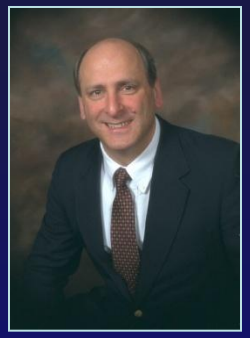
Laboratory Detection and Reporting of CRE

June 6, 2014

Illinois Department of PUBLIC HEALTH

Featured Presenters



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Illinois Department of Public Health,
Division of Patient Safety and Quality

June 6, 2014

Laboratory Detection and Reporting of CRE

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Learning Objectives

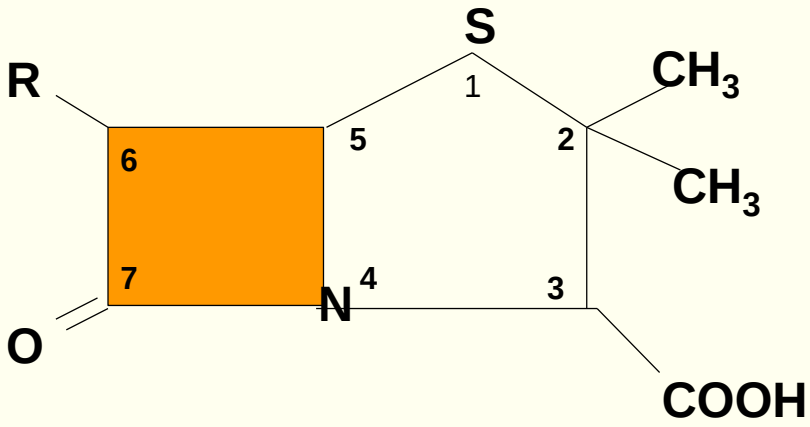
At the conclusion of this Session, participants will be able to:

1. Describe mechanisms of carbapenem resistance
2. List criteria to be used for screening laboratory isolates for CRE
3. Describe the procedure, interpretation and application of the Hodge Test and MBL Etest.
4. List the pitfalls of susceptibility testing for the detection of CRE
5. Prepare appropriate comments for reporting CRE

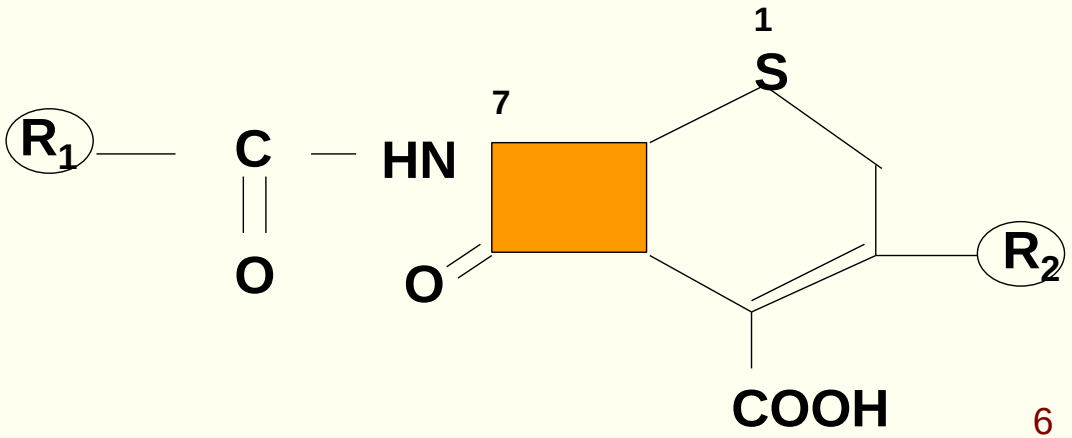
Financial Disclosures

Type of Affiliation/Financial Interest	Name of Commercial Interest
Salaried Employee	Loyola University Medical Center
Stocks/Stock Options	None
Independent contractor/Speaker's Bureau	bioMerieux, Cubist, Forest Laboratories, Hardy Diagnostics, Merck, Remel, Siemens
Consultant/Advisory Committees	Abbott Molecular, BioFire, Forest Laboratories, Quidel, Thermo Fisher Scientific, Theravance
Research Grants	Abbott Molecular, Becton-Dickinson, BioFire, bioMerieux, Cepheid, Siemens

Penicillin nucleus



Cephalosporin nucleus



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The β-lactam family of antibiotics

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

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MODE OF ACTION OF BETA LACTAMS IN GRAM NEGATIVES

SUSCEPTIBLE	RESISTANT
β-Lactam Antibiotic	
↓	
Diffusion through	← Porin Blocks Entry
Outer Membrane	← Efflux Pump
↓	
Diffusion through	← Beta-Lactamase
Peptidoglycan	Hydolyzes Beta-Lactam
↓	
Penicillin Binding Proteins	← Changes in PBP results in Failure to Bind to β-Lactam
↓	
Cell Death	

The β-lactam family of antibiotics

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Ampicillin	Cefuroxime 2nd	Cefmetazole	Ertapenem	
Carbenicillin	Cefotaxime 3rd		Doripenem	
Mezlocillin	Ceftazidime 3rd			
Ticarcillin	Ceftriaxone 3rd			
	Cefepime 4th			

ESBLs hydrolyze all

Penicillins
Cephalosporins
Monobactams

The β-lactam family of antibiotics

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Mezlocillin	Ceftazidime 3rd			
Ticarcillin	Ceftriaxone 3rd			
	Cefepime 4th			

ampCs hydrolyze all

Penicillins

Cephalosporins except 4th generation (cefepime)

Cephamycins

Monobactams

The β-lactam family of antibiotics

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Mezlocillin	Ceftazidime 3rd			
Ticarcillin	Ceftriaxone 3rd			
	Cefepime 4th			

Metallo BL hydrolyze all

Penicillins
Cephalosporins
Cephamycins
Carbapenems

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The β-lactam family of antibiotics

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Mezlocillin	Ceftazidime 3rd			
Ticarcillin	Ceftriaxone 3rd			
	Cefepime 4th			

KPCs hydrolyze all

Penicillins
Cephalosporins
Cephamycins
Carbapenems
Monobactams

Carbapenems

- By way of review the following antibiotics are classified as carbapenems
  - Ertapenem
  - Doripenem
  - Imipenem
  - Meropenem

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 b-lactam drugs
- These isolates are clearly MDR and infection control measures are recommended. Healthcare institutions may reserve more aggressive measures for carbapenemase-producing isolates

Carbapenemases in the U.S.

Molecular Class	Carbapenemase	Found in:	Some Key Features
A	KPC	*K. pneumoniae* and other Enterobacteriaceae	Some are chromosomal (NmcA, Sme, IMI-1, SFC-1) others are plasmid encoded (KPC, IMI-2, GES). All hydrolyze carbapenems and are partially inhibited by clavulanic acid
	SME	*S. marcescens*	
	also IMI, NMCA, GES	Enterobacteriaceae	
B	Metallo beta-lactamases (IMP, VIM, GIM, SPM, NDM-1)	*S. maltophilia* *P. aeruginosa,* Enterobacteriaceae, *Acinetobacter,*	Hydrolyze all ß-lactams except aztreonam. Activity inhibited by EDTA but not by clavulanic acid
D	OXA	*Acinetobacter baumannii,* Enterobacteriaceae	OXA-48 first reported in Turkey in 2003. Not inhibited by EDTA or clavulanic acid

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

When to Suspect a Carbapenemase

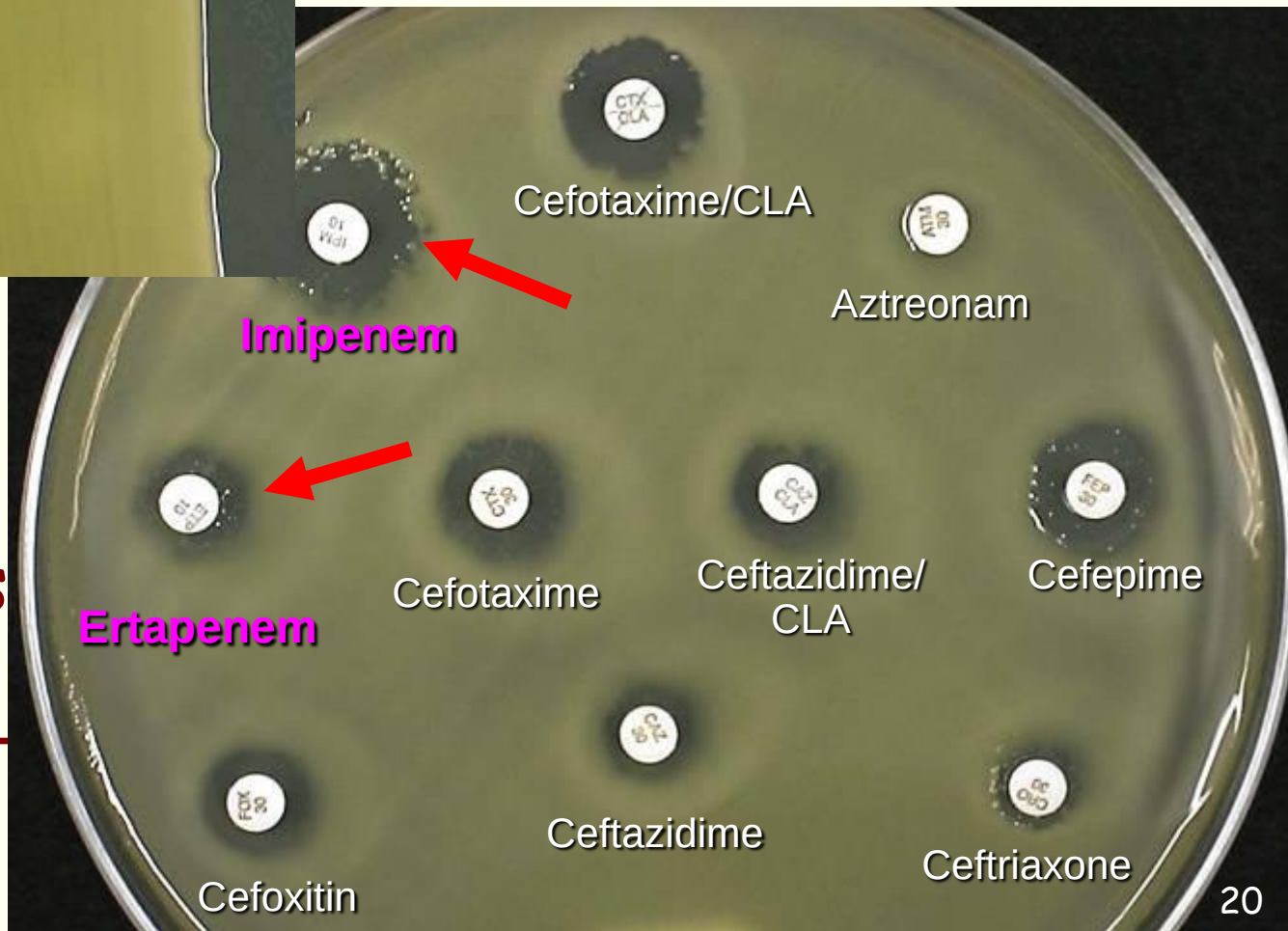
- Enterobacteriaceae – especially K. pneumoniae that are resistant to extended-spectrum cephalosporins:
  - Carbapenemase-producing Enterobacteriaceae test resistant to extended-spectrum cephalosporins
  - KPC producers show variable susceptibility to cefotetan, cefoxitin, and cefepime
  - Metallo-β-lactamas producers show variable susceptibility to aztreonam

Strategy for Laboratory Detection of Carbapenemases

- CLSI Screening Criteria for KPCs (M100-S-19 Jan 2009)
  - Disk zone of < 22 mm for ertapenem or meropenem
  - MIC of >1 μg/ml for imipenem, ertapenem or meropenem
- CLSI Confirmatory Test (M100-S19, Jan 2009)
  - Modified Hodge Test
- 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

Imipenem disk showing susceptible zone but many break-through colonies

Ertapenem Etest showing many break-through colonies



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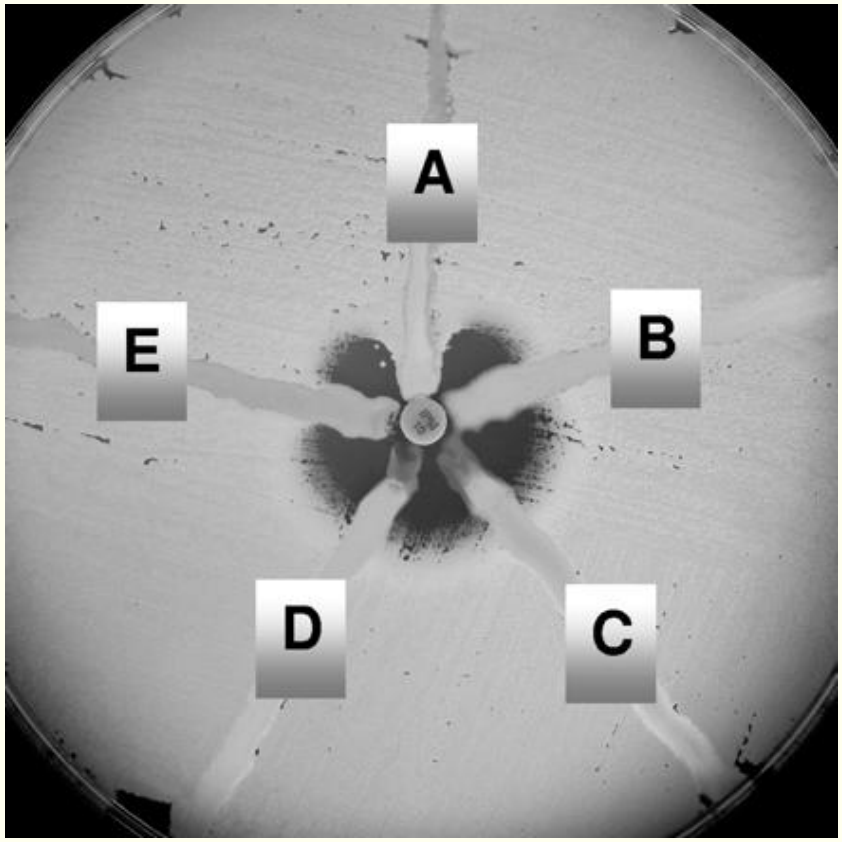
Modified Hodge Test



- 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-µg 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.

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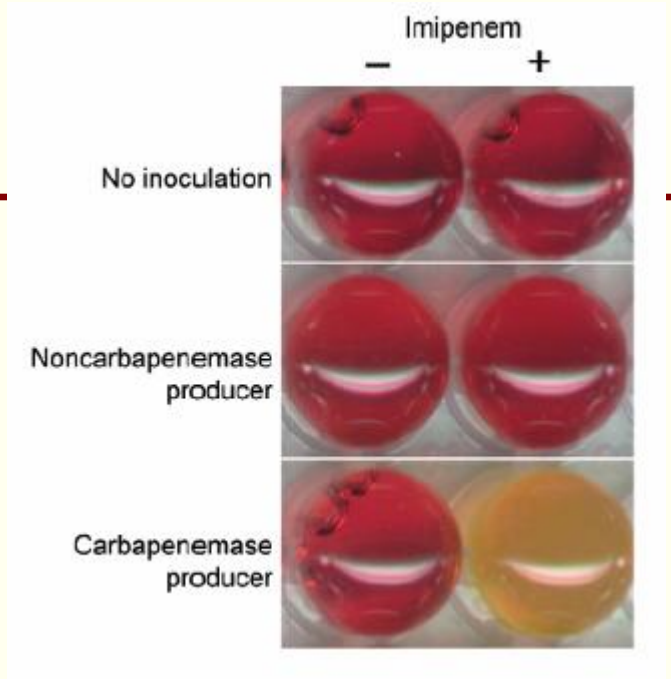
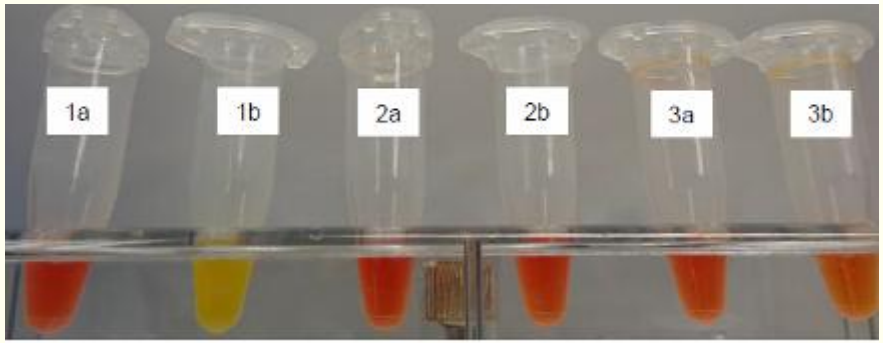
Carba NP Test for Carbapenemase Production



- Isolated colonies (lyse / centrifuge)
- Hydrolysis of imipenem
- Detected by change in pH of indicator (red to yellow/orange)
- Rapid <3h
- Microdilution plate or microtube method



Nordmann et al. 2012. Emerg Infect Dis. 18:1503.
Tijet et al. 2013. Antimicrob Agent Chemo. 57:4578.
Vasoo et al. 2013. J Clin Microbiol. 51:3092.

"a" tubes – Solution A
"b" tubes Solution A + imipenem

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(slide courtesy Janet Hindler

EPI-CRE®

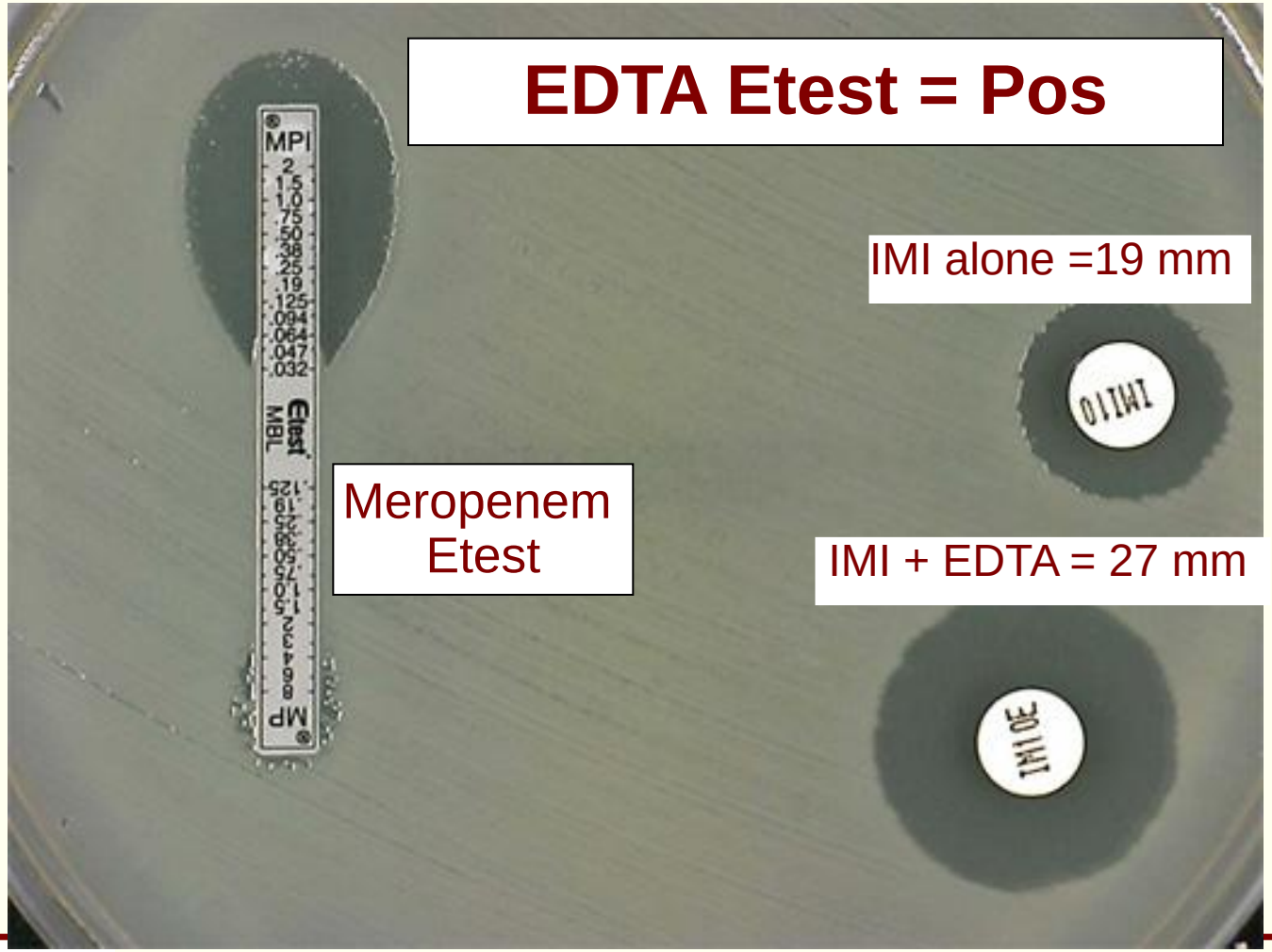
Enterobacteriaceae (CRE)

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.

Rosco Diagnostica IMI/EDTA Disks MBL Etest bioMerieux



KPC - Questions

- If I have detected KPC-production, should I change susceptible carbapenem results to resistant?
  - If using old CLSI carbapenem breakpoints:
    - Isolates that are MHT positive and have an ertapenem MIC of 2-4 ug/mL, imipenem MIC of 2-8 ug/mL, or meropenem MIC of 2-8 ug/mL, Report carbapenems as resistant
  - If using new CLSI carbapenem breakpoints
    - Report MIC, interpret with new breakpoints

(CLSI Jan 2011 M100-S21, p. 55)

Enterobacteriaceae - Revised Carbapenem Breakpoints (MIC μg.ml)

Agent	CLSI M100-S19 (2009)			CLSI M100-S20-U (2010) Supplement		
	Susc	Int	Res	Susc	Int	Res
Doripenem	-	-	-	≤1	2	≥4
Ertapenem*	≤2	4	≥8	≤0.5	1	≥2
Imipenem	≤4	8	≥16	≤1	2	≥4
Meropenem	≤4	8	≥16	≤1	2	≥4

Special CLSI M100-S20-U Supplement published June 2010 with Enterobacteriaceae Tables with these new breakpoints

* Ertapenem BP revised in CLSI document M100-S22 Jan 2012

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CLSI M100-S20-U. Table 2A

Enterobacteriaceae - Revised Carbapenem Breakpoints (disk mm)

Agent	CLSI M100-S19 (2009)			CLSI M100-S20 (2010)		
	Susc	Int	Res	Susc	Int	Res
Doripenem	-	-	-	≥ 23	20-22	≤19
Ertapenem*	≥ 19	16-18	≤15	≥ 22	19-21	≤18
Imipenem	≥ 16	14-15	≤13	≥ 23	20-22	≤19
Meropenem	≥ 16	14-15	≤13	≥ 23	20-22	≤19

Special CLSI M100-S20-U Supplement published June 2010 with Enterobacteriaceae Tables with these new breakpoints

* Ertapenem BP revised in CLSI document M100-S22 Jan 2012

CLSI M100-S20-U. Table 2A

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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 Resistant Enterobacteriacea (CRE) and implementation of infection control practices are necessary to limit spread

CDC Definition of CRE (Carbapenem Resistant Enterobacteriaceae)

- Enterobacteriaceae that are:
  - **Nonsusceptible** to one of the following carbapenems: doripenem, meropenem, or imipenem AND
  - **Resistant** to all of the following 3rd-generation cephalosporins that were tested: **ceftriaxone, cefotaxime, and ceftazidime**. (Note: All three of these antimicrobials are recommended as part of the primary or secondary susceptibility panels for Enterobacteriaceae)

http://www.cdc.gov/hai/organisms/cre/

CDC Definition of CRE

- *Klebsiella spp.* and *E. coli* that meet the CRE definition are a priority for detection and containment in all settings; however, other *Enterobacteriaceae* (e.g., *Enterobacter* species) might also be important in some regions.
- For bacteria that have intrinsic imipenem nonsusceptibility (i.e., *Morganella morganii, Proteus* spp., *Providencia* spp.), requiring nonsusceptibility to carbapenems other than imipenem as part of the definition might increase specificity.

http://www.cdc.gov/hai/organisms/cre/

Imipenem vs. Proteeae

- MIC_{90}S of imipenem are ≤ 1 ug/mL for most Enterobacteriaceae, but are 4-8 ug/mL for Proteeae and therefore may test non-susceptible to imipenem using the new CLSI/FDA breakpoints
- 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
- Meropenem, doripenem and ertapenem are not affected and will test in susceptible range in absence of a carbapenemase (eg. KPC)

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Villar HE et al JAC 1997, 40:365-370
Neuwirth C, et al. 1995, 36:335-342

Imipenem Disclaimers

- FDA Indications for imipenem: *Acinetobacter* spp., *Citrobacter* spp., *Enterobacter* spp., *E. coli*, *M. morganii*, *P. vulgaris*, *Prov. rettgeri*, *Prov. stuartii*, *P. aeruginosa*, *Serratia* spp., including *S. marcescens*
- Note: there is no FDA indication for imipenem and *P. mirabilis*
- Consider not reporting imipenem results for *P. mirabilis*

Detect and Protect

- CDC is funding some states who are testing the use of “Detect and Protect” strategies to find germs causing healthcare-associated infections (HAI) and prevent their spread.
- Detect and Protect strategies include: Tracking CRE, including use of the National Healthcare Safety Network (NHSN), and Prevention activities, such as those found in CDC guidelines and HAI prevention toolkits.

http://www.cdc.gov/hai/organisms/cre/

Creation of XDRO Registry

- In response to the CRE public health threat, IDPH has amended the Control of Communicable Diseases Code (77 Ill. Adm. Code 690) Rules (see addendum) to require reporting of CREs to IDPH.
- All hospitals, hospital-affiliated clinical laboratories, independent or free-standing laboratories, longer-term care facilities, and long-term acute care hospitals in Illinois will be required to report CRE isolates that meet surveillance criteria to IDPH through a tool called the XDRO registry, effective **November 1, 2013.**

Report CRE Isolates to XDRO Registry with one of following test results:

1. Molecular test (e.g., PCR) specific for carbapenemase

OR

2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production

OR

3. For ***E. coli*** **and** ***Klebsiella*** species only: non-susceptible to ONE of the carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime).

Report 1st CRE event per patient per encounter

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

- Knowing the resistance mechanism is important
- The following cases demonstrate 3 different mechanisms of carbapenem resistance. Some require changes in antibiotic reporting, some require infection control notification, some require reporting to XDRO registry, and some require no action
- Can you tell the difference between them by MIC alone?

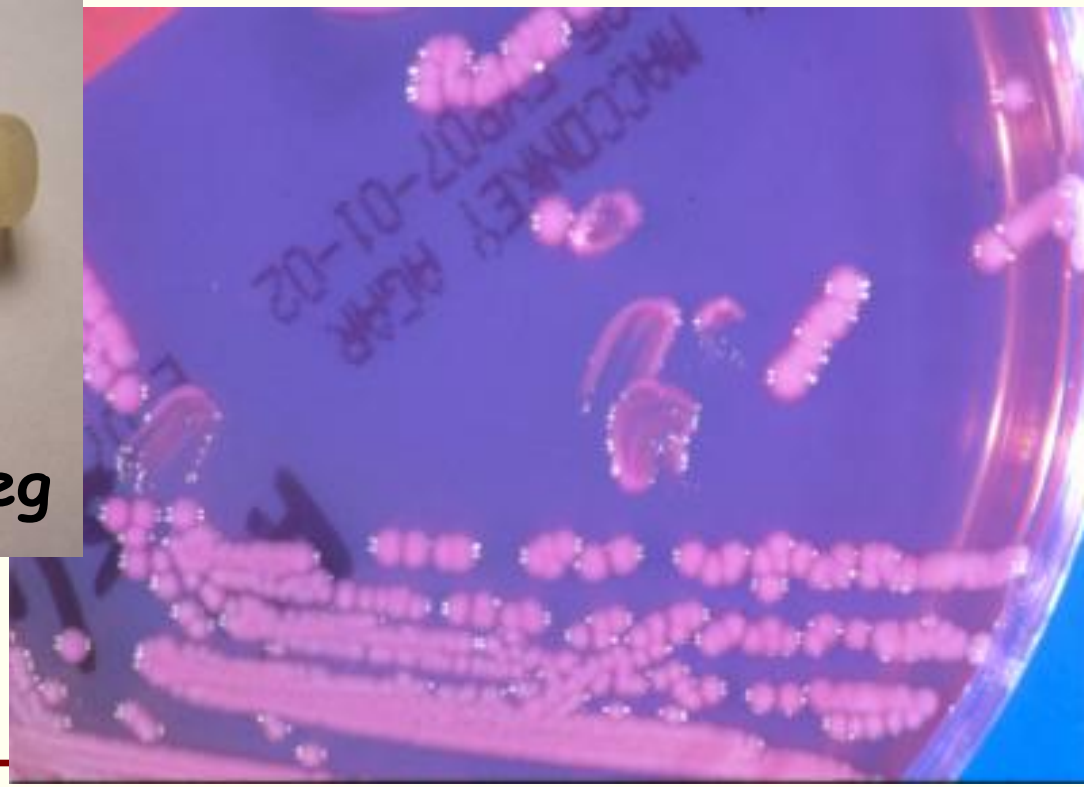
Patient History Case 1

- 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), 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*…

- **Spot Indole Neg**



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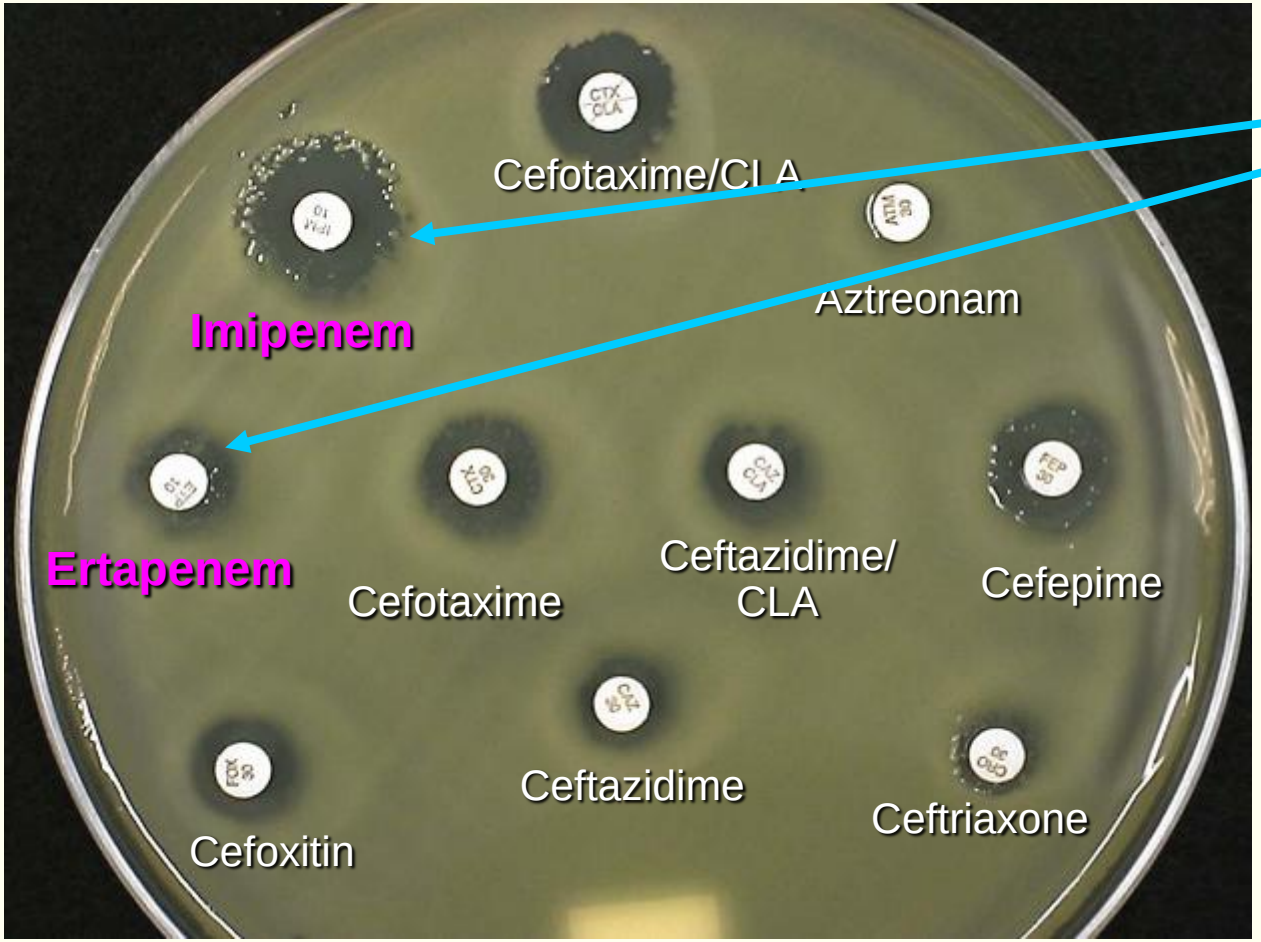
Vitek ID: [redacted] Oxidase -
Type: Gram Negative General Susceptibility 143 (GNS-143)
Status: Final
Elapsed Time: 13 hours
Organism: Klebsiella pneumoniae
Source: Manual
Demographics: [redacted]

	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	
Aztreonam	>=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

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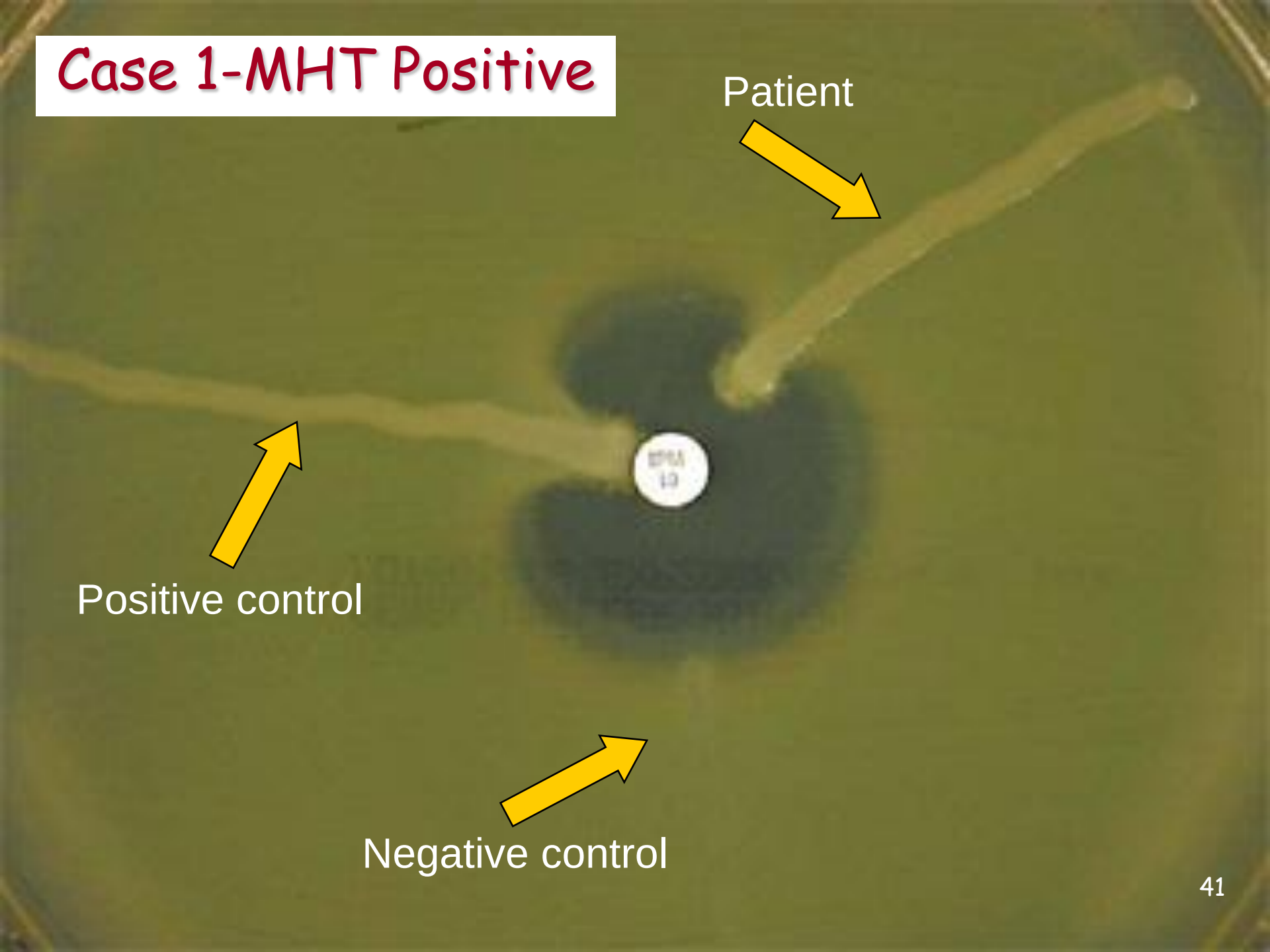
Case 1-MHT Positive



And the Answer is …….

Carbapenemases in the U.S.

Molecular Class	Carbapenemase	Found in:	Some Key Features
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	also IMI, NMCA, GES	Enterobacteriaceae	
B	Metallo beta-lactamases (IMP, VIM, GIM, SPM, NDM-1)	*S. maltophilia* *P. aeruginosa,* Enterobacteriaceae, *Acinetobacter,*	Hydrolyze all ß-lactams except aztreonam. Activity inhibited by EDTA but not by clavulanic acid
D	OXA	*Acinetobacter baumannii,* Enterobacteriaceae	OXA-48 first reported in Turkey in 2003. Not inhibited by EDTA or clavulanic acid

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

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."
- REPORT TO XDRO REGISTRY

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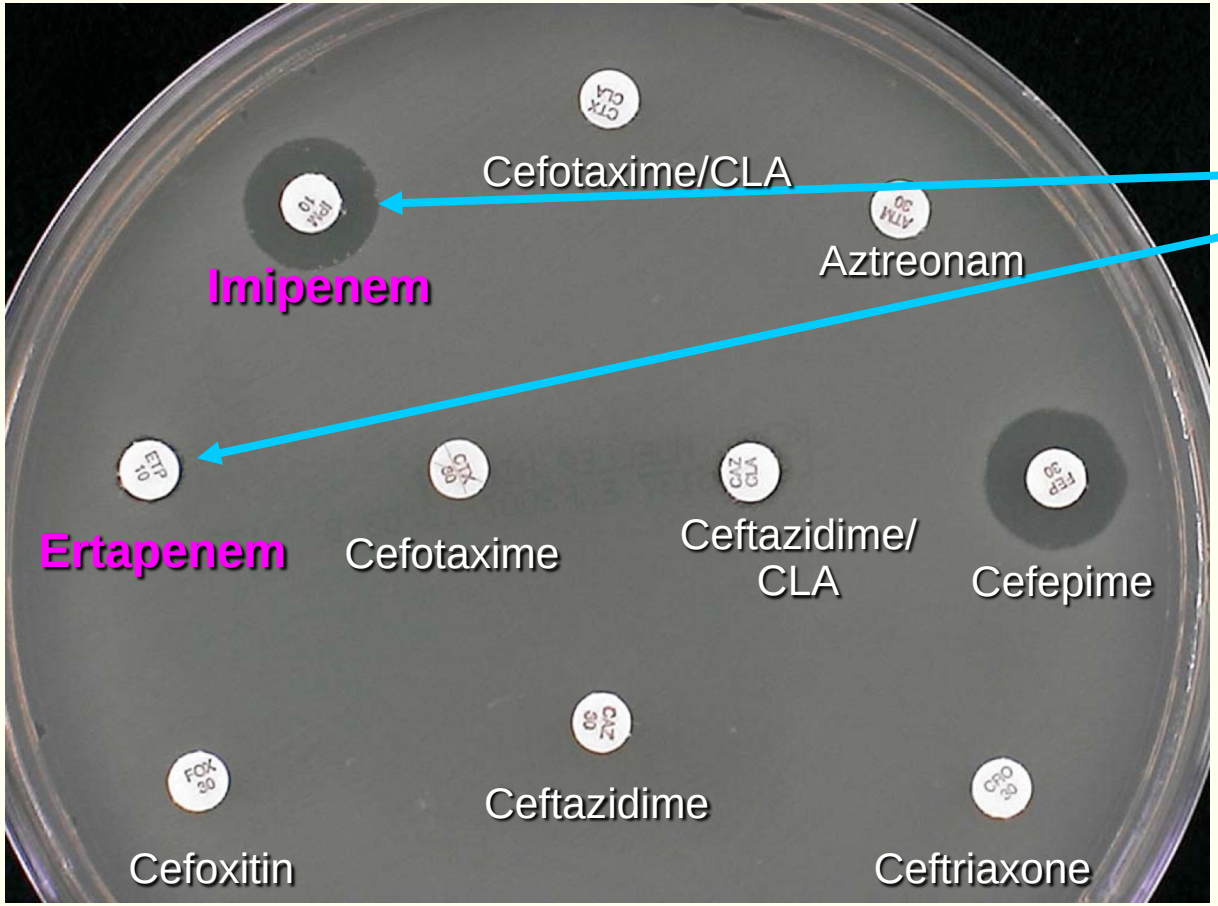
Double Disk Potentiation Method – Case 2 Blood Culture with *Enterobacter cloacae*



Imipenem - S
Ertapenem - R

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

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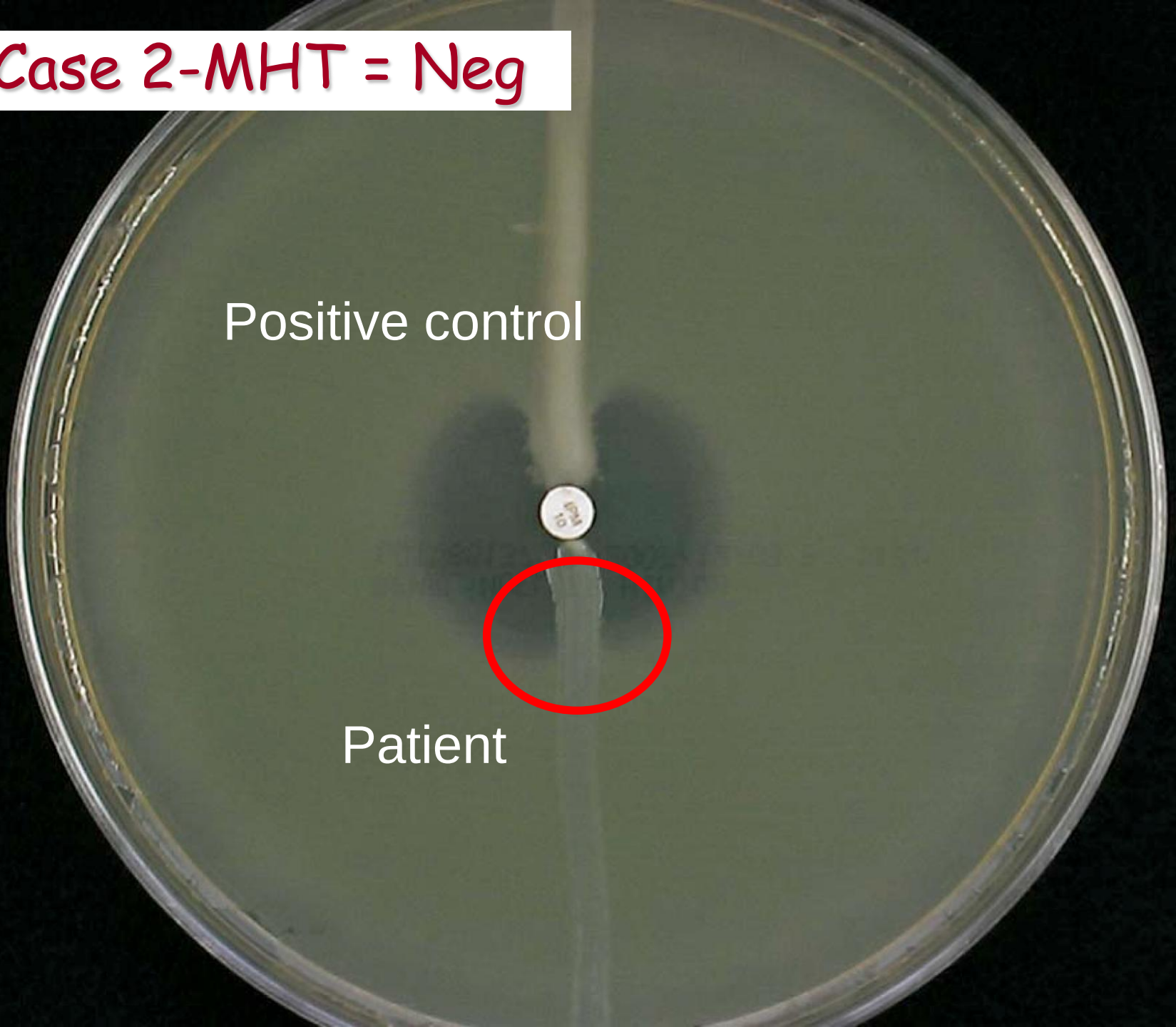
Case 2-MHT = Neg



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 ß-lactamase. Isolates may become resistant to all cephalosporins after initiation of therapy. Avoid ß-lactam-inhibitor drugs"
- DO NOT REPORT TO XDRO REGISTRY

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Case 3

- Patient is a 40 Y.O. male paraplegic who traveled to New Delhi 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 3

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)

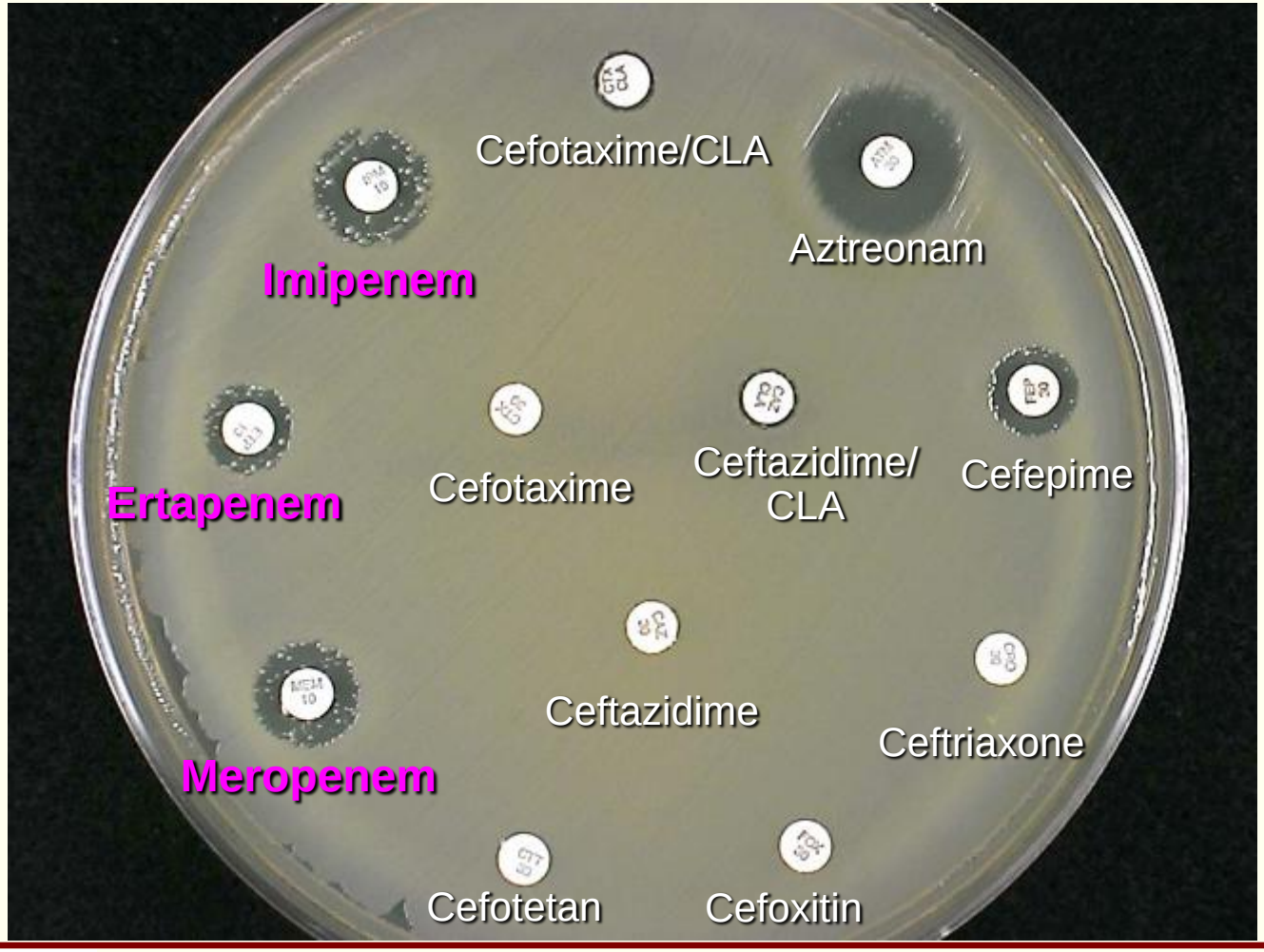
AM	A/S	P/T	CFZ	CAX	CAZ	CPE	MER	GM	Ø TE	TO	CP	T/S	Ø FD	AK
>16	>16/8	>64	>16	>32	>16	>16	>8	>8	>8	>8	>4	>2/38	<=32	>32
R	R	R	R	R	R	R	R	R	R	R	R	R		R

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 -

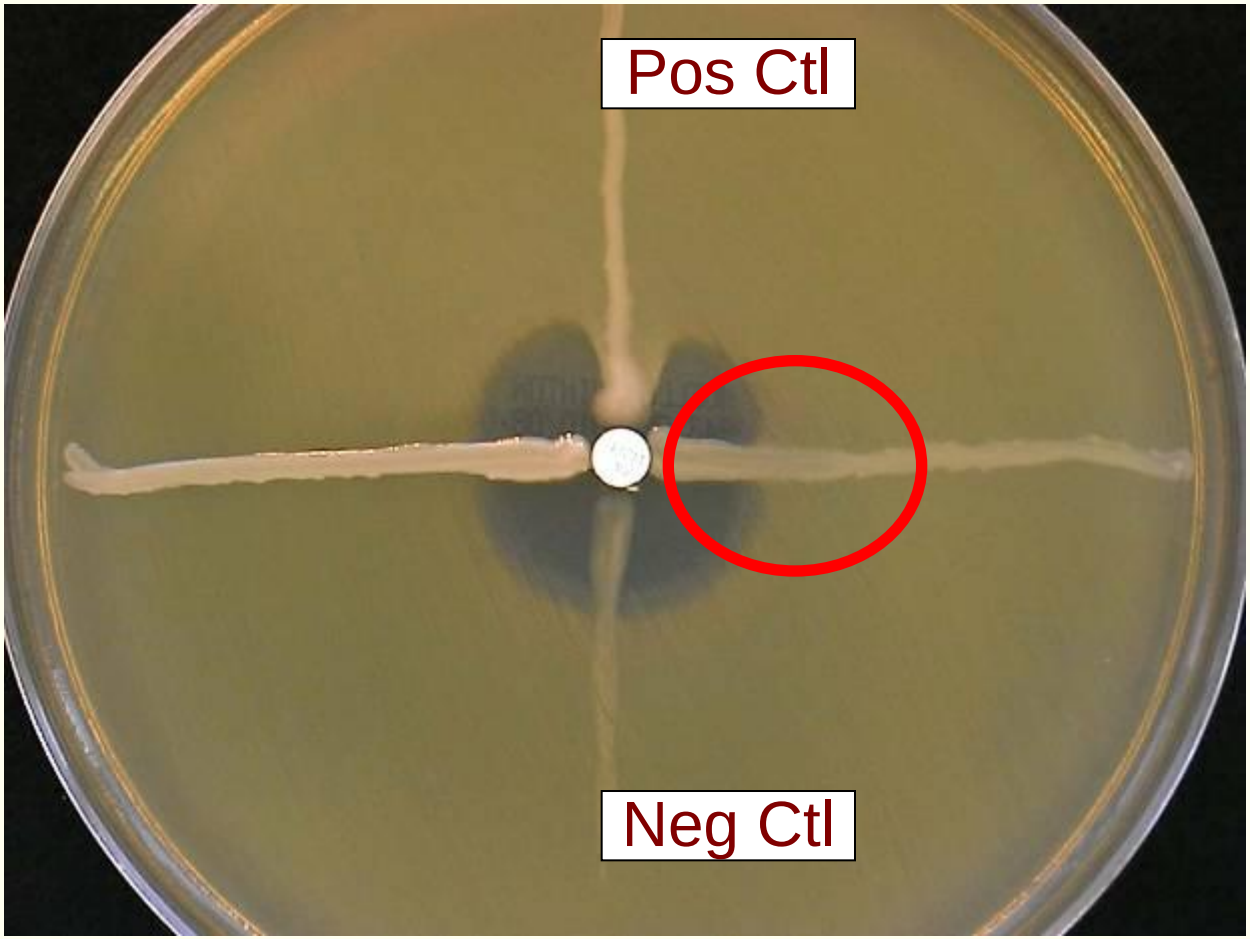
LOYOLA UNIVERSITY CHICAGO

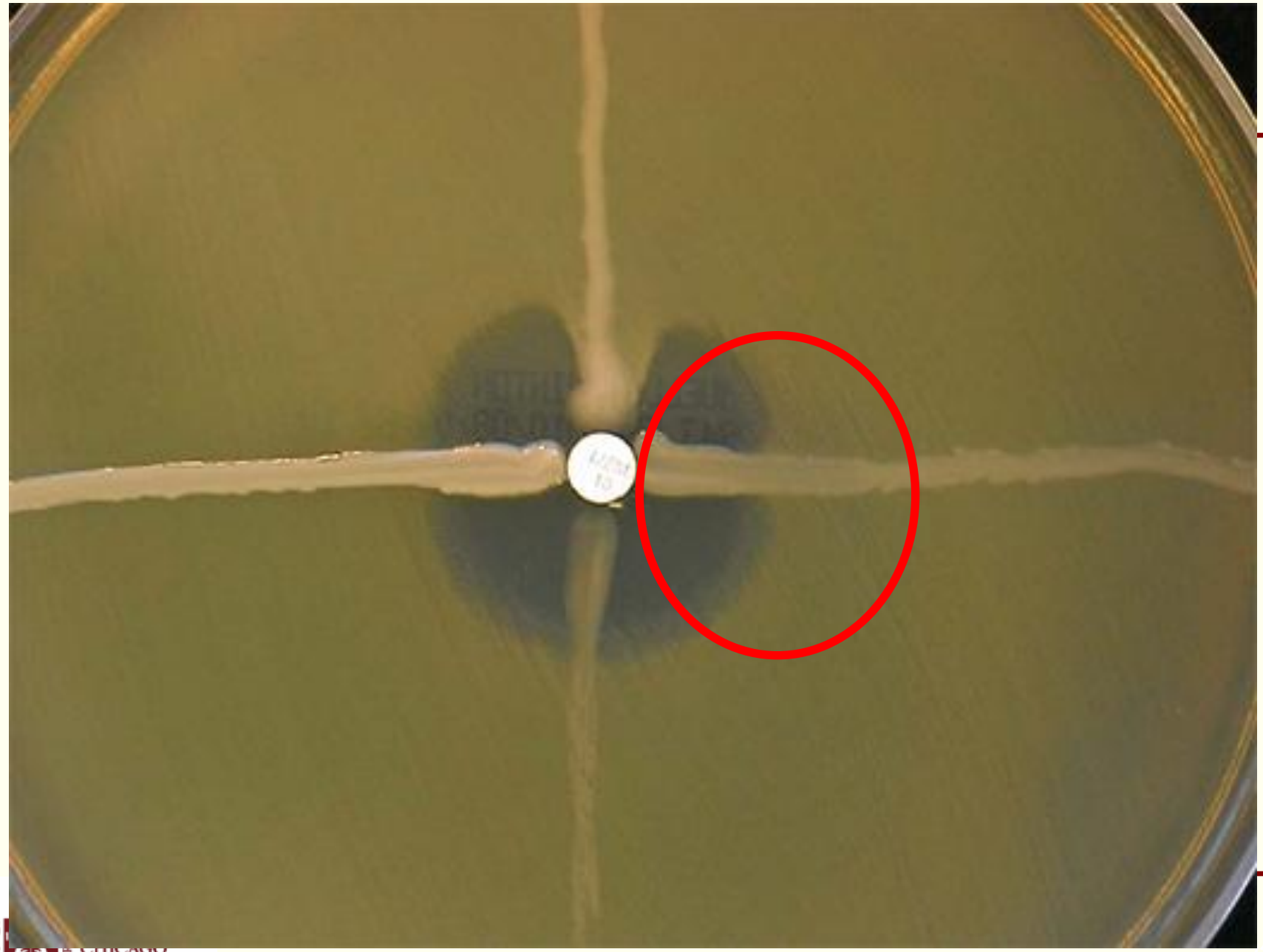
Case 3. 12 Disk



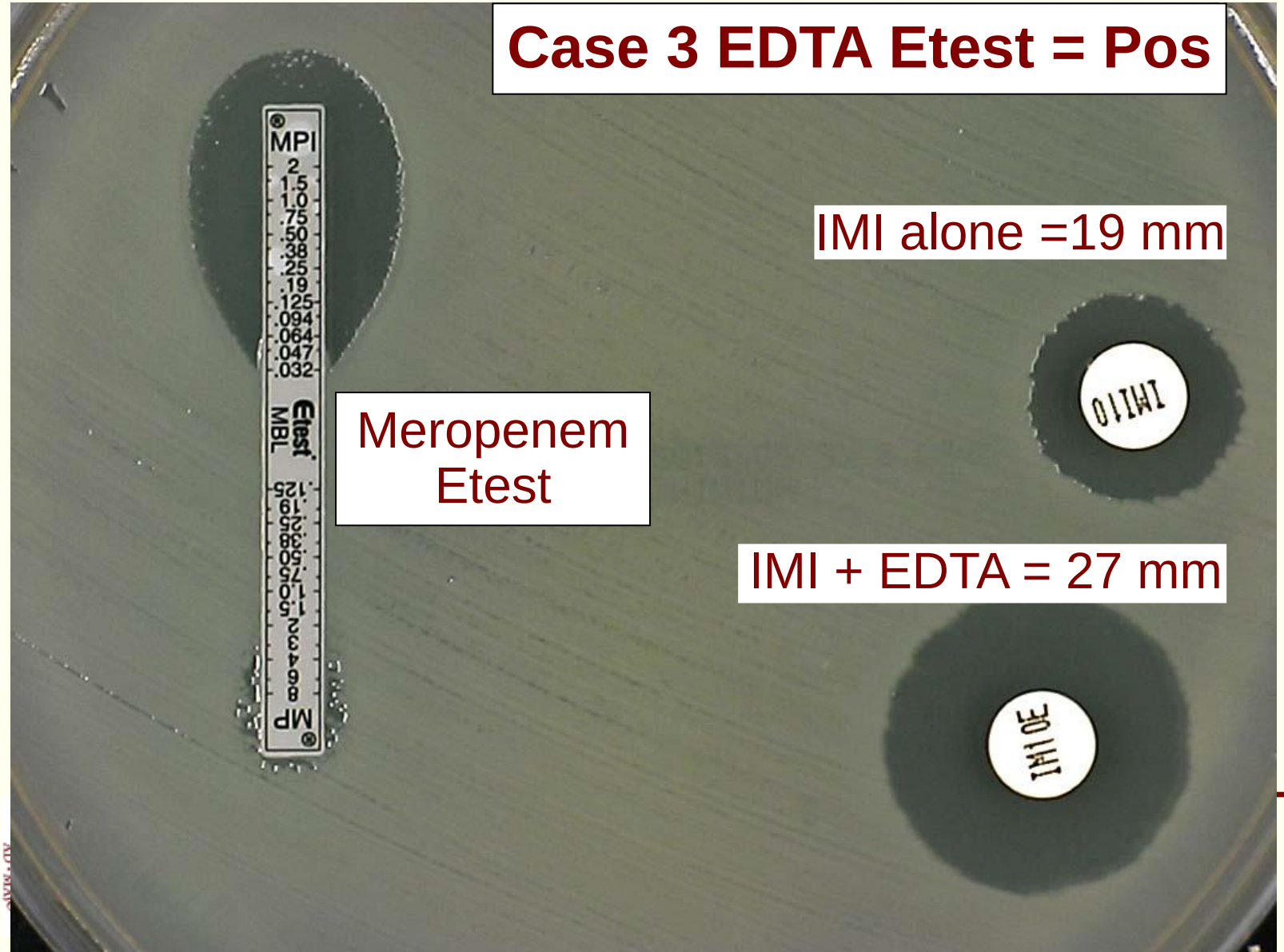
LOYOLA UNIVERSITY CHICAGO

Case 3 - Modified Hodge Test





Rosco Diagnostica IMI/EDTA Disks
MBL Etest bioMerieux



And the Answer is …….

Carbapenemases in the U.S.

Molecular Class	Carbapenemase	Found in:	Some Key Features
A	KPC	*K. pneumoniae* and other Enterobacteriaceae	Some are chromosomal (NmcA, Sme, IMI-1, SFC-1) others are plasmid encoded (KPC, IMI-2, GES). All hydrolyze carbapenems and are partially inhibited by clavulanic acid
	SME	*S. marcescens*	
	also IMI, NMCA, GES	Enterobacteriaceae	
B	Metallo beta-lactamases (IMP, VIM, GIM, SPM, NDM-1)	*S. maltophilia* *P. aeruginosa,* Enterobacteriaceae, *Acinetobacter,*	Hydrolyze all ß-lactams except aztreonam. Activity inhibited by EDTA but not by clavulanic acid
D	OXA	*Acinetobacter baumannii,* Enterobacteriaceae	OXA-48 first reported in Turkey in 2003. Not inhibited by EDTA or clavulanic acid

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

NDM-1
New Class B: Metallo-β-Lactamases

- First reported in Swedish patient of Indian origin traveled to New Delhi, acquired a urinary tract infection caused by NDM-1-producing *K. pneumoniae*
- MBLs hydrolyze all β-lactams, including carbapenems, penicillins, extended-spectrum cephalosporins, but not aztreonam
- MBLs pose a serious threat in terms of infection control because of their high mobility
- MBLs require zinc for enzymatic activity which is not diminished by serine β-lactamase inhibitors but is inhibited by EDTA and other chelators of divalent cations

Antimicrobial Agents and Chemotherapy. December, 2009. 53:5046-5054.

Courtesy Brandi Limbago, CDC

MicroScan Report

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	MER	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 -

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Enterobacteriaceae - Revised Carbapenem Breakpoints (MIC μg.ml)

Agent	CLSI M100-S19 (2009)			CLSI M100-S20 (2010) Supplement		
	Susc	Int	Res	Susc	Int	Res
Doripenem	-	-	-	≤1	2	≥4
Ertapenem	≤2	4	≥8	≤0.5	1	≥2
Imipenem	≤4	8	≥16	≤1	2	≥4
Meropenem	≤4	8	≥16	≤1	2	≥4

CLSI. Performance Standards for Antimicrobial Susceptibility Testing: Twentieth Informational Supplement (June 2010 Update). CLSI document M100-S20-U. Wayne, PA; 2010

CLSI M100-S20-U. Table 2A

Patient Report Case 3

- 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 EDTA Inhibition Test –probable MBL type. Implement infection control measures according to facility"
- REPORT TO XDRO REGISTRY

LOYOLA UNIVERSITY CHICAGO

Carbapenem-Resistant Enterobacteriaceae (CRE): Submitting Samples to IDPH

- IDPH and CDC want to prioritize sample submission of CRE isolates **other than KPC** for further (genotypic) testing.
- At a *minimum*, prior to submission, labs should confirm ID, ensure pure cultures, and **repeat resistance testing,** with a different method if possible, to confirm resistance patterns.
- Submit **likely MBL-producing CRE isolates to IDPH**

Carbapenem-Resistant Enterobacteriaceae (CRE): Submitting Samples to IDPH

- **Likely MBL-producing CRE isolates:**

  1) Must exhibit carbapenem resistance (I or R to imipenem, doripenem, or meropenem using updated breakpoints) and resistance (R) to all tested third-generation cephalosporins

     AND

  2) Must have phenotypic testing suggesting MBL (e.g. + MBL Etest or + multi-disk test) OR, if phenotypic testing not done, be isolated from a patient with international travel in last 6 months or epidemiologic link to a patient with non-KPC CRE.

QUESTIONS?

XDRO Registry

for Laboratories

June 2014

Michael Lin, MD MPH

William Trick, MD

Chicago CDC Prevention Epicenter

XDRO registry

Objectives

1. Review epidemiology and registry data (2 slides)

2. XDRO registry website orientation

CRE in Chicagoland

Facility type	CRE colonization prevalence
Short stay acute care hospitals (adult ICUs)	3%
Long term acute care hospitals (LTACHs)	30%

- CRE common in some Chicago healthcare facilities, particularly LTACHs
- Data suggest that skilled nursing facilities with ventilated patients have rates similar to LTACHs

Lin et al. CID, 2013. 57(9): 1246-1252.
Prabaker et al. ICHE 2012. 33(12): 1193-1199.

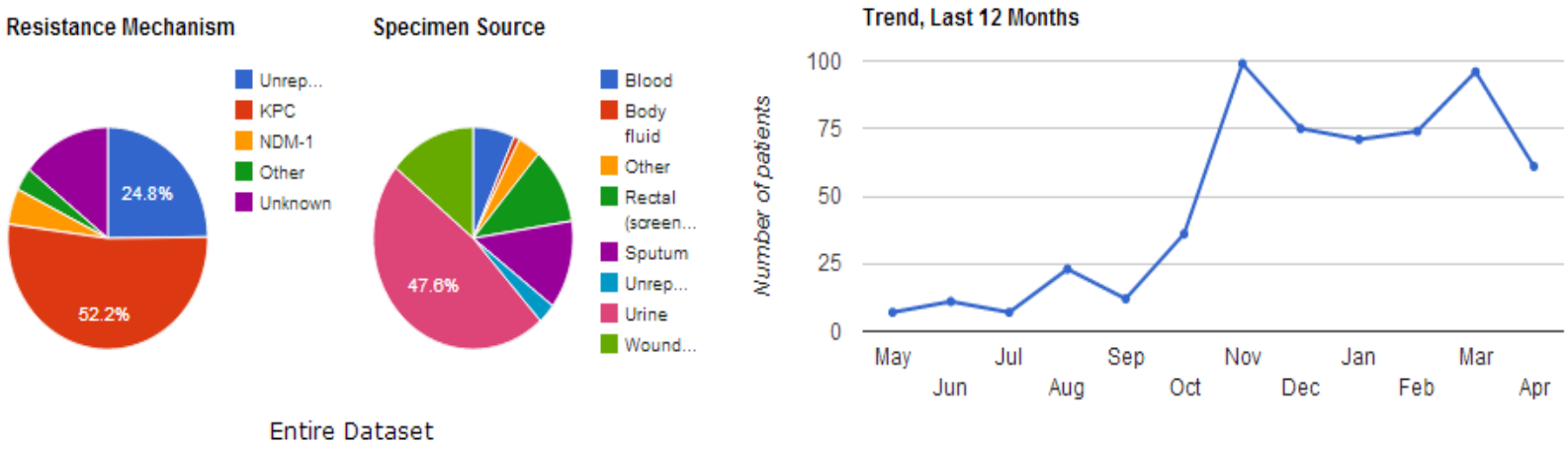
XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report

State Data [b]



Entire Dataset

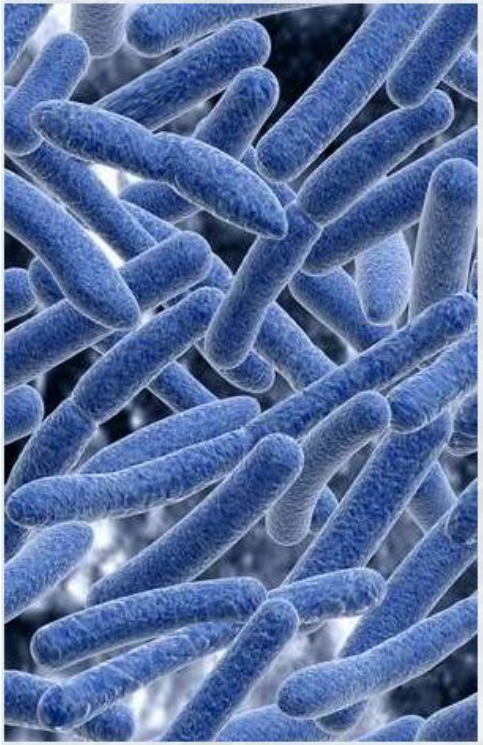
Since Nov. 2013, average 2-3 patients reported per day

XDRO registry website: orientation and updates

XDRO registry

XDRO registry

Extensively drug resistant organism registry Help Login



The XDRO registry is a product of collaboration between IDPH, Medical Research Analytics and Informatics Alliance (MRAIA), and the Chicago CDC Prevention Epicenter.

Carbapenem-resistant Enterobacteriaceae (CRE) are extremely drug resistant organisms (XDROs) that have few treatment options and high mortality rates. CRE are increasingly detected among patients in Illinois, including acute and long term care healthcare facilities.

In response to the CRE public health threat, the Illinois Department of Public Health (IDPH) has guided development an infection control tool called the XDRO registry. The purpose of the XDRO registry is two-fold:

1. **Improve CRE surveillance:** The first CRE-positive culture per patient stay must be reported to the XDRO registry.
2. **Improve inter-facility communication:** Healthcare facilities can query the XDRO registry to see whether a patient has been previously reported as CRE-positive.

For access to the XDRO registry, click here

UPDATES

IL CRE Detect and Protect Campaign. More...

CRE are reportable to IDPH via the XDRO registry. Links: [IDPH letter to facilities, September 2013][Reporting rule]

XDRO registry orientation webinar [Slides][Recording]

CDC guidance on control of CRE: [The 2012 Toolkit]

As of November 1, 2013, the XDRO registry is open for CRE submissions and queries.

View FAQs: [FAQs PDF]

www.xdro.org

IDPH Web Portal
Applications, Alerting & Resources

Illinois Department of Public Health
Health Alert Network
Web Portal

Welcome to the IDPH Web Portal

From here, you can:

- Find all your public health related information at one secure site.
- Join online communities to share files, discussions, calendars and more.
- Access Web-based applications.

To access the IDPH Web Portal, users must be running Internet Explorer 6.0 or higher. Some portal applications may not function properly with other browsers such as Mozilla Firefox.

Current Users: click here to access the portal: Login

I need to...

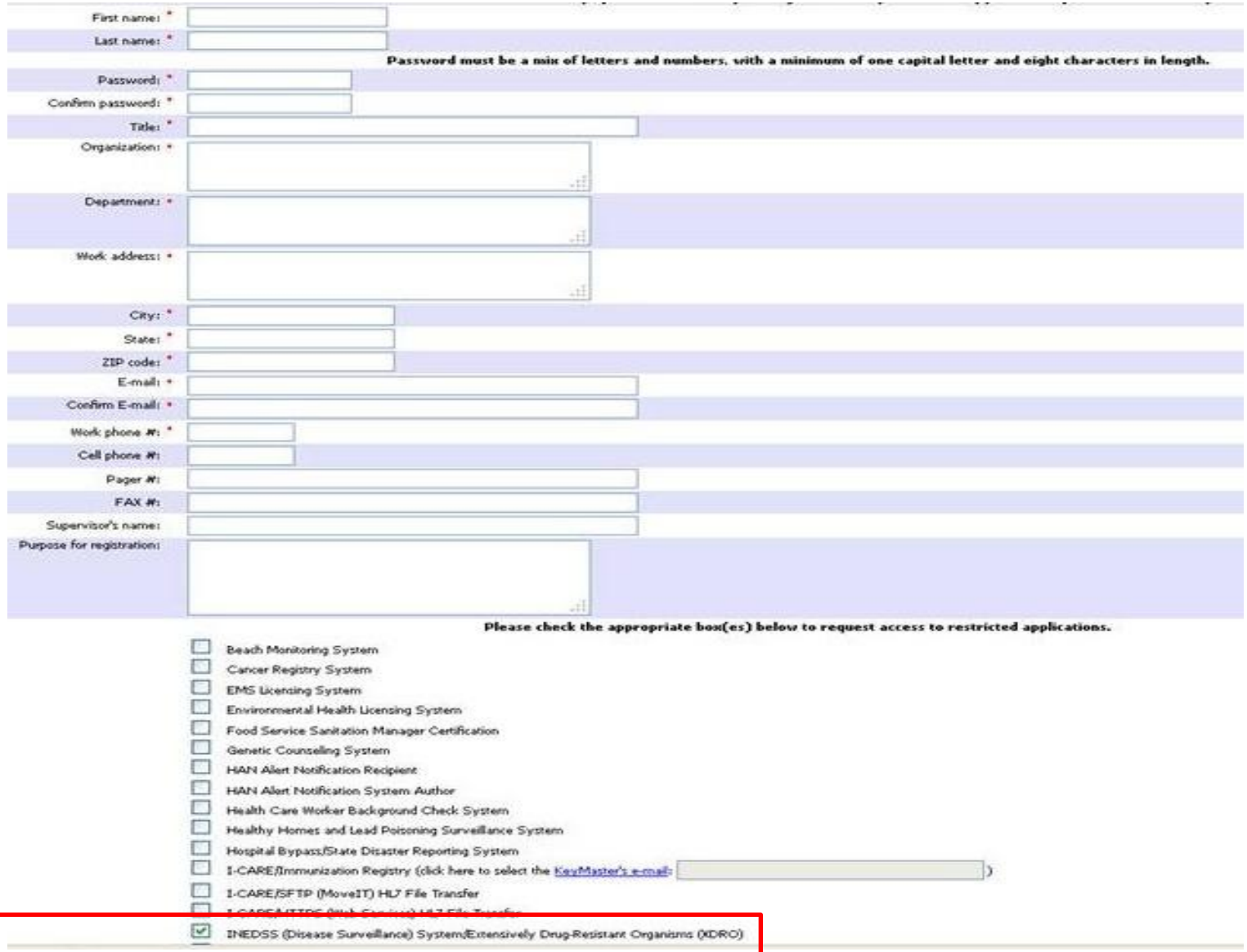
Register for a Portal Account

Contact Customer Service Center
1-800-366-8768

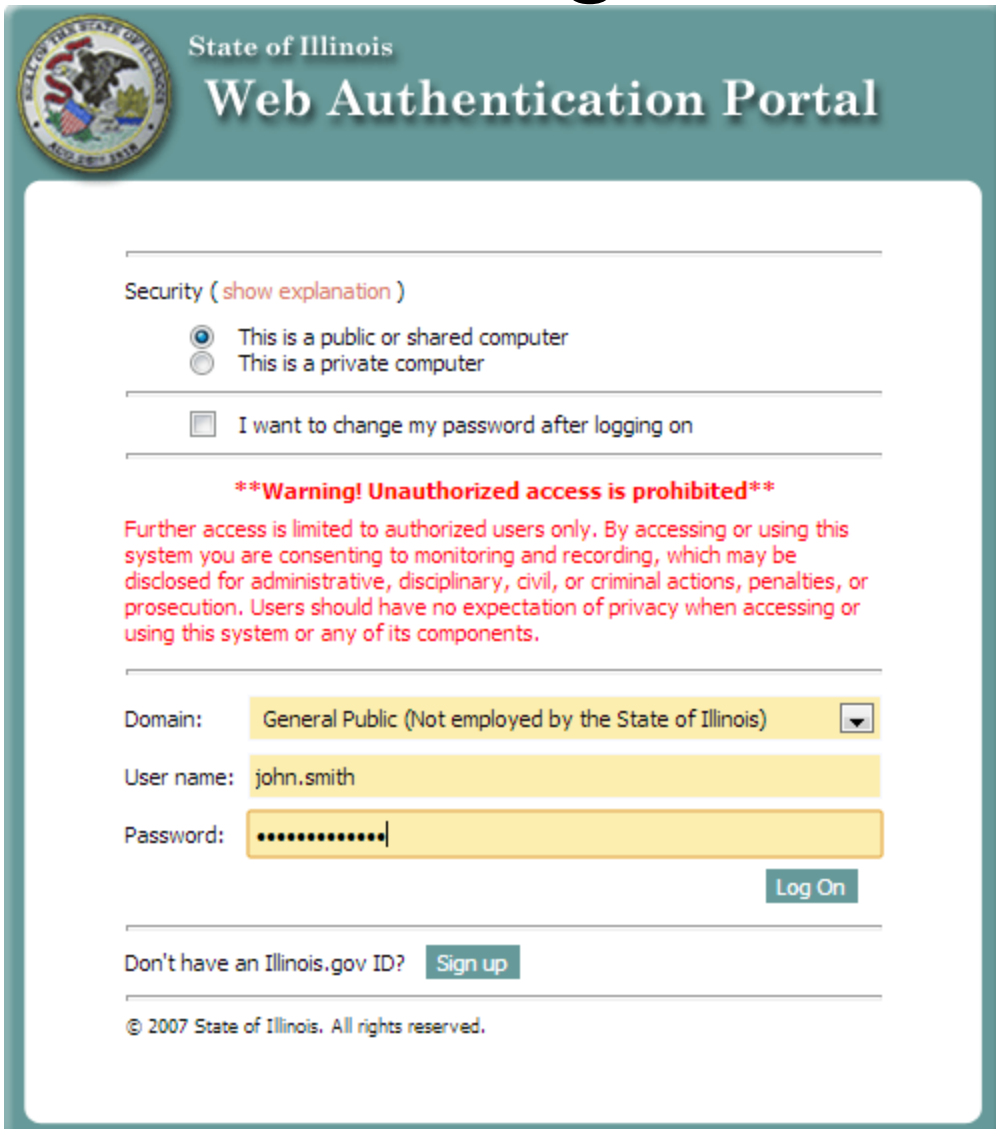
For assistance with IDPH portal access and web-based application support, contact the Customer Service Center at 1-800-366-8768, Option 1, then Option 1 for password reset assistance or Option 7 to reach support personnel for the Department of Public Health.

Please indicate to the CSC staff that you are an IDPH Health Alert Network (portal) user when placing the call to ensure you are routed to the correct support staff to resolve the problem. Include your name, phone number, and specific application name, detail of the issue and error messages, if any, in your description of the problem to ensure efficient resolution.

Registration Page: New Users



User Sign-In


State of Illinois
Web Authentication Portal
Security (show explanation)
This is a public or shared computer
This is a private computer
I want to change my password after logging on
Warning! Unauthorized access is prohibited
Further access is limited to authorized users only. By accessing or using this system you are consenting to monitoring and recording, which may be disclosed for administrative, disciplinary, civil, or criminal actions, penalties, or prosecution. Users should have no expectation of privacy when accessing or using this system or any of its components.
Domain:
General Public (Not employed by the State of Illinois)
User name:
john.smith
Password:
Log On
Don't have an Illinois.gov ID?
Sign up
© 2007 State of Illinois. All rights reserved.


https://dph.partner.illinois.gov/Pages/AppTest.aspx
Most Visited
Getting Started
Latest Headlines
Customize Links
Free Hotmail
DPH Partner
IDPH
Web Portal
Applications, Alerting & Resources
DPH Partner
DPH Partner
Applications
Communities
Discussion Board
Production Apps
Test Apps
Development Apps
View All Site Cont
Documents
Lists
Local Health Departments
Portal Registration Authorities
Communities
Communicable Disease
Division of Laboratories
Environmental Health
Test Applications
Business Objects 3.1 - NEW VERSION (Test)
Extensively Drug-Resistant Organisms (XDRO)
I-NEDSS Provider Reporting Test

Sample Hospital change facility

Test User1 Home Help Go Back Logout

Submit Report

Search Registry

Facility Submission History

Facility Alert History

XDRO Dashboard


XDRO registry
Sample Hospital change facili
Test User1
Home Help Go Back Logou
XDRO Report
XDRO culture information
*XDRO criteria (select all that apply)
Reporting rule
Molecular test (e.g. PCR) specific for carbapenemase
Phenotypic test (e.g. Modified Hodge) specific for carbapenemase production
For E. coli and Klebsiella spp. only:
Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. Ignore ertapenem.
* Organism name (genus/species)
Please Select Organism:
* Date (culture acquisition)
mm / dd / yyyy
* Specimen source
Please Select Specimen:
* Mechanism of resistance
Please Select Mechanism:
(molecular test required)
Facility information
Facility name
Sample Hospital
Culture obtaine
Change Facility
Sample Hospital
Change
Sample Hospital
Test Nursing Home
Patient demograph
* First name
* Last name
Maiden name(if applicable)
* Gender
Male Female
* Date of birth(mm/dd/yyyy)
mm / dd / yyyy
Social Security Number(last4)
Race
Please Select One:
Ethnicity
Hispanic or Latino
Not Hispanic or Latino
* Street address
* City
Chicago
* County
Cook
* State
Illinois
* Zip code

Sample Hospital change facility

Test User1 Home Help Go Back Logout

Submit Report

Search Registry

Facility Submission History

Facility Alert History

XDRO Dashboard

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report

XDRO culture information

* **Organism name (genus/species)**
Please Select Organism:

* **Specimen source**
Please Select Specimen:

*XDRO criteria (select all that apply)
Reporting rule

- ☐ **Molecular test** (e.g. PCR) specific for carbapenemase
- ☐ **Phenotypic test** (e.g. Modified Hodge) specific for carbapenemase production
- ☐ **For E. coli and Klebsiella spp. only:** Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. **Ignore ertapenem.**

* **Date (culture acquisition)**
mm / dd / yyyy

* **Mechanism of resistance**
Please Select Mechanism:
(molecular test required)

Facility information

Facility name
Sample Hospital

* **Patient MRN**

* **Date of admission/Encounter Date**
mm / dd / yyyy

☐ Culture obtained as outpatient

Patient demographics

* **First name**

* **Last name**

Maiden name(if applicable)

* **Gender**
○ Male ○ Female

* **Date of birth(mm/dd/yyyy)**
mm / dd / yyyy

Social Security Number(last4)

Race
Please Select One:

Ethnicity
○ Hispanic or Latino
○ Not Hispanic or Latino

* **Street address**

* **City**
Chicago

* **County**
Cook

* **State**
Illinois

* **Zip code**

Comments

For laboratories and IDPH only
* **Select facility that sent specimen:**
Please Select Facility:

CANCEL | SAVE DRAFT | SUBMIT

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report

XDRO culture information

* **Organism name (genus/species)**
Please Select Organism:

* **Specimen source**
Please Select Specimen:

* **XDRO criteria** (select all that apply)
Reporting rule

☐ **Molecular test** (e.g. PCR) specific for carbapenemase

☐ **Phenotypic test** (e.g. Modified Hodge) specific for carbapenemase production

☐ **For E. coli and Klebsiella spp. only:**
Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. **Ignore ertapenem.**

* **Date (culture acquisition)**
mm / dd / yyyy

* **Mechanism of resistance**
Please Select Mechanism:

Facility information

Facility name
Sample Hospital

* **Patient MRN**

* **Date of admission/Encounter Date**
mm / dd / yyyy

☐ Culture obtained as outpatient

XDRO registry

Sample Hospital change facilit

Test User1 | Home | Help | Go Back | Logout

XDRO Report

XDRO culture information

* **Organism name (genus/species)**

Please Select Organism:

- Please Select Organism:
- Citrobacter freundii
- Citrobacteri koseri
- Citrobacter spp.
- Enterobacter aerogenes
- Enterobacter cloacae
- Enterobacter spp.
- Escherichia coli
- Klebsiella oxytoca
- Klebsiella pneumoniae
- Klebsiella spp.
- Morganella morganii
- Pantoea agglomerans
- Proteus mirabilis
- Proteus spp.
- Providencia stuartii
- Providencia spp.
- Salmonella spp.
- Serratia marcescens
- Serratia spp.

* **XDRO criteria** (select all that apply)

Reporting rule

☐ **Molecular test** (e.g. PCR) specific for carbapenemase

☐ **Phenotypic test** (e.g. Modified Hodge) specific for carbapenemase production

☐ **For E. coli and Klebsiella spp. only:** Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. **Ignore ertapenem.**

* **Date (culture acquisition)**

mm / dd / yyyy

* **Mechanism of resistance**

Please Select Mechanism:

Fa

* **Patient MRN**

* **Date of admission/Encounter Date**

mm / dd / yyyy

utpatient

Pa s

* **First name**

* **Last name**

Maiden name(if applicable)

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report

XDRO culture information

* **Organism name (genus/species)**
Klebsiella pneumoniae

* **Specimen source**
Please Select Specimen:

* **XDRO criteria** (select all that apply)
Reporting rule

☐ **Molecular test** (e.g. PCR) specific for carbapenemase

☐ **Phenotypic test** (e.g. Modified Hodge) specific for carbapenemase production

☐ **For E. coli and Klebsiella spp. only:** Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. **Ignore ertapenem.**

* **Date (culture acquisition)**
mm / dd / yyyy

* **Mechanism of resistance**
Please Select Mechanism:

Facility information

Facility name
Sample Hospital

* **Patient MRN**

* **Date of admission/Encounter Date**
mm / dd / yyyy

☐ Culture obtained as outpatient

Patient demographics

* **First name**

* **Last name**

Maiden name(if applicable)

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report

XDRO culture information

* **Organism name (genus/species)**
Klebsiella pneumoniae

* **Specimen source**
Please Select Specimen:

* **XDRO criteria** Reporting rule

☑ **Molecular test** (e.g. PCR) specific for carbapenemase

☐ **Phenotypic test** (e.g. Modified Hodge) specific for carbapenemase production

☑ **For E. coli and Klebsiella spp. only:** Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. **Ignore ertapenem.**

* **Date (culture acquisition)**
mm / dd / yyyy

* **Mechanism of resistance**
Please Select Mechanism:

Facility information

Facility name
Sample Hospital

* **Patient MRN**

* **Date of admission/Encounter Date**
mm / dd / yyyy

☐ Culture obtained as outpatient

Patient demographics

* **First name**

* **Last name**

Maiden name(if applicable)

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report

XDRO culture information

* **Organism name (genus/species)**
Klebsiella pneumoniae

* **Specimen source**
Please Select Specimen:

* **XDRO criteria** Reporting rule

☑ **Molecular test** (e.g. PCR) specific for carbapenemase

☐ **Phenotypic test** (e.g. Modified Hodge) specific for carbapenemase production

☑ **For E. coli and Klebsiella spp. only:**
Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. **Ignore ertapenem.**

* **Date (culture acquisition)**
mm / dd / yyyy

* **Mechanism of resistance**
KPC (Klebsiella pneumonia

Please Select Mechanism:
KPC (Klebsiella pneumoniae carbapenemase)
NDM-1 (New Delhi Metallo-ß-lactamase)
OXA
Other
Unknown

Facility information

Facility name
Sample Hospital

* **Patient MRN**

* **D**
mm / dd / yyyy

☐ Culture obtained as outpatient

Patient demographics

* **First name**

* **Last name**

Maiden name(if applicable)

Patient demographics

* First name

* Last name

Maiden name(if applicable)

* Gender
Male Female

* Date of birth(mm/dd/yyyy)
mm / dd / yyyy

Social Security Number(last4)

Race
Please Select One:

Ethnicity
Hispanic or Latino
Not Hispanic or Latino

* Street address

* City
Chicago

* County
Cook

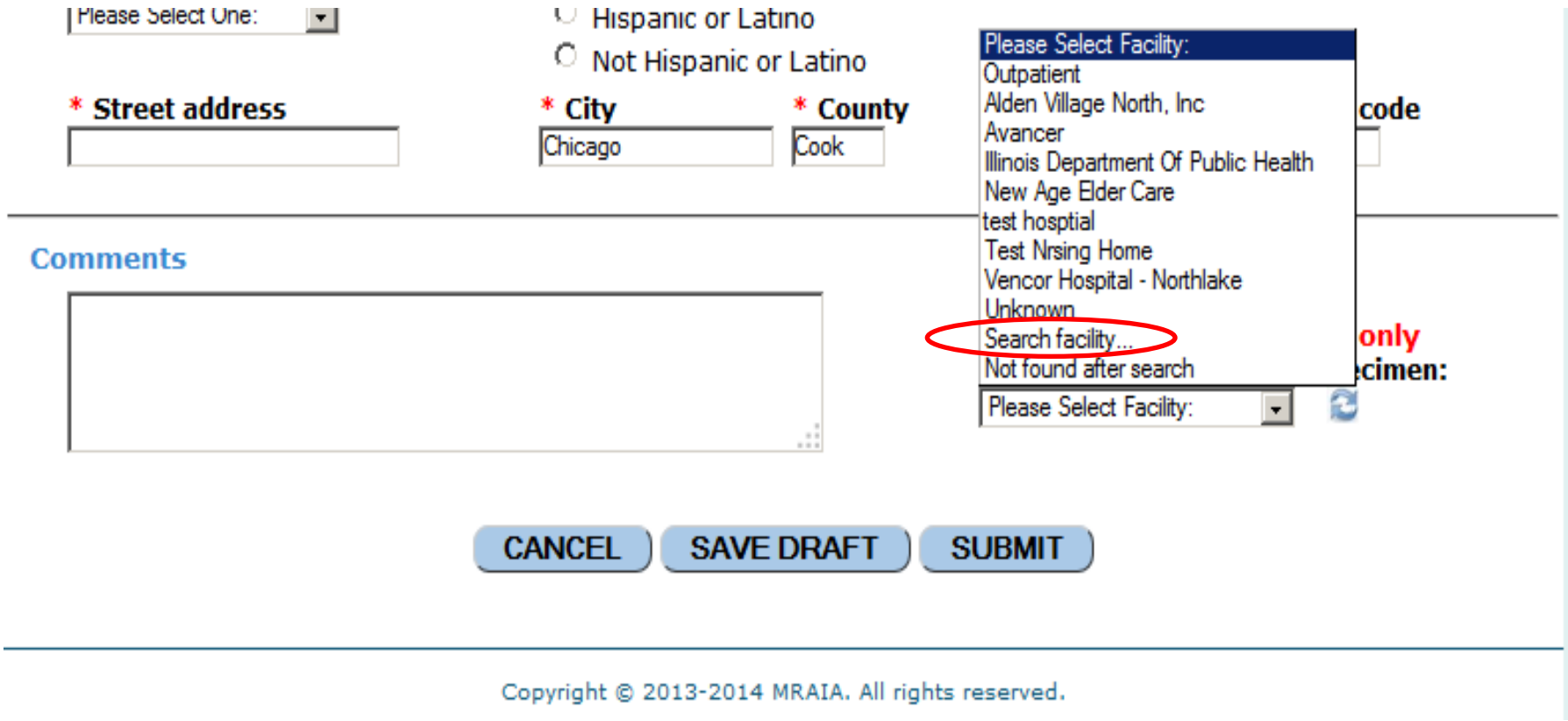
* State
Illinois

* Zip code

Comments

For laboratories and IDPH only
* Select facility that sent specimen:
Vencor Hospital - Northlake

CANCEL SAVE DRAFT SUBMIT


Please Select One:
Hispanic or Latino
Not Hispanic or Latino
* Street address
* City
Chicago
* County
Cook
Please Select Facility:
Outpatient
Alden Village North, Inc
Avancer
Illinois Department Of Public Health
New Age Elder Care
test hosptial
Test Nrsing Home
Vencor Hospital - Northlake
Unknown
Search facility...
Not found after search
Please Select Facility:
code
only
ecimen:
Comments
CANCEL
SAVE DRAFT
SUBMIT
Copyright © 2013-2014 MRAIA. All rights reserved.

XDRO registry

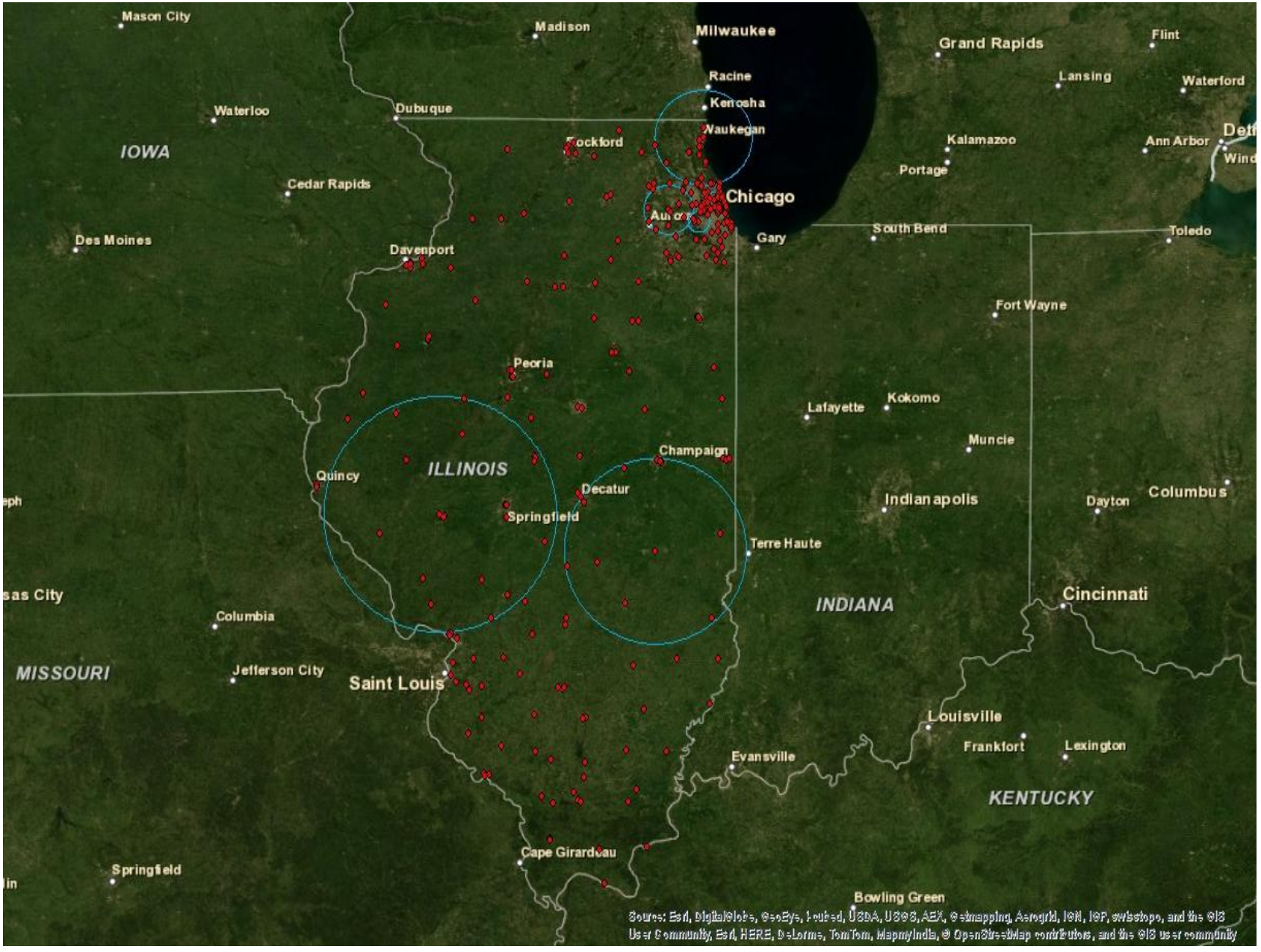
Sample Hospital change facili

Add Facility to Dropdown

Facility Name | **DPHSiteCode** | **ZipCode** (60612) | Search

Action	Facility Name	DPHsitecode	Street	City State Zip
ADD	Veterans Rehabilitation Cent..	6075	2449 West Washington	Chicago, Illinois 60612
ADD	Vet Administration West Side..	6074	820 South Damen Avenue	Chicago, Illinois 60612
ADD	University Of Illinois Hospi..	6072	1740 West Taylor	4 West O.b. - 4th Floor ..
ADD	U Of I College Of Medicine	6070	1819 West Polk Street	Chicago, Illinois 60612
ADD	Rush University Medical Cent..	6053	1753 West Congress Parkway	Chicago, Illinois 60612
ADD	John H. Stroger, Jr. Hospita..	6020	1835 West Harrison Street	Chicago, Illinois 60612
ADD	Illinois State Psychiatric I..	6033	1601 West Taylor Street	Chicago, Illinois 60612
ADD	Ill Research And Education H..	6031	1819 West Polk Street	Chicago, Illinois 60612
ADD	City Morgue	6018	1828 West Polk Street	Chicago, Illinois 60612

SatScan Cluster Detection



XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

Submit Report

Search Registry

Facility Submission History

Facility Alert History

XDRO Dashboard

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

Search Patient

* Last name

* Date of birth mm / dd / yyyy

First name

Query

Search Instruction

a. Available fields

Last name (required), first name (optional), DOB (required).

b. Search algorithm

i. If you enter all 3 fields, then attempt to match (exact; case insensitive) on all 3 fields.

ii. If no match returns on 3 fields, then attempt to match (exact; case insensitive) on last name and DOB (ignore first name completely).

c. Results display

i. In general, You will see the search results for exactly how you entered the information. If there are no exact matches for last name and dob, you will see a NULL result.

XDRO registry

Sample Hospital change facility

Test1 Test | Home | Help | Go Back | Logout

XDRO Report - Rush-presb-st Lukes Medical Center

Patient information

Patient name: J, J
MRN:
Admission date: 10/10/2012
Date of birth: 10/10/1999
SSN (last 4):
Race: Black/African American
Address: 2200, Chicago, IL 60612

XDRO culture information

Organism: Other Enterobacteriaceae
Culture date: 10/10/2012
XDRO criterion:
Specimen source: Blood
Mechanism of resistance:
Comments:

Submitted by Vicky G, 10/10/2013, Rush-presb-st Lukes Medical Center

Go Back Print

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

Submit Report

Search Registry

Facility Submission History

Facility Alert History

XDRO Dashboard

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

Sample Hospital Submission History

First name | Last name | Date of birth (mm / dd / yyyy) | SSN(last4) | RID | Report (All) | Search

RID	Name	Date of Birth	MRN	Organism	▼Culture Date	Status	Username
585	Q, Q	12/12/2010	1212	Citrobacter spp.	03/01/2014	Pending	devxtest
835	Duck, Daffy	11/13/1973	1234	Klebsiella pneumoniae	02/14/2014	Submitted	rleidig
1017	T, Test	01/01/1955	1234536	Escherichia coli	12/31/2013	Submitted	devxtest
1018	B, A	11/11/2011	1234536	Escherichia coli	12/31/2013	Submitted	devxtest
846	S, B	11/11/1950	32152	Citrobacter spp.	12/12/2013	Submitted	devxtest
777	E, Ds	11/11/1982	1110	Enterobacter aerogenes	11/22/2013	Submitted	devxtest
861	, Test Criteria			Escherichia coli	11/12/2013	Pending	devxtest
871	Gao, TestUI	11/11/1958	lkdsfkj	Klebsiella oxytoca	11/11/2013	Submitted	devxtest
872	D, Testzip	11/12/1950	2321321	Enterobacter aerogenes	11/11/2013	Submitted	devxtest
899	T, Test	01/23/1980	3232132	Citrobacter spp.	11/11/2013	Submitted	devxtest

previous | 1 | 2 | 3 | next

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report - Sample Hospital

Patient information

Patient name: Duck, Daffy
MRN: 1234
Admission date: 03/13/2014
Date of birth: 11/13/1973
SSN (last 4):
Race:
Address: 122 S. Michigan, Chicago, IL 60603

XDRO culture information

Organism: Klebsiella pneumoniae
Culture date: 02/14/2014
XDRO criterion: Molecular test
Specimen source:
Mechanism of resistance: KPC
Comments:

Submitted by ROBYNN LEIDIG, 03/14/2014, Sample Hospital

Go Back | Edit | Delete | Print

XDRO registry

Sample Hospital change facility

Test User1 | Home | Help | Go Back | Logout

XDRO Report - Sample Hospital

Patient information

Patient name: Duck, Daffy
MRN: 1234
Admission date: 03/13/2014
Date of birth: 11/13/1973
SSN (last 4):
Race:
Address: 122 S. Michigan, Chicago, IL 60603

XDRO culture information

Organism: Klebsiella pneumoniae
Culture date: 02/14/2014
XDRO criterion: Molecular test
Specimen source:
Mechanism of resistance: KPC
Comments:

Submitted by ROBYNN LEIDIG, 03/14/2014, Sample Hospital

Reason for deleting the above record: Please Select Reason: **Comment:**

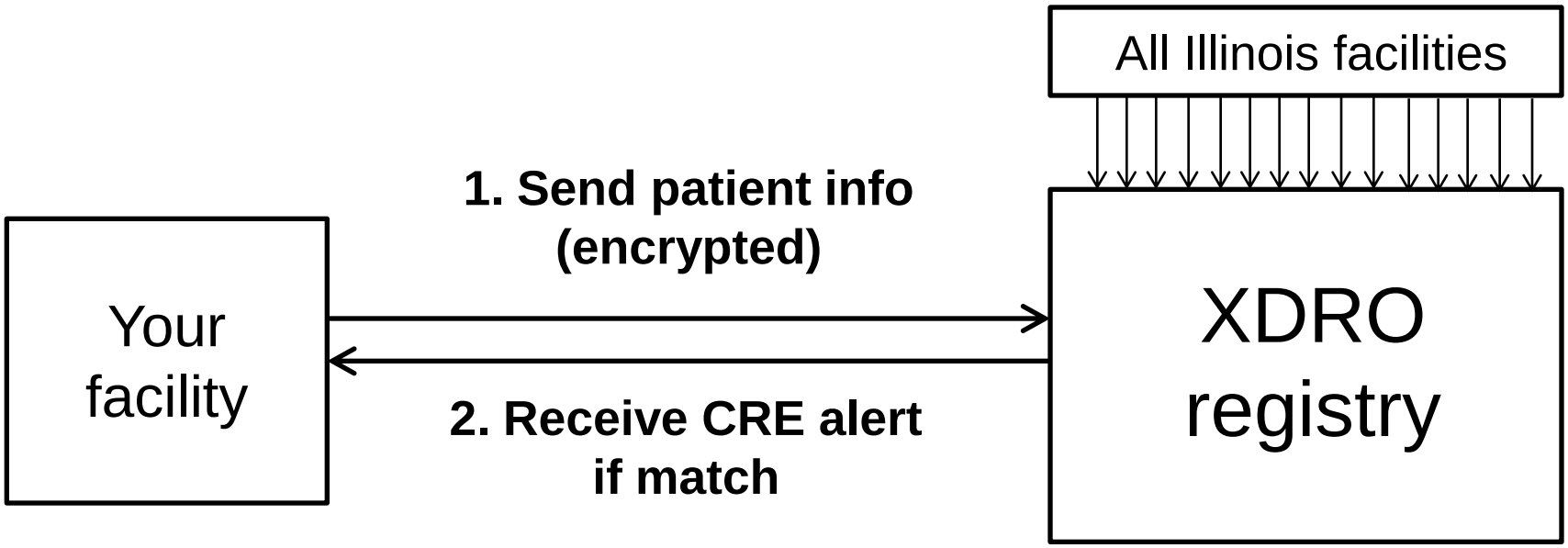
De-colonization or infection resc on to delete the record.

- Please Select Reason:
- Data entry error
- Laboratory testing error
- Patient deceased
- Not a CRE
- Other

Querying the XDRO registry

XDRO registry

Planned: Automated CRE Alerts



Automated alerts will be piloted at limited hospitals in 2014; anticipate wider availability in 2015

Take home points

1. Stand alone reference labs
   - Report labs on behalf of facilities
   - If the facility is not listed, let us know by email: DPH.XDROregistry@Illinois.gov
   - Encourage facilities to register and report on their own
2. Hospital-based labs
   - Submit under your hospital name
   - Coordinate submission with the infection prevention dept.
3. Hospital-based reference labs
   - Ideally, the IP will submit “local” isolates
   - The laboratory would submit on behalf of other facilities

Question and answer forum

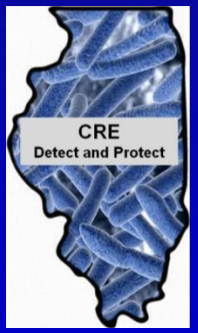
XDRO registry

Upcoming Webinar

Target Audience	Topics	Date
Long Term Care	Antibiotic Use in Nursing Homes	June 26

CRE webinar recordings and slides will be available at https://www.xdro.org/cre-campaign/index.html

Illinois Department of PUBLIC HEALTH



Survey and Continuing Education

- Fill out webinar evaluation on SurveyMonkey at: https://www.surveymonkey.com/s/cre-labs
- Instructions on applying for CEUs will appear at the end of the SurveyMonkey
- Surveys and CEU applications must be completed by **Monday, June 16**!

Illinois Department of PUBLIC HEALTH

Contact: Robynn.Leidig@illinois.gov or Angela.Tang@illinois.gov