



# Identification of CRE Using Techniques That Every Laboratory Can Perform

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Type of Affiliation/Financial Interest	Name of Commercial Interest
Salaried Employee	Loyola University Medical Center
Stocks/Stock Options (Does not include Mutual Funds)	None
Independent contractor/Speaker's Bureau	bioMerieux, Cubist, Forest Laboratories, Hardy Diagnostics, Merck, Remel, Siemens
Consultant/Advisory Committees	Abbott Molecular, BioFire, Forest Laboratories, Thermo Fisher Scientific, Quidel
Research Grants	Abbott Molecular, Becton-Dickinson, BioFire, bioMerieux, Cepheid, Siemens

# Why labs should continue to perform Modified Hodge Test and EDTA Inhibition Test on isolates that test non-susceptible to carbapenems

- Knowing the resistance mechanism is important
- The following cases demonstrate different mechanisms of carbapenem resistance. Some require changes in antibiotic reporting, some require infection control notification and some require no action
- Can you tell the difference between them by MIC alone?

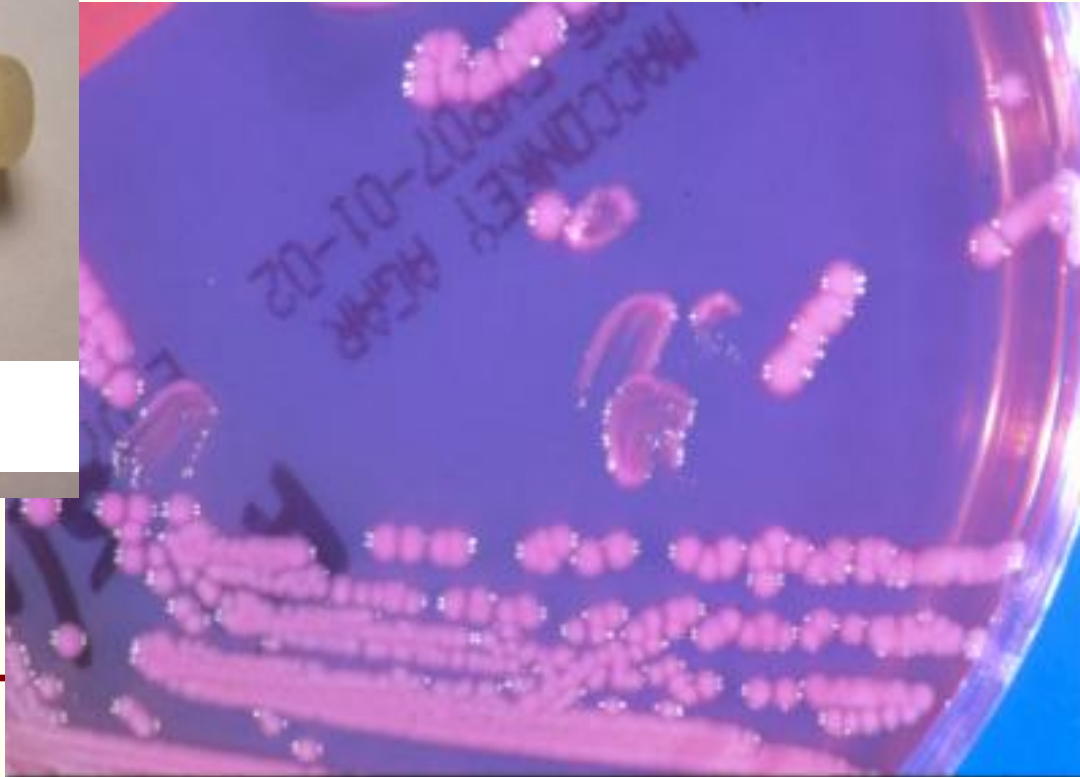
# Patient History Case 1

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- 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), currently vent dependent
  - ◆ Chronic foley catheter
  - ◆ Diabetes mellitus type 2
  - ◆ ESRD
- Exam:
  - ◆ Afebrile
  - ◆ Multiple decubitus ulcers (sacrum, spine, right leg)
  - ◆ Urine is grossly dirty

# Patient History

- Concerned that septic => Pan-cultures
  - ◆ Urine: *Klebsiella*...



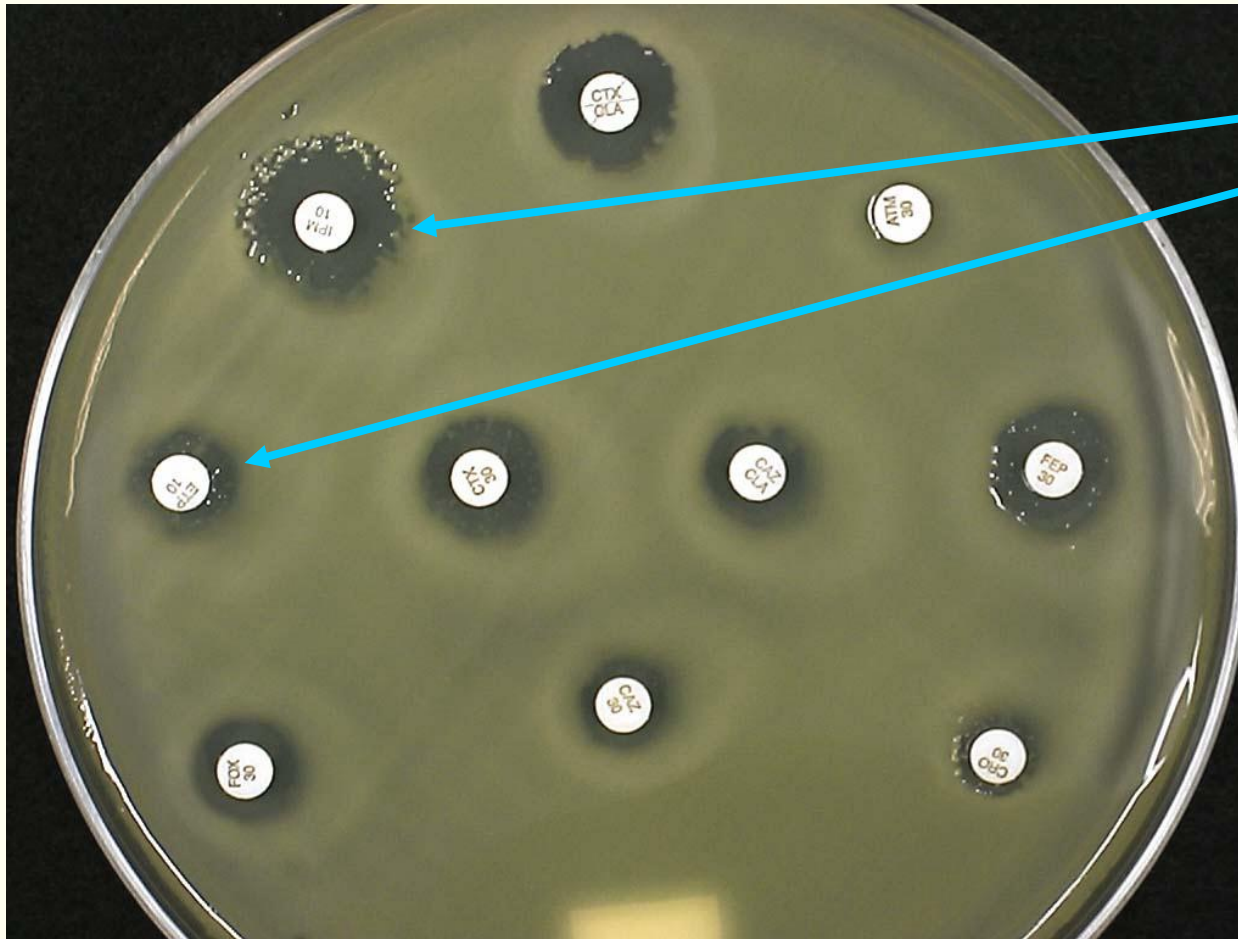
Vitek ID: [REDACTED] Oxidase -  
Type: Gram Negative General Susceptibility 143 (GNS-143)  
Status: Final  
Elapsed Time: 13 hours  
Organism: *Klebsiella pneumoniae*  
Source: Manual  
Demographics: [REDACTED]

	MIC	Instrument	Expert
Ampicillin	>=32	R	
Ampicillin/Sulbactam	>=32	R	
Piperacillin/Tazobactam	>=128	R	
Cefazolin	>=32	R	
Ceftriaxone	>=64	R	
Ceftazidime	>=32	R	
Cefepime	8	S	
Aztrennam	>=32	R	
Imipenem	<=4	S	
Gentamicin	4	S	
Tobramycin	>=16	R	
Ciprofloxacin	>=4	R	
Levofloxacin	>=8	R	
Trimeth-sulfa	>=320	R	
Nitrofurantoin	64	I	
ESBL		Negative	

MIC values in mcg/ml ( M1 ) Wait for All  
The presence of other Beta-lactamases (e.g. AmpC, IRT) may mask ESBL production.



# 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



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And the Answer is .....

# Carbapenemases in the U.S.

Molecular Class	Carbapenemase	Found in:
A	KPC	<i>K. pneumoniae</i> and other Enterobacteriaceae
	SME	<i>S. marcescens</i>
	also IMI, NMCA, GES	Enterobacteriaceae
B	Metallo beta-lactamases (IMP, VIM, GIM, SPM, NDM-1)	<i>P. aeruginosa</i> , <i>Enterobacteriaceae</i> , <i>Acinetobacter</i> , <i>S. maltophilia</i>
D	OXA	<i>Acinetobacter baumannii</i> , <i>Enterobacteriaceae</i>

Adapted from Queenan & Bush. 2007. Clin Microbiol Rev. 20:440.

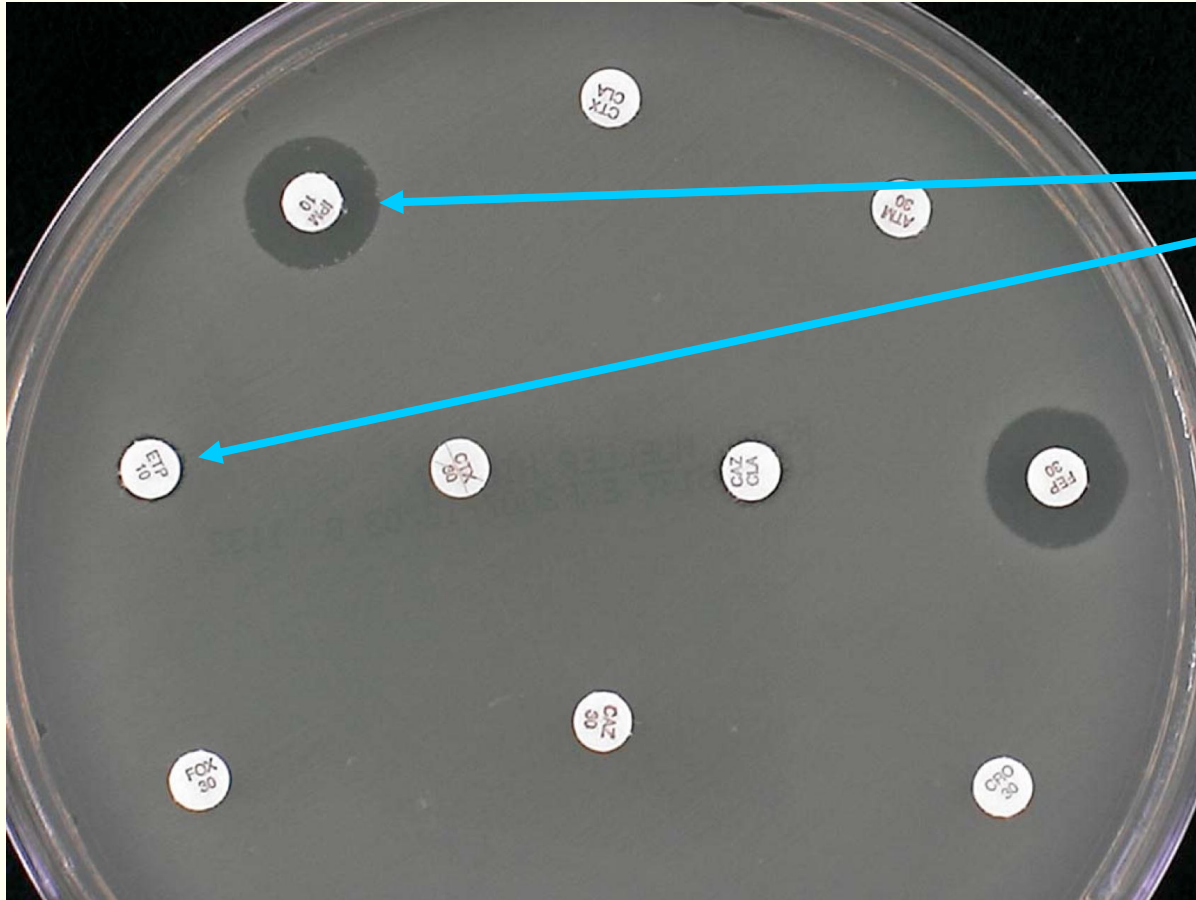
# Patient Report Case 1

If using FDA breakpoints change all carbapenems to resistant and add following statement to report:

“Multiple drug resistant organism, KPC identified. Treatment with any beta lactam drug including carbapenems is not reliable, Patient requires contact isolation.”

# 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

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And the Answer is .....

Chromosomal AmpC\_(Derepressed mutant)\_ + Porin mutation



# Patient Report Case 2

Note the susceptibility pattern in Case 2 is identical to susceptibility pattern seen in Case 1, except in this case we have a chromosomal AmpC that is not MDRO, is not an infection control risk, and does not require modification of the susceptibility report. The following comment is added to our patient report:

“This organism is known to possess an inducible  $\beta$ -lactamase. Isolates may become resistant to all cephalosporins after initiation of therapy. Avoid  $\beta$ -lactam-inhibitor drugs”

# Case 3 #227-1 (9-27-10)

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- 88 Y.O. female, bed ridden with Alzheimer's
- Urinary incontinence for >10 years
- Foley cath for 1 year
- Gastrostomy tube since 2001
- Admitted for gastrostomy tube replacement
- Patient pulled out foley catheter
- PMH UTI including MRSA
- Urine culture grew >100,000 *Serratia marcescens*

# MicroScan Report – Case 3

## Panel Data

Biotype: 70405346  
Organism: *S. marcescens*

Biochemical Results: (Biochemicals that are bolded and underlined are atypical for the stored organism)

GLU + RAF - INO + URE - LYS + TDA - CIT + CL4 + ACE - K4 - P4 +  
SUC + RHA - ADO - H2S - ARG - ESC + MAL - CF8 + CET - NIT - TAR -  
SOR + ARA - MEL - IND - ORN + VP + ONPG - OXI - FD64 + OF/G + TO4 -

MIC Results: (Antimicrobics marked with "Ø" are suppressed from Long and Short Format Patient Reports)

AM	A/S	P/T	CFZ	CAX	CAZ	CPE	MER	GM	Ø TE	TO	CP	T/S	FD	Ø AK
>16	>16/8	<=16	>16	<=8	<=1	<=4	<=1	<=4	8	<=4	<=1	<=2/38	>64	<=16
R	R	S	R	S	S	S		S	I	S	S	S	R	S
CAZ/CA	CFT	CFT/CA	ETP	Ø IMP	Ø AUG	Ø CRM	Ø LVX	Ø MXF	Ø TIM					
<=0.25	<=2	4	<=2	4 = R	>16/8	>16	<=2	<=2	<=16					
	S		S	S	R	R	S		S					

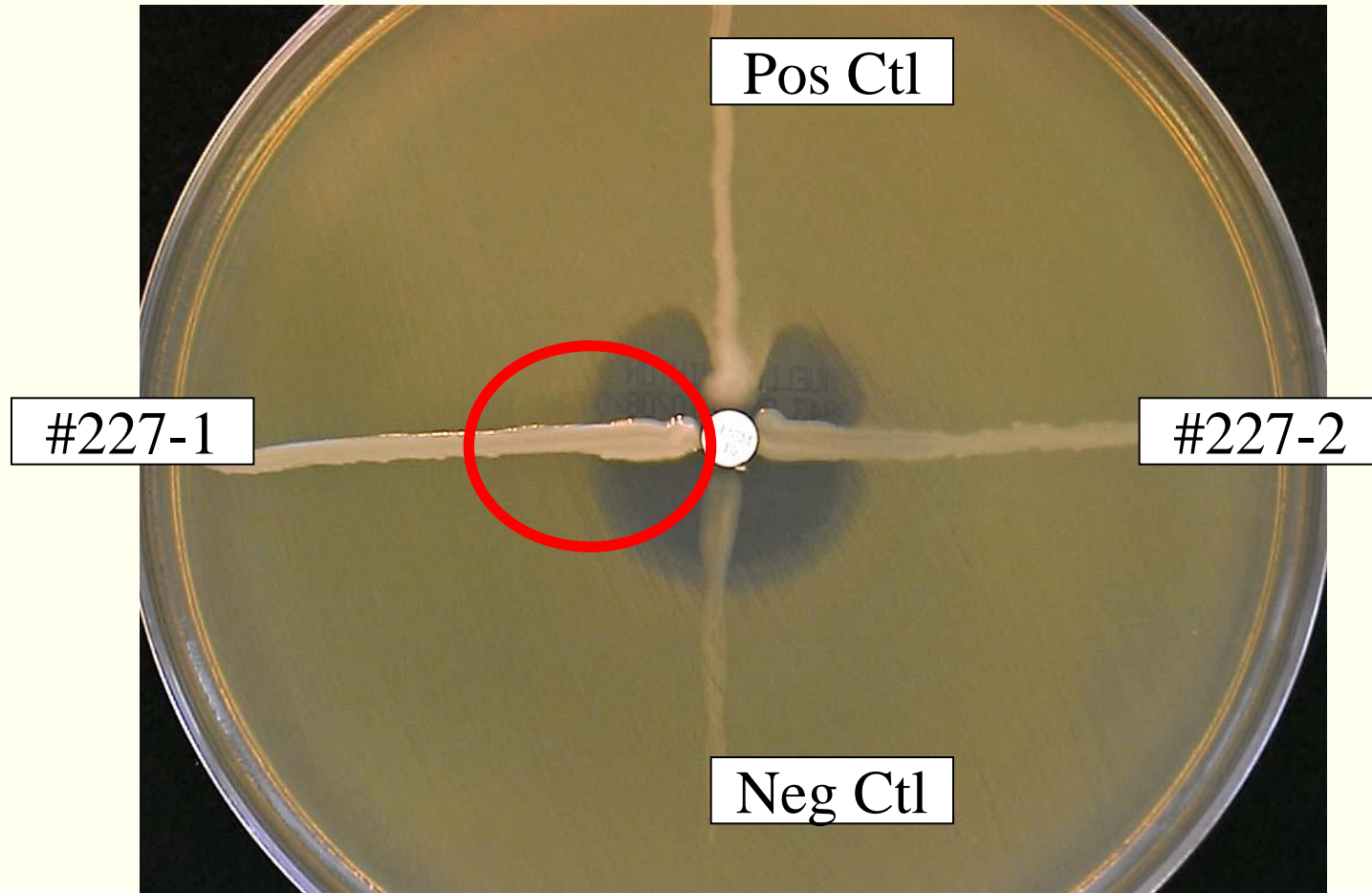
Extra Tests: ESBL ...

# Case 3 – 12 Disk



# Case 3 #227-1

## Modified Hodge Test



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And the Answer is .....



# Carbapenemases in the U.S.

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A	KPC	<i>K. pneumoniae</i> and other Enterobacteriaceae
	SME	<i>S. marcescens</i>
	also IMI, NMCA, GES	Enterobacteriaceae
B	Metallo beta-lactamases (IMP, VIM, GIM, SPM, NDM-1)	<i>P. aeruginosa</i> , <i>Enterobacteriaceae</i> , <i>Acinetobacter</i> , <i>S. maltophilia</i>
D	OXA	<i>Acinetobacter baumannii</i> , <i>Enterobacteriaceae</i>

Adapted from Queenan & Bush. 2007. Clin Microbiol Rev. 20:440.

Specimen: Urine

Diagnosis: UTI

## Case 3 Final report

*Serratia marcescens*

### MIC (µg/ml)

amikacin	1 S
ampicillin	>32 R
cefazolin	>32 R
ceftriaxone	≤0.5 S
ciprofloxacin	≤0.25 S
gentamicin	≤0.5 S
imipenem	>16 R
piper-tazobactam	≤8 S
tobramycin	1 S
trimeth-sulfa	≤1/19 S

### **Report comment:**

“Imipenem-R is due to carbapenemase production (but not KPC). The effectiveness of other β-lactams (that test “S”) in treating infections due to carbapenemase-producing *S. marcescens* has not been established. Infectious Disease consult suggested.”

## Case 5. (5-12-10)

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- Patient is a 40 Y.O. male paraplegic who traveled to New Dehli India for a surgical procedure. 3-4 months after returning to the U.S. patient presents to outpatient center in Chicago with multiple decubitus ulcers and urinary tract infection. Urine collected from foley cath is submitted for culture.

# MicroScan Report – Case 5

## Panel Data

Biotype: 73115012

### Organism Identification:

Organism	% Probability	Footnotes	Special Characteristics
1 E. coli	99.99		

Biochemical Results: (Biochemicals that are bolded and underlined are atypical for the first choice organism)

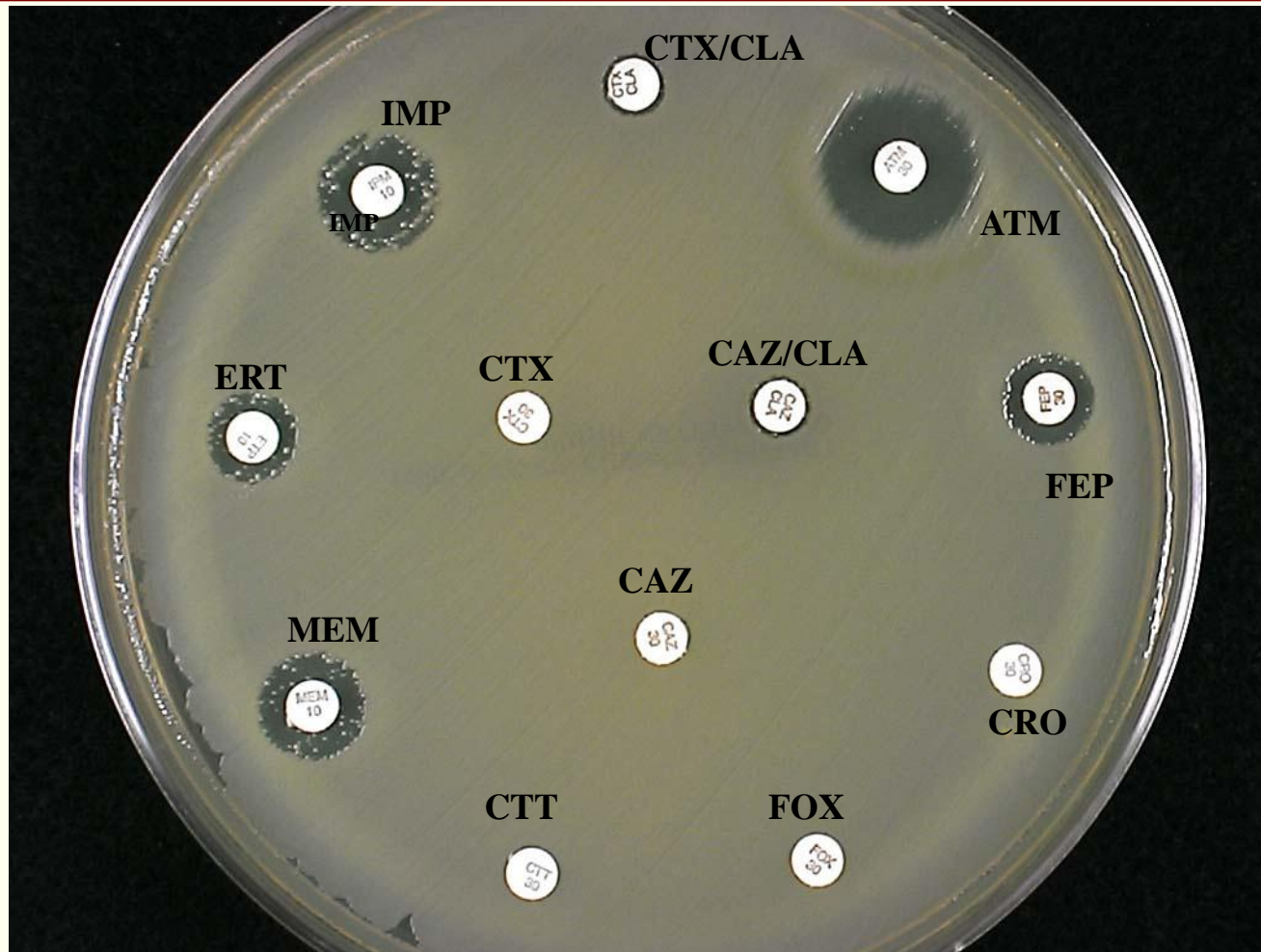
GLU + RAF - INO - URE - LYS + TDA - CIT - CL4 - ACE - K4 + P4 +  
 SUC + RHA + ADO - H2S - ARG - ESC - MAL - CF8 + CET - NIT + TAR -  
 SOR + ARA + MEL + IND + ORN + VP - ONPG + OXI FD64 - OF/G + TO4 +

MIC Results: (Antimicrobics marked with "Ø" are suppressed from Long and Short Format Patient Reports)

AM	A/S	P/T	CFZ	CAX	CAZ	CPE	<b>MER</b>	GM	Ø TE	TO	CP	T/S	Ø FD	AK
>16	>16/8	>64	>16	>32	>16	>16	>8	>8	>8	>8	>4	>2/38	<=32	>32
R	R	R	R	R	R	R	R	R	R	R	R	R		R
CAZ/CA	CFT	CFT/CA	ETP	IMP	Ø AUG	Ø CRM	Ø LVX	Ø MXF	Ø TIM					
>2	>32	>4	>4	4	>16/8	>16	>4	>4	>64					
	R		R	S	R	R	R	R	R					

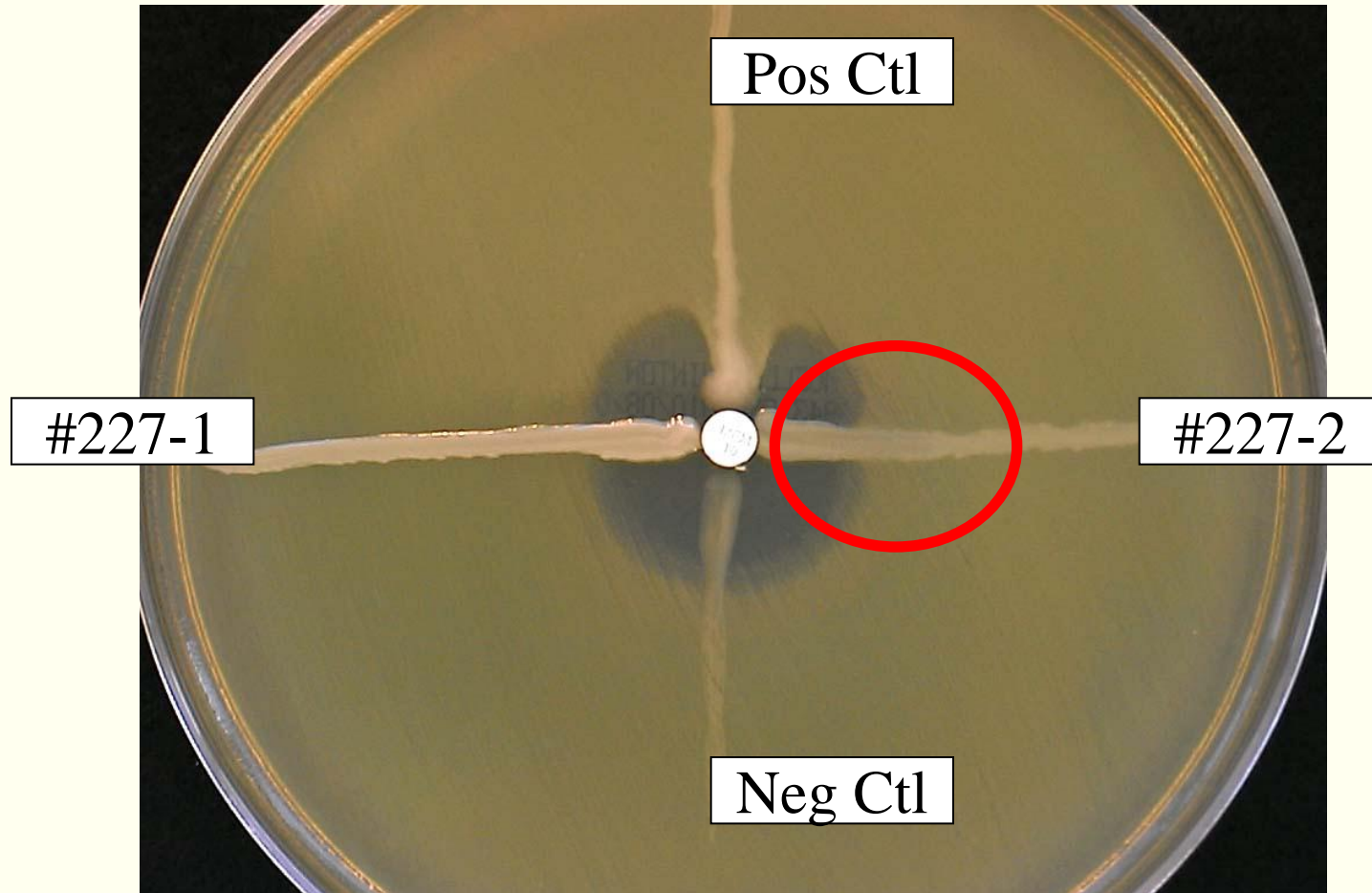
Extra Tests: ESBL -

# Case 5. 12 Disk



# Case 5 #227-2

## Modified Hodge Test





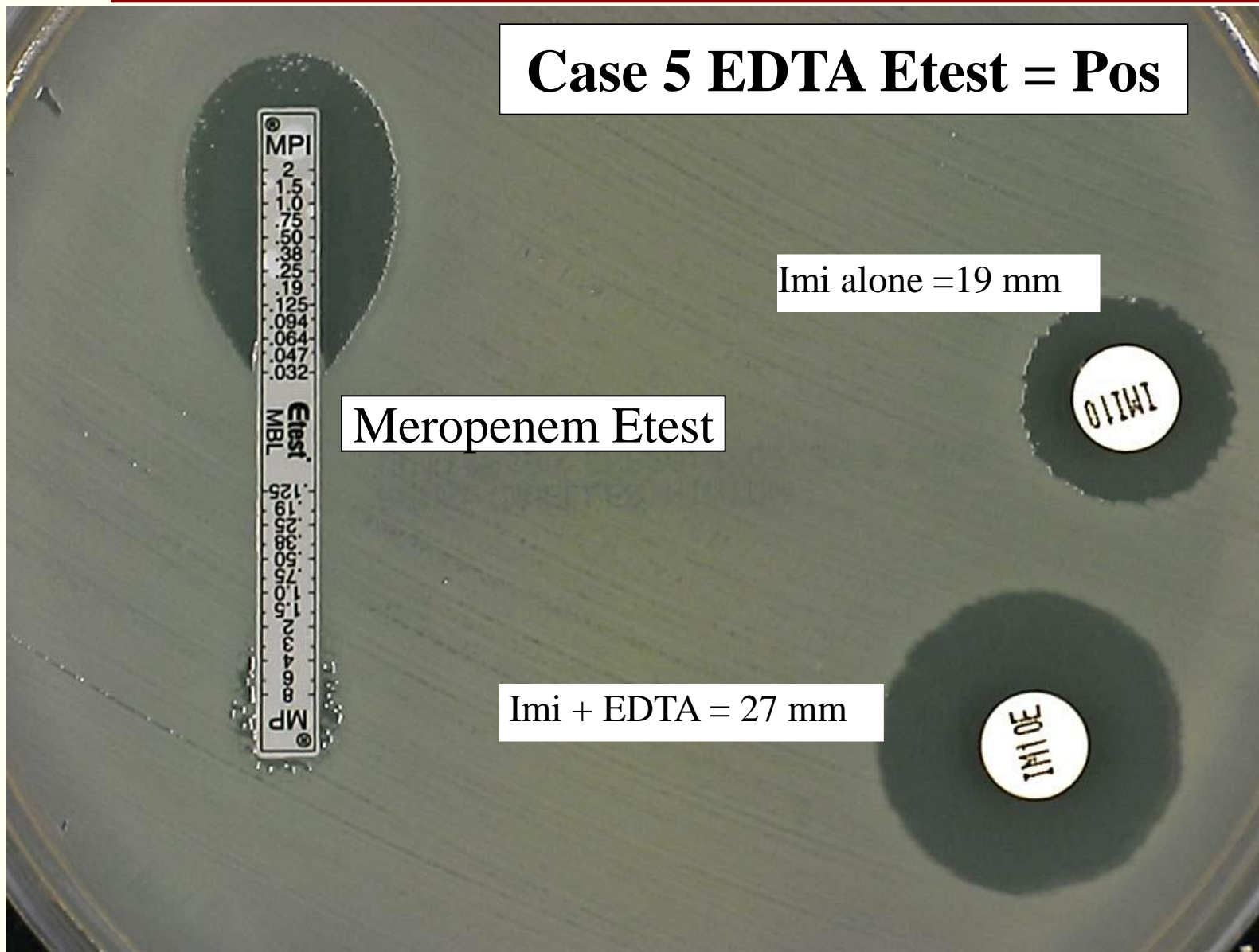
# Rosco Diagnostica IMI/EDTA Disks (Available from Key Scientific)

**Case 5 EDTA Etest = Pos**

Imi alone = 19 mm

Meropenem Etest

Imi + EDTA = 27 mm



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D	OXA	<i>Acinetobacter baumannii</i> , <i>Enterobacteriaceae</i>

Adapted from Queenan & Bush. 2007. Clin Microbiol Rev. 20:440.

# Patient Report Case 5

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- If using FDA breakpoints change all carbapenems to resistant and add following statement to report:
- “Multiple drug resistant organism, NDM-1 identified. Treatment with any beta lactam drug including carbapenems is not reliable, Patient requires contact isolation.”

# Recommendations

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- Apply new (lower) breakpoints to clinical isolates as soon as testing capability becomes available
- Perform Hodge Test and MBL Etest on all Enterobacteriaceae with carbapenem MIC > 1 mg/ml (except Proteus, Providencia and Morganella)
- If not using new breakpoints, Report MIC and Change AST result to I or R when resistant mechanism detected
- Report Resistant mechanism to clinicians and infection control practitioners