 1 st	Cefoxitin	Imipenem	Aztreonam
Methicillin	Cefamandole 2 nd	Cefotetan	Meropenem	
Ampicillin	Cefuroxime 2 nd	Cefmetazole	Ertapenem	
Carbenicillin	Cefotaxime 3 rd		Doripenem	
Mezlocillin	Ceftazidime 3 rd			
Ticarcillin	Ceftriaxone 3 rd			
	Cefepime 4 th			

The β -lactam family of antibiotics

Penicillins

Benzyl-
penicillin

Methicillin

Ampicillin

Carbenicillin

Mezlocillin

Ticarcillin

Cephalosporins

Cephalothin
1st

Cefamandole
2nd

Cefuroxime
2nd

Cefotaxime 3rd

Ceftazidime
3rd

Ceftriaxone 3rd

Cefepime 4th

Cephameycins

Cefoxitin

Cefotetan

Cefmetazole

Carbapenems

Imipenem

Meropenem

Ertapenem

Doripenem

Monobactams

Aztreonam

ESBLs hydrolyze all

Penicillins

Cephalosporins

Monobactams

The β -lactam family of antibiotics

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Carbenicillin	Cefotaxime 3 rd		Doripenem	
Mezlocillin	Ceftazidime 3 rd	<p><u>ampCs hydrolyze all</u></p> <p>Penicillins</p> <p>1st, 2nd, 3rd Cephalosporins</p> <p>Cephameycins</p> <p>Monobactams</p>		
Ticarcillin	Ceftriaxone 3 rd			
	Cefepime 4 th			

The β -lactam family of antibiotics

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Mezlocillin	Ceftazidime 3 rd			
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The β -lactam family of antibiotics

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Benzyl-penicillin	Cephalothin 1 st	Cefoxitin	Imipenem	Aztreonam
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Ampicillin	Cefuroxime 2 nd	Cefmetazole	Ertapenem	
Carbenicillin	Cefotaxime 3 rd	<u>KPCs hydrolyze all</u> Penicillins Cephalosporins Cephameycins Carbapenems Monobactams		
Mezlocillin	Ceftazidime 3 rd			
Ticarcillin	Ceftriaxone 3 rd			
	Cefepime 4 th			

Carbapenem-Resistance in Enterobacteriaceae

- Two mechanisms of resistance
 - Carbapenemase (β -lactamase that can hydrolyze carbapenems)
 - Cephalosporinase combined with porin loss
 - Some cephalosporinases (e.g., AmpC-type β -lactamases or certain ESBLs i.e. CTX-M) have a low-level carbapenemase activity
 - Porin loss limits entry of the carbapenem into the periplasmic space

Need to Distinguish Between Mechanisms of Carbapenem Resistance – Why?

- Carbapenemase
 - Isolate likely to be resistant to all carbapenems and other β -lactam agents
 - May need to change susceptible reports to resistant for β -lactam drugs
 - Need to implement infection control measures such as contact precautions and possibly active surveillance testing
 - **These are an Infection Control Emergency**

Need to Distinguish Between Mechanisms of Carbapenem Resistance – Why?

- Cephalosporins combined with porin-loss
 - Class A ESBL' s (CTX-M) + reduced permeability
 - Class C High AmpC + reduced permeability
- These hydrolyze ertapenem more than meropenem or imipenem
 - Not necessarily resistant to all carbapenems (i.e., would not need to change susceptible results to resistant reports for β -lactam drugs)
- These isolates are clearly MDR and infection control measures are recommended. Healthcare institutions may reserve more aggressive measures for carbapenemase-producing isolates

5 Most Common Carbapenemases

Class	Carbapenemases	Enterobacteriaceae	Non-fermenters
A ¹	KPC ²	+++	+
B (metallo)	NDM ³ , IMP, VIM,	+++	+++
D	OXA-48-like	+++	+/-

¹also includes SME; ²most common in USA; ³increasing in USA

....but several types within 5 groups and other types of carbapenemases

(slide courtesy Janet Hindler)

Strategy for Laboratory Detection of Carbapenemases

- **Antibiogram** – CDC approach: if any Enterobacteriaceae tests non-susceptible to any carbapenem call it CRE.
- **Phenotypic testing**
 - Modified Hodge Test
 - Boronic Acid Synergy Test
 - EDTA inhibition test (MBL Etest)
- **Rapid Colorimetric**
 - Carba NP
 - NEO-Rapid CARB Kit by Rosco Diagnostica (Hardy, Key Scientific)
 - RAPIDEC® CARBA NP (bioMerieux)
 - EPI-CRE® (Pilots Point, Sarasota, FL)
- **Molecular – PCR**
- **Other**

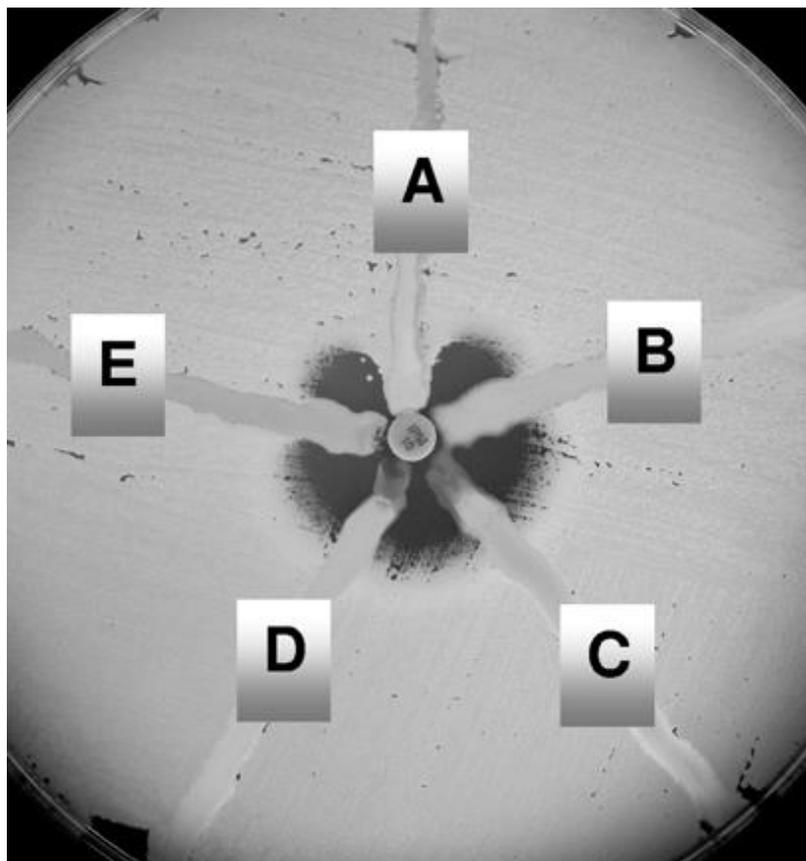
Strategy for Laboratory Detection of Carbapenemases

- CLSI Carbapenemase Screening Criteria (M100-S-25 Jan 2015 p.48)
 - “Laboratories **should perform** the modified Hodge test (MHT), the Carba NP test, and/or a molecular assay when isolates of *Enterobacteriaceae* are suspicious for carbapenemase production”

Strategy for Laboratory Detection of Carbapenemases

- CLSI Carbapenemase Screening Criteria (M100-S-25 Jan 2015 p.48)
 - Disk zone of < 22 mm for ertapenem or meropenem
 - MIC of >1 $\mu\text{g/ml}$ for imipenem, ertapenem or meropenem
- Procedure Notes
 - Imipenem disk test is not a good screen
 - Imipenem MIC does not work as a screen for *Proteus/Providencia/Morganella* due to slightly elevated MICs in this group by mechanisms other than carbapenemases

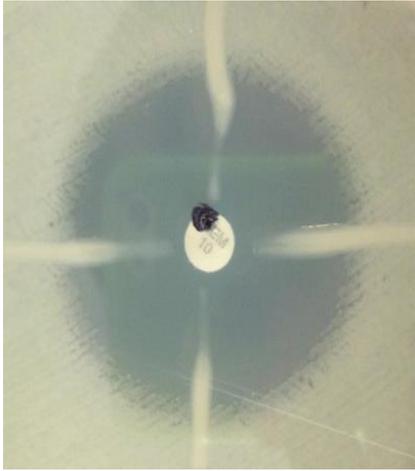
Modified Hodge Test



- Inoculate MH agar with a 1:10 dilution of a 0.5 McFarland suspension of *E. coli* ATCC 25922 and streak for confluent growth using a swab.
- Place 10- μ g ertapenem or **meropenem (best)** disk in center
- Streak each test isolate from disk to edge of plate
- Isolate A is a KPC producer and positive by the modified Hodge test.

Anderson KF et al. JCM 2007 Aug;45(8):2723-5.

Modified Hodge Test



Neg Control

-



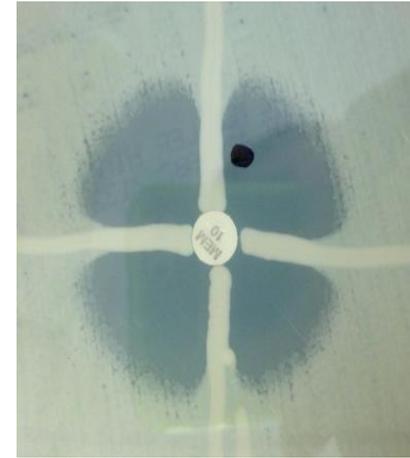
KPC

+



NDM

False -



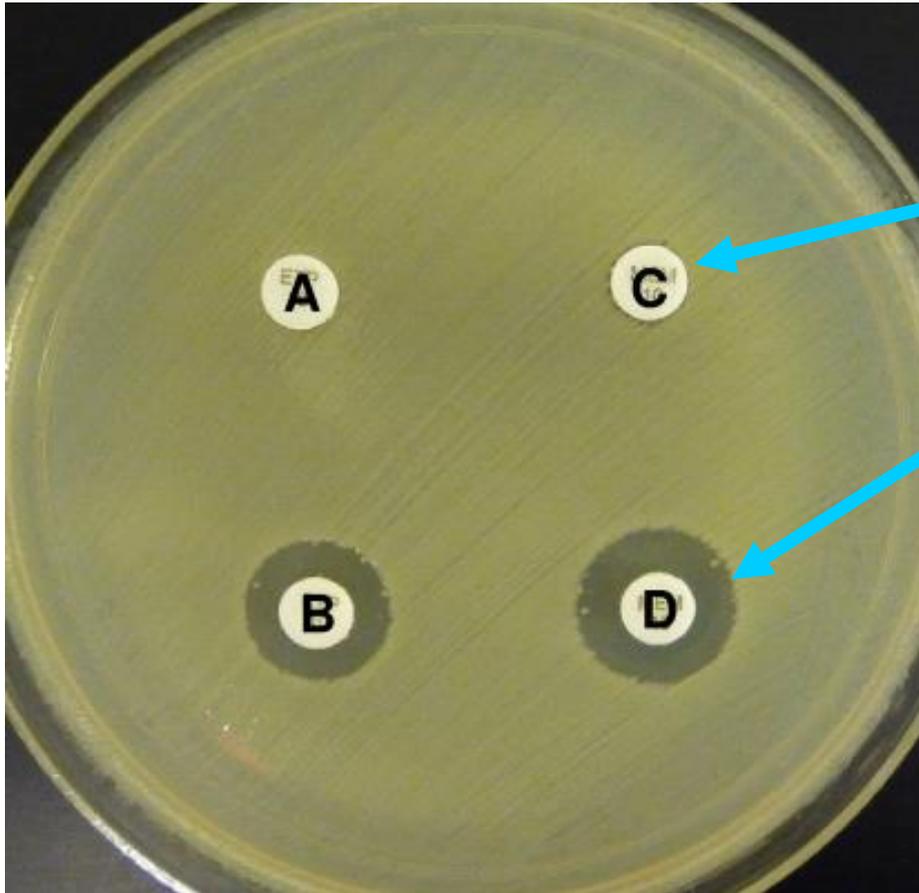
OXA 232

+

UCLA

(slide courtesy Janet Hindler)

Boric Acid Synergy Test



Meropenem

Meropenem plus
3-aminophenyl
boronic acid

Potential of carbapenems by APB in *K. pneumoniae* producing KPC-2. (A) Ertapenem (10 μ g); (B) ertapenem plus APB (300 μ g); (C) meropenem (10 μ g); (D) meropenem plus APB (300 μ g).

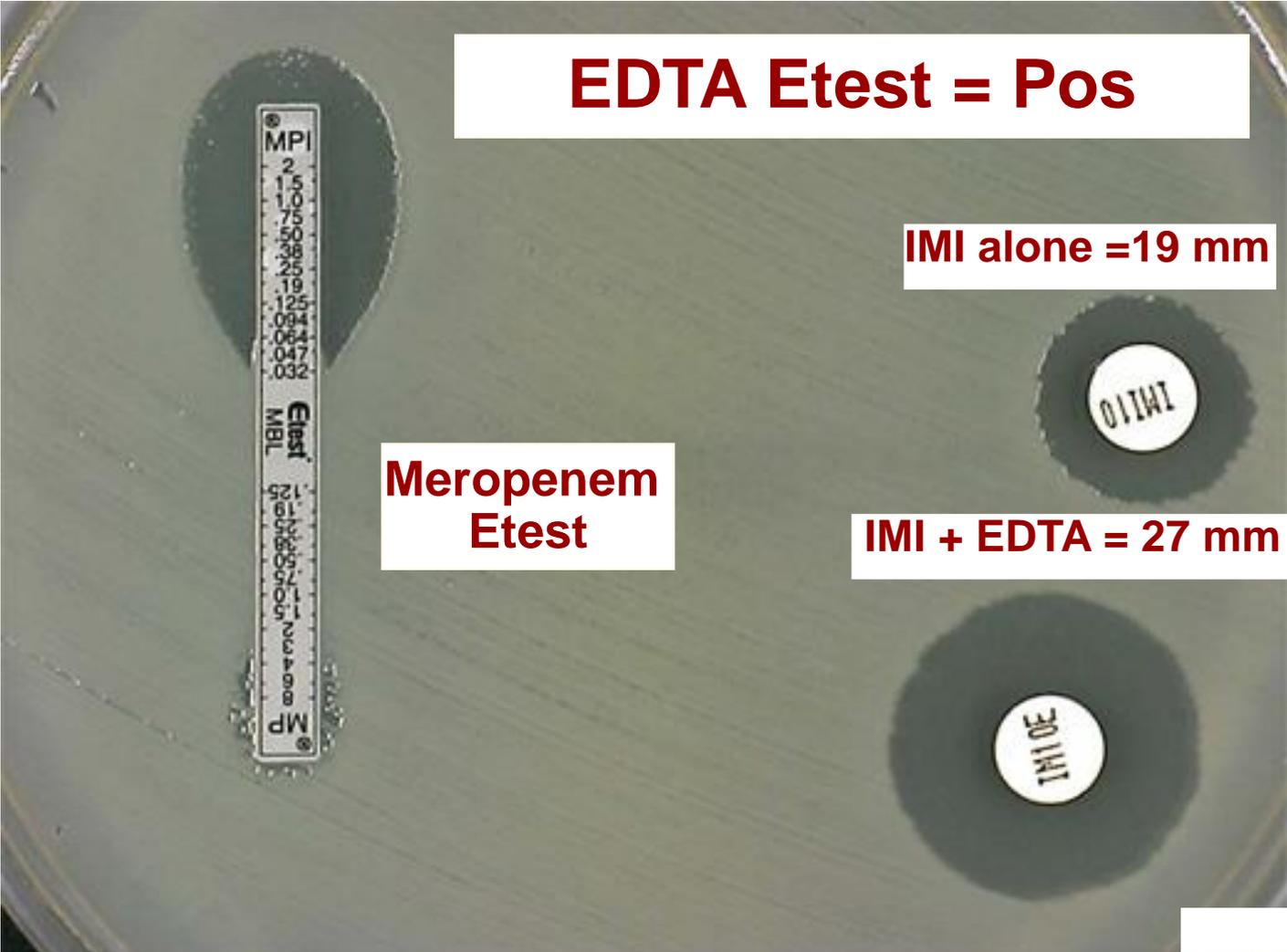
[Doi Y et al. J Clin Microbiol. 2008 Dec;46\(12\):4083-6.](#)

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Rosco Diagnostica IMI/EDTA Disks MBL Etest bioMerieux



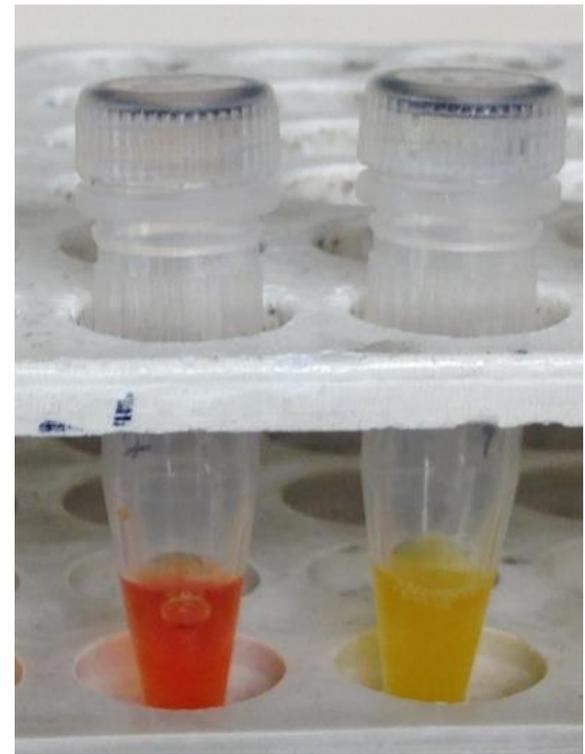
(Only Detects MBL's eg. NDM, IMP, VIM)

What is the Carba NP test?

- A **colorimetric test for carbapenemase** production by Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter*
 - Uses imipenem as the target substrate, phenol red as the pH indicator; positive hydrolysis turns yellow
 - Color usually turns fast, test ends at 2 hours
 - Good at detecting KPC, NDM, VIM, SPM, and SME, not so good at OXA
 - Will pick up carbapenem resistance if the MIC is 2 or 4 and you haven't changed your breakpoints

Carba NP Test for Carbapenemase Production

- ◆ Isolated colonies (lyse)
- ◆ Hydrolysis of imipenem
- ◆ Detected by change in pH of indicator (red to yellow/orange)
- ◆ Rapid <2h
- ◆ Microtube method



NO **+**
imipenem imipenem

Nordmann et al. 2012. Emerg Infect Dis. 18:1503.
Tijet et al. 2013. Antimicrob Agents Chemother. 57:4578.
Vasoo et al. 2013. J Clin Microbiol. 51:3092.
Dortet et al. 2014. J Med Microbiol. 63:772.
Dortet et al. 2014. Antimicrob Agents Chemother. 58:2441.

(slide courtesy Janet Hindler)

Results for Patient and QC Tubes

Tube "a": Solution A (serves as internal control)	Tube "b": Solution B	Interpretation
Red or red-orange	Red or red-orange	Negative, no carbapenemase detected
Red or red-orange	Light-orange, dark yellow, or yellow	Positive, carbapenemase producer
Red or red-orange	Orange	Invalid
Orange, light-orange, dark yellow, or yellow	Any color	Invalid

Solution A



Red

Orange **Invalid**

Red

Light Orange **+**

Red

Dark Yellow **+**

Red-orange

Yellow **+**

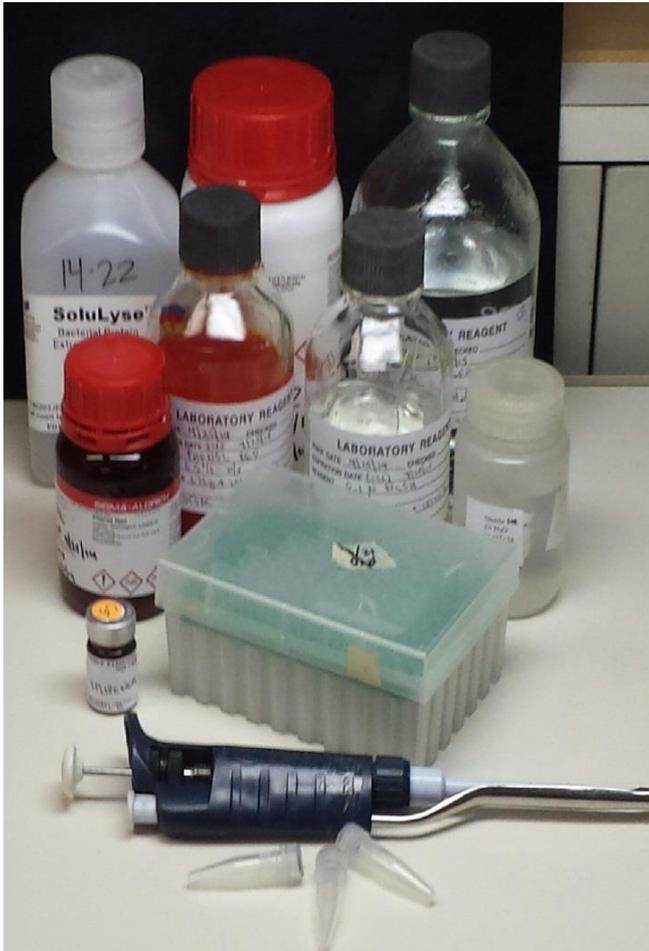
Red-orange

Yellow **+**

M100-S25.
p.120-126.

(slide courtesy Janet Hindler)

Carba NP Test Materials/Reagents



(slide courtesy Janet Hindler)

- ◆ Testing simple
- ◆ Reagent Preparation takes time

Reagents Must be Prepared Fresh

10 mM Zinc sulfate heptahydrate

Phenol red solution

0.1 N NaOH

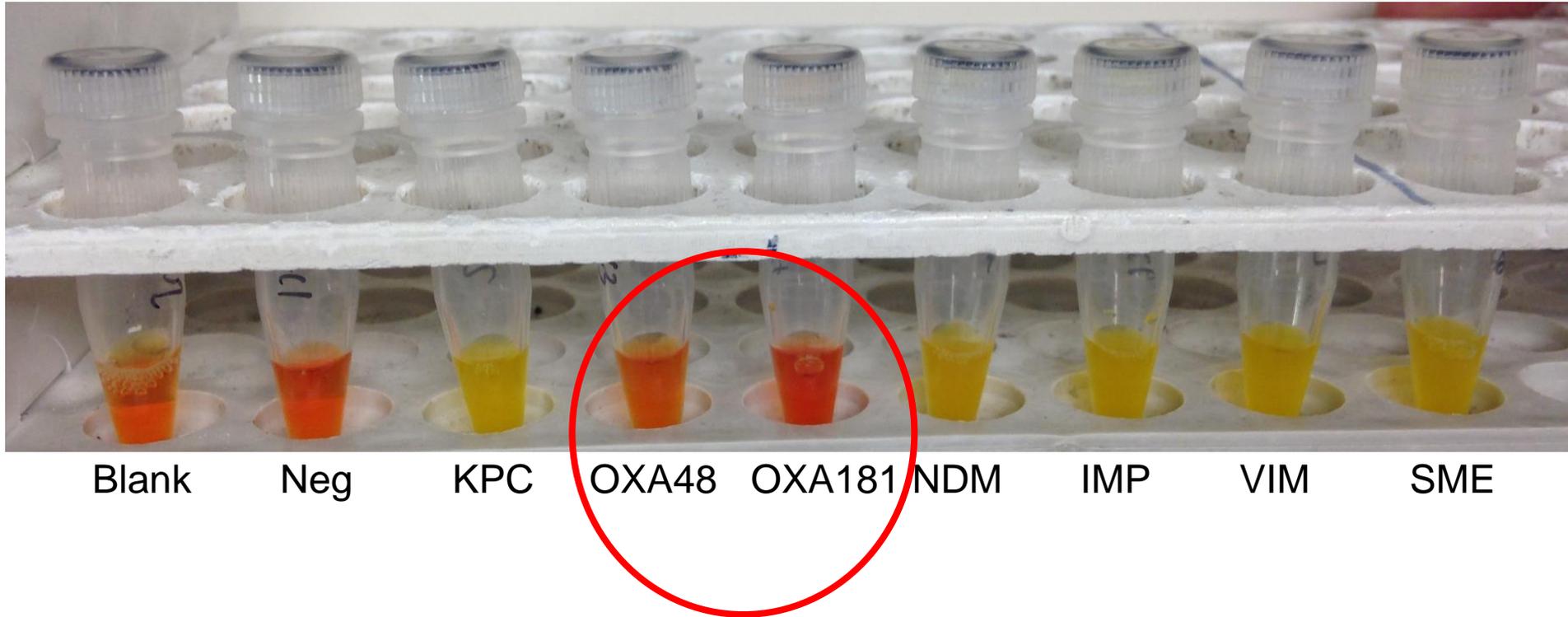
Carba NP Solution A

(phenol red + zinc solutions)

Carba NP Solution B

(Carba NP Solution A + imipenem)

Carba NP Test



UCLA

(slide courtesy Janet Hindler)

Commercial Test Rapid CARB Screen Kit

- Commercial kit; similar to Carba NP
- Enterobacteriaceae and *P. aeruginosa*
- Tablets
 - Imipenem + indicator
 - Negative control
- ≤2 hours
- CLSI study isolates – UCLA results:
 - More difficult to read than Carba NP
 - Good agreement with Carba NP but more initial invalids that required repeating
 - Most problems with *Acinetobacter baumannii* – NDM (not indicated for this species)



www.rosco.dk

NOT FDA cleared

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Enterobacteriaceae Carbapenemase Detection

Study	N	Carba NP	Rapid CARB Screen Kit	MHT
1	235	97% sens 100% spec	98% sens 83% spec	-
2	92	91% sens 100% spec	73% sens 100% spec	-
3	150	-	98% sens 100% spec	75% sens 91% spec

1 Huang et al. 2014. J Clin Microbiol. 52:3060.

2 Yousef et al. 2014. Eur J Clin Microbiol Infect Dis. Jul 10 epub.

3 Simner et al. 2015. J Clin Microbiol. 53:105.

Rapid CARB Screen Kit discontinued !!!!
Reformatted Product is Neo-Rapid CARB Screen Kit

(slide courtesy Janet Hindler)

Commercial Test RAPIDEC® CARBA NP

- 1) Phenol red: pH indicator
- 2) A carbapenem: imipenem (carbapenemase substrate) + Zinc, required for the detection of metallodependent carbapenemase-producing strains



**Detects (without distinction)
Class A, B and D Carbapenemases**

bioMerieux

NOT FDA cleared

<https://www.youtube.com/watch?v=3YXCBs34zyA>

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EPI-CRE®

Enterobacteriaceae (CRE)

It's Easy to See...



Specifications

Time to Results: **Positive** – as soon as the sample changes from gold to magenta.

Negative – after 24 hours if no color change from gold occurs.

Storage: From 2 to 28 °C under dry conditions, EPI-CRE® is stable for 1 year from date of manufacture.

Sensitivity & Specificity: EPI-CRE® detects ONLY living bacteria. It is 100% specific.

Regulatory: CE/IVD approved.

EPI-CRE®

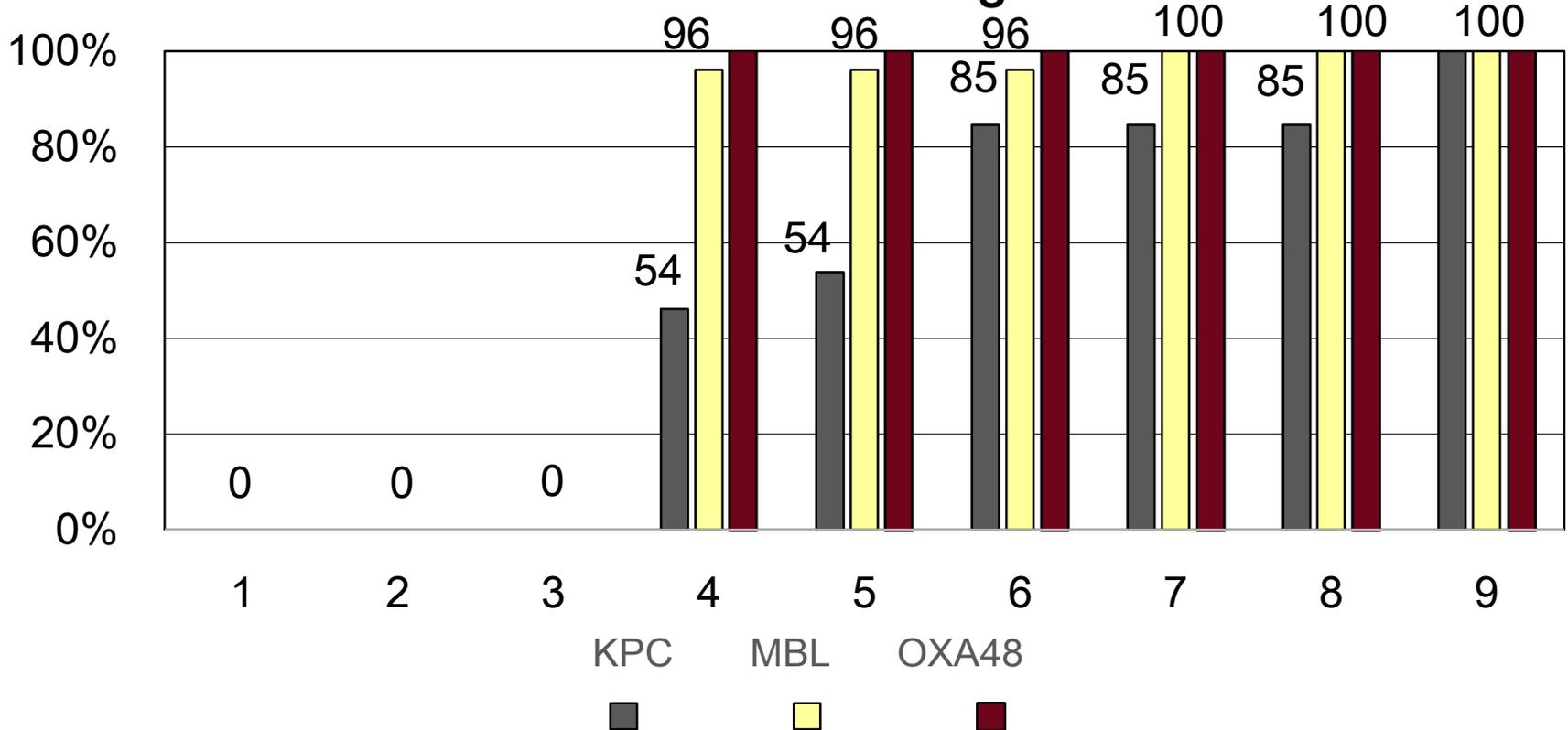
	MBL E-test			Modified Hodge Test				EPI-CRE			PCR		
	Pos	Neg	Total	Pos	Weak	Neg	Total	Pos	Neg	Total	Pos	Neg	Total
KPC	0	13	13	13	0	0	13	13	0	13	13	0	13
MBL	26	0	26	1	16	9	26	26	0	26	26	0	26
OXA48	0	3	3	2	1	0	3	3	0	3	3	0	3
ESBL	0	20	20	0	0	20	20	0	20	20	0	20	20
AmpC	0	21	21	0	0	21	21	0	21	21	0	21	21
Total Tested	26	57	83	16	17	50	83	42	41	83	42	41	83
Total CRE	42			42				42			42		
Sensitivity (%)	61.9			38.1				100			100		
Specificity (%)	100			100				100			100		

EPI-CRE inoculated with 50 µl 0.5 McFarland suspension

Slesar AJ, Schreckenberger PC. Evaluation of Modified EPI-CRE Tet for Rapid Carbapenemase Detection. Abstr. 115th Gen. Mtg. Am. Soc. Microbiol, New Orleans, LA, June 2, 2015.

EPI-CRE®

Table 3. Cumulative Percentage of Positives



EPI-CRE inoculated with 50 µl 0.5 McFarland suspension

Slesar AJ, Schreckenberger PC. Evaluation of Modified EPI-CRE Tet for Rapid Carbapenemase Detection. Abstr. 115th Gen. Mtg. Am. Soc. Microbiol, New Orleans, LA, June 2, 2015.



Molecular Tests for Carbapenemases

- ◆ Biofire *
 - KPC
- ◆ Nanosphere *
 - KPC, NDM, OXA, IMP, VIM
- ◆ BD Max
 - KPC, NDM, OXA-48
- ◆ Cepheid
 - KPC, NDM, OXA-48, IMP-1, VIM
- ◆ Check-Points
 - KPC, NDM, OXA-48, IMP, VIM
- ◆ Others?

* FDA cleared

(slide courtesy Janet Hindler)

Tests for Carbapenemases in *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter* spp.

	MHT	Carba NP	Molecular
Use	Enterobacteriaceae	Enterobacteriaceae P. aeruginosa Acinetobacter	Enterobacteriaceae P. aeruginosa Acinetobacter
Strengths	Simple	Rapid	Determines type of carbapenemase
Limitation	Some false pos (eg, ESBL/ampC + porin) Some false neg (eg NDM) Enterobacteriaceae only	Special “fresh” reagents Some invalid results False neg for OXA-type carbapenemase	Special reagents Specific to targeted gene High Cost

Other New Approaches

- Immunochromatographic confirmatory test for the detection of OXA-48



OXA-48 K-SeT

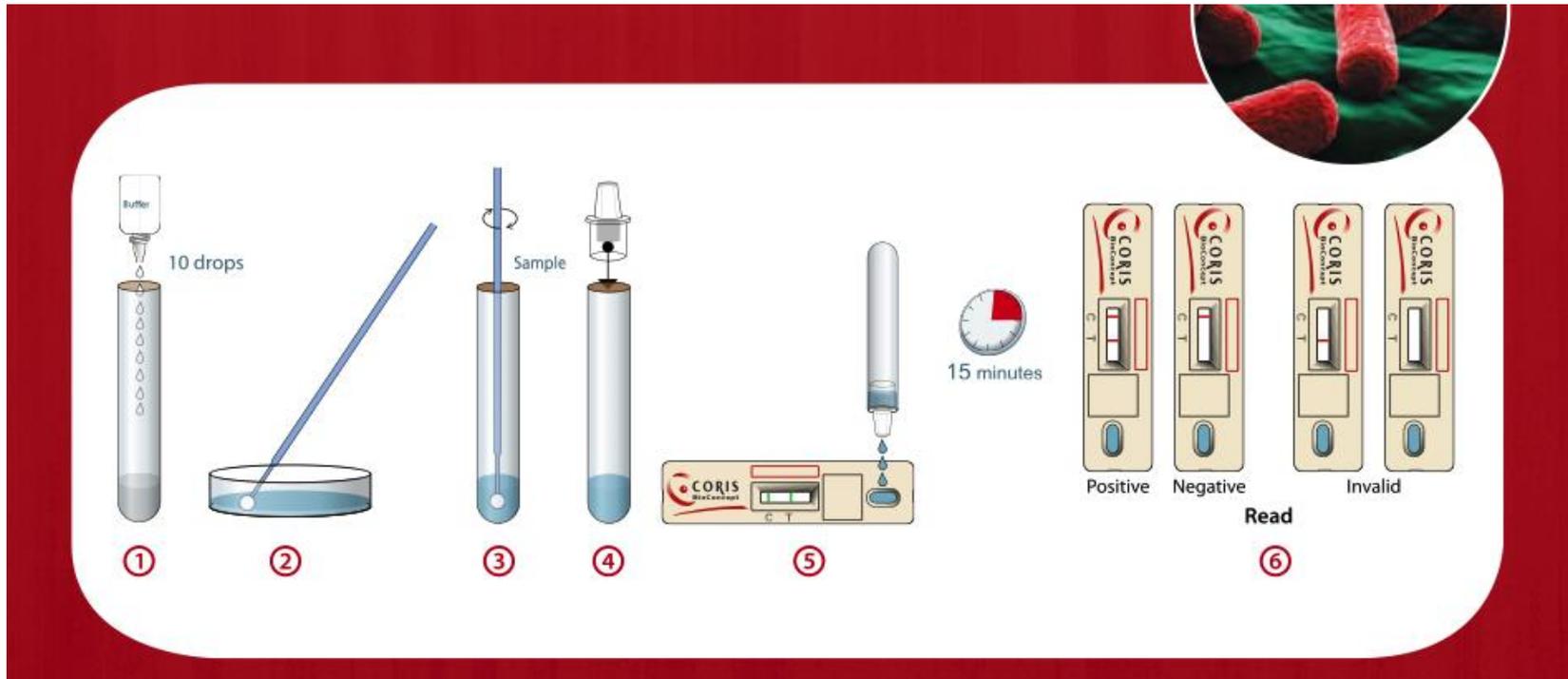
Carbapenemase
Producing
Enterobacteriaceae



Made in Belgium

The image shows a red rectangular graphic with a white curved top edge. At the top left is the RESIST logo, which consists of a red circle with a white vertical bar and a horizontal line through it, followed by the word RESIST in a stylized font with dots between the letters. Below this, the text 'OXA-48 K-SeT' is written in white. Underneath that, the text 'Carbapenemase Producing Enterobacteriaceae' is written in white. In the center is a white circle containing the CORIS BioConcept logo, which features a red swoosh and the text 'CORIS BioConcept'. At the bottom, the text 'Made in Belgium' is written in white, flanked by two sets of three small white dots.

Other New Approaches



Ote Isabelle, et al. Development of a novel immunochromatographic confirmatory test for the detection of OXA-48 carbapenemase in Enterobacteriaceae, ECCMID 4-26-15

<https://www.youtube.com/watch?v=BbiX5-aWQ9w>

Other New Approaches

- Electrochemical Detection of Imipenem Hydrolysis
 - Validation of a new electrochemical assay (BYG Carba test) for the rapid laboratory detection of carbapenemase-producing Enterobacteriaceae
 - P. **B**ogaerts, S. **Y**unus, Y. **G**lupezyndki
National Reference Laboratory for monitoring antimicrobial resistance in Gram-negative bacteria, Belgium ECCMID 4-26-15
- Based on modification of conductivity of sensor Polyaniline which is coated on the electrode which results due to change in pH and redox potential during imipenem hydrolysis
- 324 clinical isolates 178 CPE (KPC, OXA, VIM, NDM)
No False Pos, 9 False Neg. Test result in 30 min.

Revolutionizing Infectious Disease Practice with
**CULTURE-FREE
Microbiology™**



Using fluorescence spectroscopy
the P-1000™ makes CULTURE-FREE Microbiology™ a reality
and establishes a new worldwide standard in infectious
disease practice.

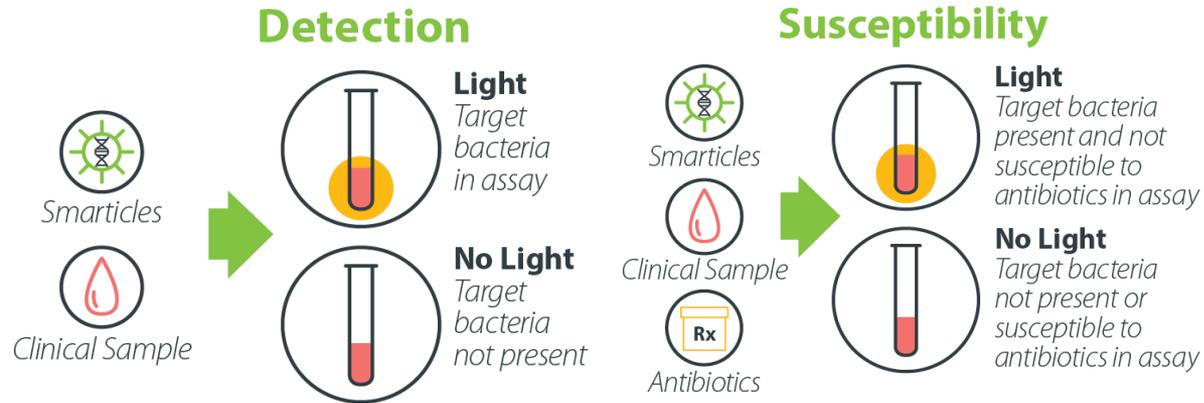
Multi-Source
Bacterial detection, Enumeration, Identification

P-1000™
Designed for quality-Built for performance

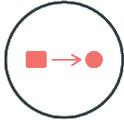
pocared.com

**Ten Minute, Reagent-Free Identification of Bacteria
Containing Resistance Genes Using a Rapid Intrinsic
Fluorescence Method. ASM Poster 548, May 31, 2015**

GeneWEAVE™



For the first time, the speed and simplicity of molecular diagnostics is combined with the antibiotic susceptibility information that is critical for MDRO surveillance and guiding antibiotic therapy.

 Test Applications	 Direct-from-Patient Sample	 Same-Shift	 MDRO Detection and Susceptibility
Surveillance Programs	<i>e.g., nasal swab, rectal swab</i>	≤ 4 hours	MDROs of interest (<i>e.g., MRSA, CRE, FRE</i>)
Guiding Therapy	<i>e.g., urine, +blood culture, wound</i>	≤ 4 hours	Ruling in therapies that will work

MALDI-TOF MS

Matrix Assisted Laser Desorption Ionization- Time of Flight Mass Spectrometry

Method	Sensitivity	Specificity
MALDI-TOF Assay	77%	100%
Carb NP Test	76%	100%
MALDI-TOF BIC Assay	98%	100%

BIC Assay includes addition of 50 mM NH_4HCO_3 to reaction buffer

Both methods experienced problems with subset of 19 isolates producing OXA-48 carbapenemase



Papagiannitsis CC et al.
J Clin Microbiol. 2015 May;53:1731-5.

Why is Carbapenem Resistance a Public Health Problem?

- Significantly limits treatment options for life-threatening infections
- No new drugs for gram-negative bacilli
- Emerging resistance mechanisms, carbapenemases are mobile
- Detection of Carbapenem Producing Organisms (CPO's) and implementation of infection control practices are necessary to limit spread

Alphabet Soup: CRE, CPE, CPO

- **What is the difference between CPO, CPE and CRE?**
 - The differences depend on type of bacteria being included and the mechanisms of resistance to carbapenem antibiotics.
 - **Carbapenem Resistant Enterobacteriaceae (CRE)** refers to bacteria in the family of Enterobacteriaceae (e.g. *E.coli*, *Klebsiella*, etc) that are resistant to carbapenem antibiotics regardless of the method of resistance, as there are a number of different ways.

Alphabet Soup: CRE, CPE, CPO

- **What is the difference between CPO, CPE and CRE?**
 - **Carbapenemase Producing Enterobacteriaceae (CPE)** refers to bacteria in the family of Enterobacteriaceae (e.g. *E.coli*, *Klebsiella*, etc) that are resistant to carbapenem antibiotics by producing an enzyme to break down the carbapenem antibiotics. This is determined by testing for the genes that produce these enzymes, such as KPC and NDM.

Alphabet Soup: CRE, CPE, CPO

- What is the difference between CPO, CPE and CRE?
 - Carbapenemase Producing Organisms (CPO) refers to bacteria in the family of Enterobacteriaceae (e.g. *E.coli*, *Klebsiella*, etc) and those that do not belong to this family such as *Pseudomonas* and *Acinetobacter*, that are resistant to carbapenem antibiotics by producing an enzyme to break down the carbapenem antibiotics. This is determined by testing for the genes that produce these enzymes, such as KPC and NDM.

Alphabet Soup: CRE, CPE, CPO

- **Why are other countries using the term CPO?**
 - Genes for carbapenem resistance can be transferred to bacteria in the Enterobacteriaceae family and to bacteria not within this family
 - The term **CPO** includes the larger group of potentially affected bacteria. This is important for surveillance purposes so that we do not miss any groups of bacteria that may be carrying and spreading these antibiotic resistant genes.
 - **CPO's are what laboratories should be looking for and what Infection Preventionists should be reporting.**

CSTE Definition of CRE

- **The 2012 definition for CRE was:** *E. coli*, *Klebsiella* spp., and *Enterobacter* spp. nonsusceptible to imipenem, meropenem, or doripenem and resistant to all 3rd-generation cephalosporins tested (e.g., ceftriaxone, cefotaxime, ceftazidime) **Ertapenem was excluded.**
- **Proposed 2015 definition for CRE is:** *E. coli*, *Klebsiella* spp., and *Enterobacter* spp. resistant to imipenem, meropenem, doripenem, **or ertapenem** or production of a carbapenemase (eg. KPC, NDM, VIM, OXA-48) demonstrated by a recognized test (e.g. PCR, MBL test, MHT, Carba NP

Problems with CSTE Definition

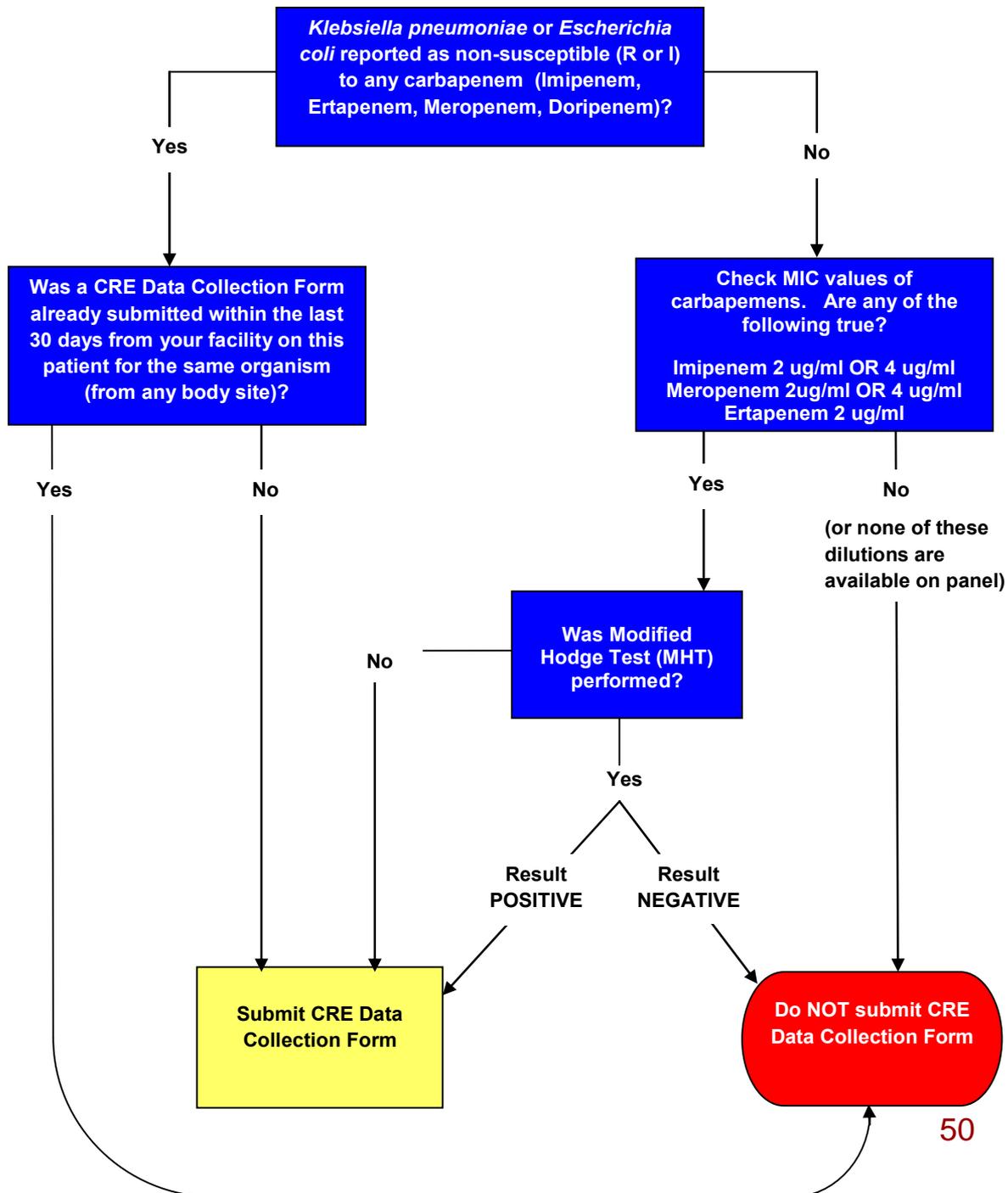
- MYSPACE Bugs (**M**organella, **Y**ersinia, **S**erratia, **P**rovidencia, **A**eromonas, **C**itrobacter, **E**nterobacter, posses chromosomal AmpC beta-lactamase) may test ertapenem non-susceptible if also have porin mutation. These are not CPO's and are not an IC threat.
- At LUMC, 12% of *E. cloacae* test non-susceptible to ertapenem.
- In 2014, **40 patients** would have been called CRE (that were not CPO's) and would have been placed in isolation and reported to XDRO registry

Problems with CSTE Definition

- Imipenem vs. Proteeae (i.e., *Morganella morganii*, *Proteus* spp., *Providencia* spp.)
- MIC₉₀ of imipenem \leq 1 ug/mL for most Enterobacteriaceae, but is 4-8 ug/mL for Proteeae and may test non-susceptible to imipenem using new CLSI/FDA BPs
- Some *P. mirabilis* are more resistant, with imipenem MICs ranging from 16 to 64 ug/mL
- Higher MICs seen with imipenem vs. *P. mirabilis* are **not due to carbapenemases** but rather diminished expression of penicillin-binding protein (PBP) 1a and reduced binding of imipenem by PBP2

Problems with CSTE Definition

- Proteeae that are non-susceptible to imipenem are not CPOs and are not an IC threat.
- At LUMC in 2014, **239 Proteeae** were NS to imipenem (141 *P. mirabilis*, 11 *P. vulgaris*, 17 *Providencia* spp., 70 *Morganella* spp.)
- These patients should not be placed in isolation and should not be reported to the XDRO registry
- *P. aeruginosa* and *Acinetobacter baumannii* have both been reported to have CPO's yet these are not reported using the CSTE definition.



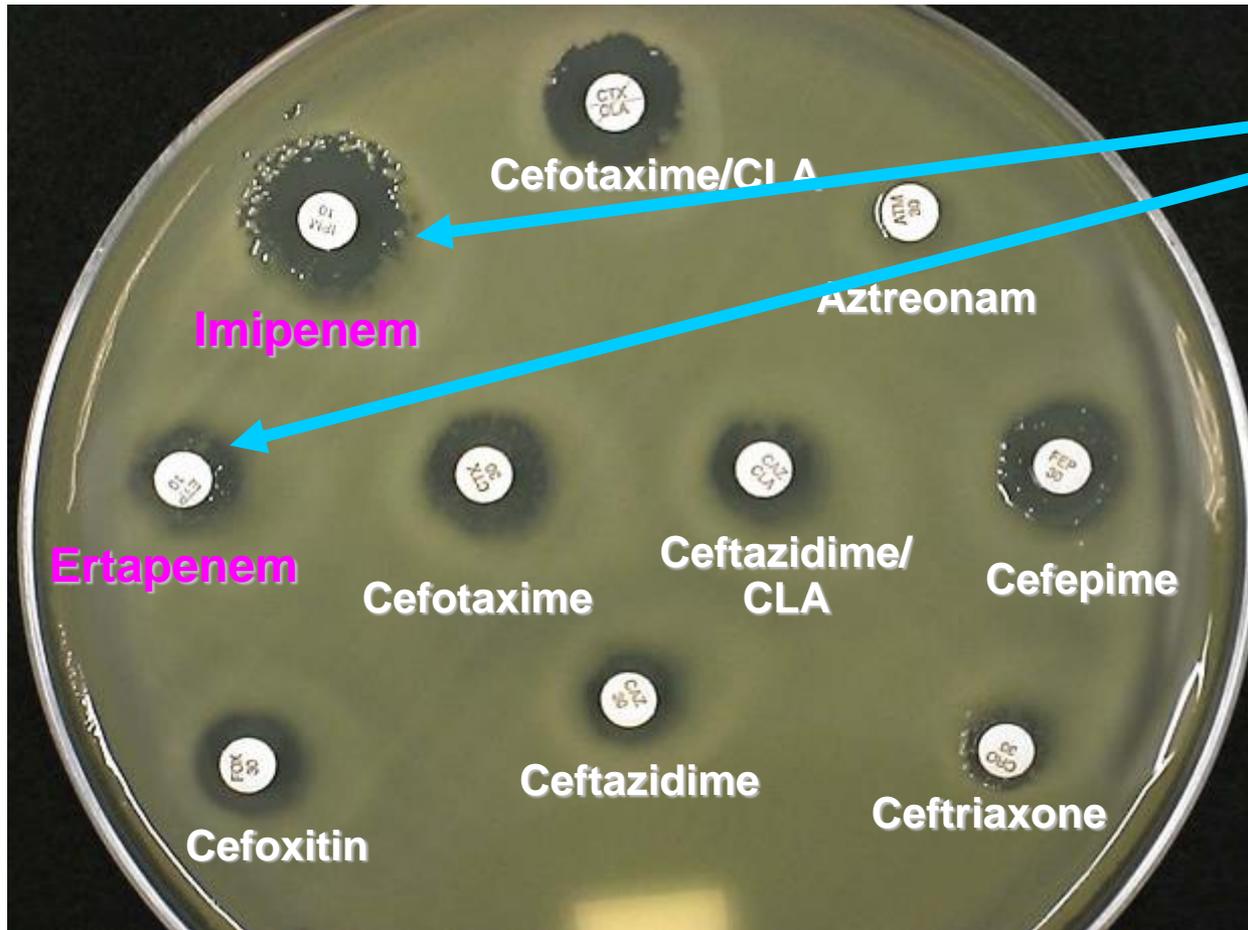
Why labs should continue to perform MHT and EDTA Inhibition Test on isolates that test Non-Susceptible to carbapenems

- Knowing the resistance mechanism is important
- Some require changes in antibiotic reporting, some require infection control notification, some require reporting to State Lab, and some require no action
- Can you tell the difference between them by MIC alone?

Patient History Case 1

- 58 y/o male, morbidly obese (>500 lbs)
- Presented to ER with episode of hypoxia and hypotension during dialysis
- PMH
 - Pt has trach for hypercapnea (COPD and OSA), vent dependent
 - Chronic foley catheter
 - Diabetes mellitus type 2
 - ESRD
- Exam:
 - Afebrile
 - Multiple decubitus ulcers (sacrum, spine, right leg)
 - Urine is grossly dirty
- Concerned that septic => Pan-cultures
 - Urine: *Klebsiella*...

Double Disk Potentiation Method – Case 1

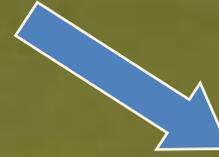


Imipenem - S
Ertapenem - R

Suggests possible KPC which should be confirmed with Hodge test or sent to reference lab for confirmation

**Case 1-MHT
Positive**

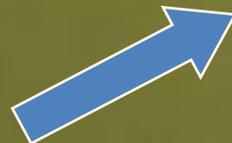
Patient



Positive control



Negative control



And the Answer is

5 Most Common Carbapenemases

Class	Carbapenemases	Enterobacteriaceae	Non-fermenters
A ¹	KPC ²	+++	+
B (metallo)	NDM ³ , IMP, VIM,	+++	+++
D	OXA-48-like	+++	+/-

¹also includes SME; ²most common in USA; ³increasing in USA

....but several types within 5 groups and other types of carbapenemases

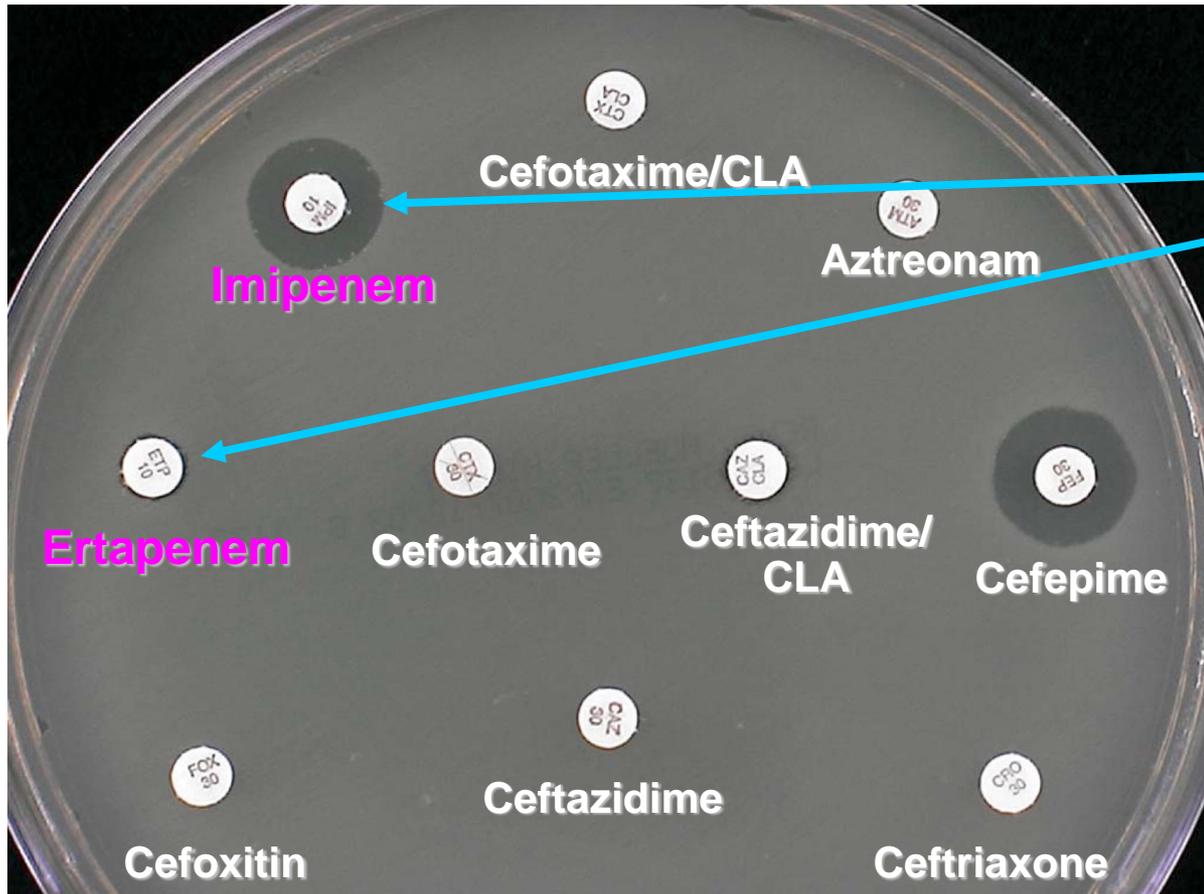
(slide courtesy Janet Hindler)

Patient Report Case 1

- If using former CLSI/FDA breakpoints change all carbapenems to resistant
- If using new CLSI/FDA breakpoints report interpretations as tested
- Add following statement to report:
“Carbapenem resistant *Enterobacteriaceae* (CRE) detected by Modified Hodge Test – probable KPC type. Implement infection control measures according to facility policy.”
- Submit CRE Data Collection Form

Double Disk Potentiation Method – Case 2

Blood Culture with *Enterobacter cloacae*



Imipenem - S
Ertapenem - R

Suggests possible KPC which should be confirmed with Hodge test or sent to reference lab for confirmation

Case 2-MHT = Neg

**Positive
control**



Patient

And the Answer is

And the Answer is

Chromosomal AmpC_ (Derepressed mutant)_ + Porin mutation

Patient Report Case 2

- Susceptibility pattern in Case 2 is identical to susceptibility pattern in Case 1, except in Case 2 we have a chromosomal AmpC that is not MDRO, is not an infection control risk, and does not require modification of susceptibility report.
- Add following statement to report:
“This organism is known to possess an inducible β -lactamase. Isolates may become resistant to all cephalosporins after initiation of therapy. Avoid β -lactam-inhibitor drugs”
- **DO NOT Submit CRE Data Collection Form**

CDC Lab Training Resources

- 5 e-learning courses in the basic curriculum—direct link: http://www.cdc.gov/labtraining/basic_courses.html
- Curriculum on antimicrobial susceptibility testing called MASTER – 3 e-learning courses offered: http://www.cdc.gov/labtraining/master_courses.html
- E-learning course on Packaging and Shipping Division 6.2 Materials. Relevant for facilities who need to send specimens to other labs for testing. Individuals who pass this course are eligible to be certified to pack and ship by their employer. http://www.cdc.gov/labtraining/course_listing/1043824.html