CRE Detect and Protect Crash Course

Illinois Infection Prevention and CRE Workshop

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Disclosures

- I have nothing to disclose

I want to cover:

- What is CRE and XDRO?
- The roles we each play
- What happens after a CRE case is reported?

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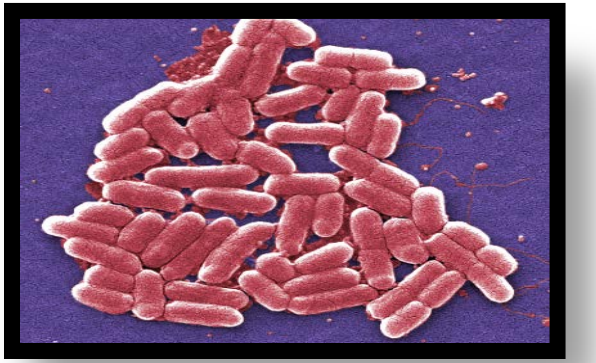
What is CRE?

Carbapenem
Resistant
Enterobacteriaceae

Carbapenem:
Class of broad-spectrum antibiotics

Resistant:
Bacteria with mutations that make antibiotics ineffective



Enterobacteriaceae:
Family of bacteria that includes *Escherichia coli*, *Klebsiella sp.*, *Enterobacter*

CRE is

- KPC
- NDM
- OXA
- VIM
- IMP

CRE is **not**…

- VRE
- Pseudomonas
- Acinetobacter
- ESBLs

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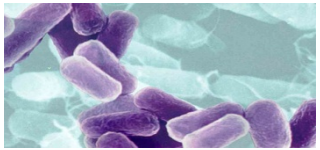
Why is CRE such a big deal?

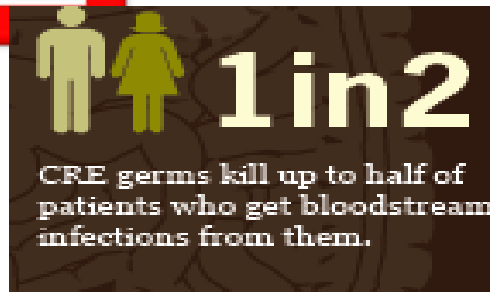


- Deadly infection
- Few treatment options (if any)
- Spreading quickly

HAZARD LEVEL
URGENT

These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

Clostridium difficile (C. difficile), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)



http://www.cdc.gov/drugresistance/threat-report-2013/

What is the XDRO registry?

XDRO = e**X**tensively **D**rug **R**esistant **O**rganisms

XDRO registry = where CRE is reported in Illinois*

Began: November 1, 2013

Required to report:

- Acute care hospitals
- Long-term acute care hospitals
- Long-term care facilities
- Laboratories

* Illinois healthcare facilities and laboratories are required to report CRE to the XDRO registry per 77 Ill. Adm. Code 690, Control of Communicable Diseases Code.

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But wait, let's take a step back…

We all have a role to play:

State Health Department (IDPH)

Local Health Departments

Health Care Facilities

Laboratories

Other?

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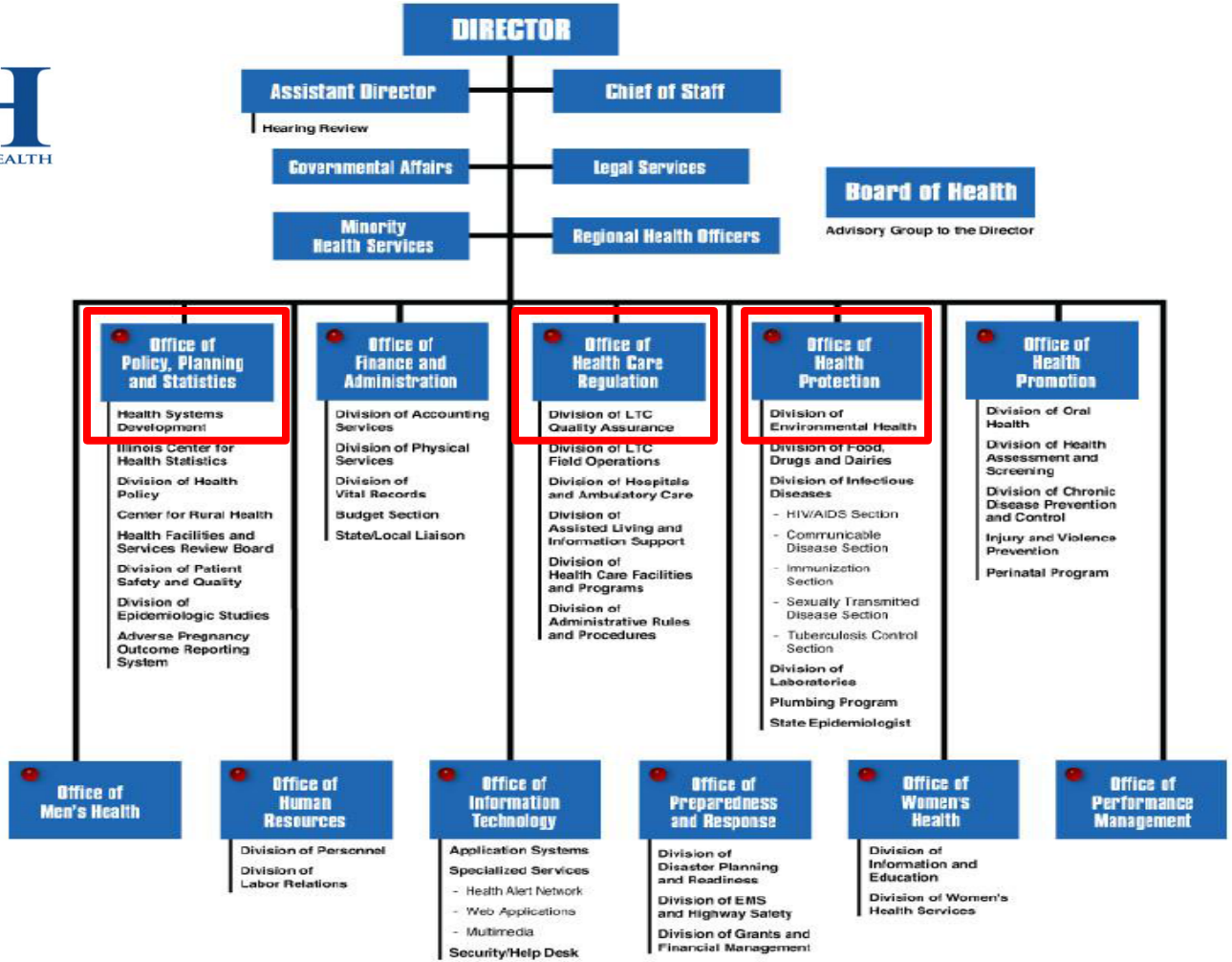

IDPH Office of Health Care Regulation

License, inspect or certify those that must comply with state and federal regulations.

May include:

- Ambulatory surgical treatment centers (ASTCs)
- Certified nurse aides
- Health maintenance organizations (HMOs)
- Home health agencies
- Hospices
- Hospitals
- Laboratories
- Nursing homes
- Physical therapists in independent practice
- Poison control resource centers
- Pregnancy termination centers
- Rural health clinics
- Sperm and tissue bank

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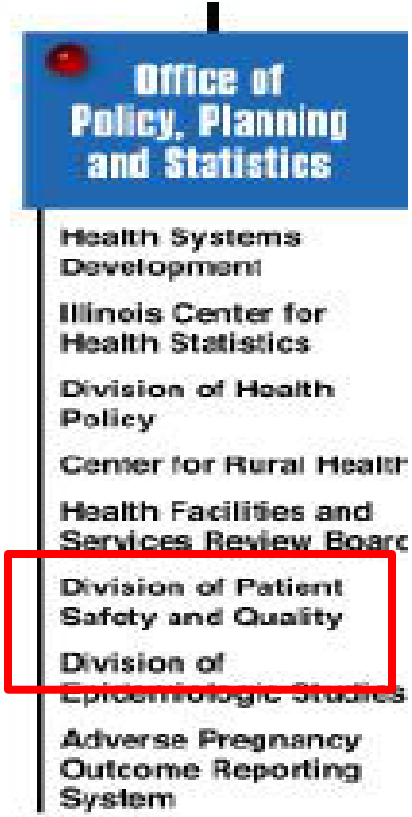
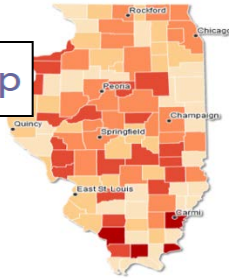


IDPH Division of Patient Safety and Quality

- Promotes health care transparency
- Collects and reports health care provider data
- **Develops and implements programs for improving the quality and value of health care**

Illinois Hospital Report Card
and Consumer Guide to Health Care

Illinois Public Health Community Map



XDRO registry

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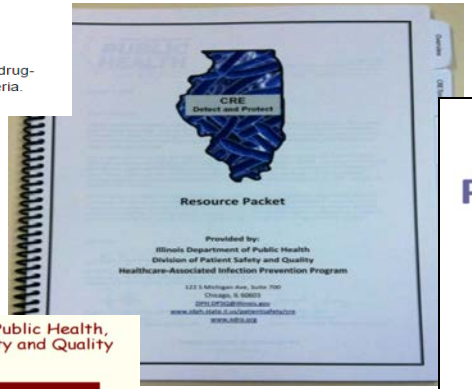
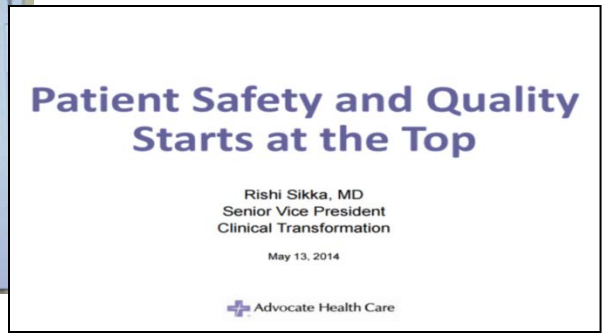
CRE "Detect and Protect" Campaign

- 30 stakeholder CRE Taskforce
- 6 webinars: 605 people
- 2 packets: 470 facilities
- 2 websites
- 1 Press release
- 3 regional workshops





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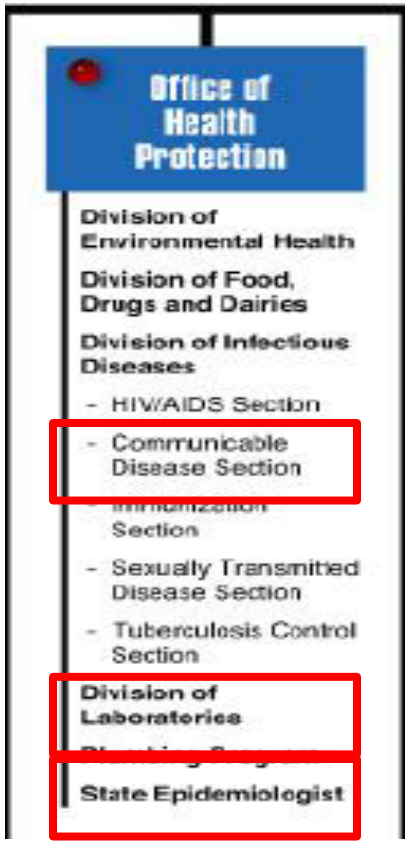
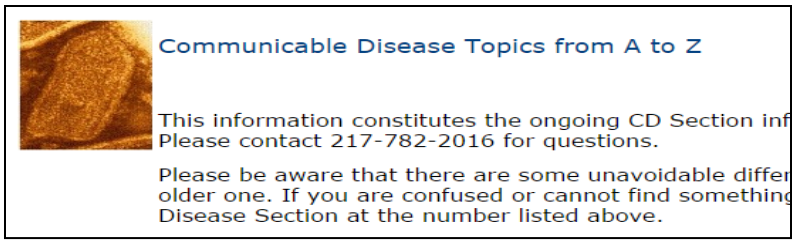
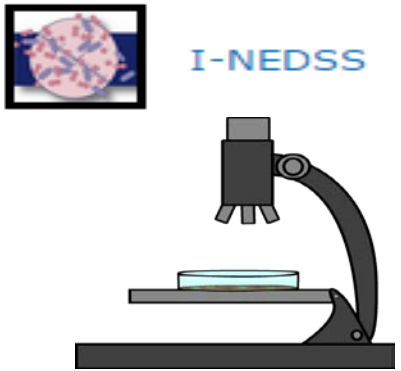
IDPH Division of Infectious Disease



- Protect people from infectious diseases through disease surveillance, analysis, immunization, and education

- Mandated reporting of certain infectious diseases to Illinois' National Electronic Disease Surveillance System (I-NEDSS)





IDPH and Local Health Departments

- Local Health Departments are typically the first point of contact

- Health care facilities are organized by Local Health Department jurisdictions

Local → State → Federal

HEALTHY CHICAGO
CHICAGO DEPARTMENT OF PUBLIC HEALTH

→

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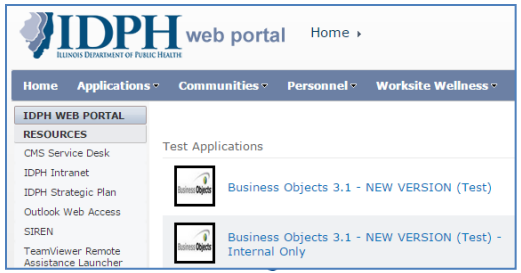
→

CDC

If I work at a Local Health Dept…

- Refer facilities to report CRE to the XDRO registry
- Notify IDPH about unusual CRE (e.g. NDM), or potential CRE clusters
- Investigate clusters in collaboration with IDPH
- Facilitate communication when patients are transferred
- Refer facilities to CDC CRE Toolkit guidelines
- Maintain vigilance for clusters of CRE via INEDSS B.O.
- Refer CRE questions to IDPH CRE Team



If I work at a Health Care Facility…

- Communicate with the lab about CRE testing
- Report CRE cases to the XDRO registry
- Use the XDRO registry to query for admitted patients/ residents
- Use the XDRO registry (or some other method) to keep track of CRE patients/ residents
- Contact your local health department about unusual CRE or potential CRE clusters
- Implement appropriate infection control measures according to the CDC CRE Toolkit*

*http://www.cdc.gov/hai/organisms/cre/cre-toolkit/

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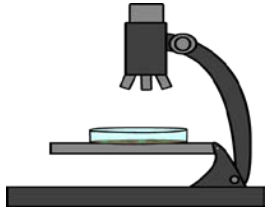
If I work at a Laboratory…



- Communicate with your facilities about what type of CRE testing you do
- Report CRE cases to the XDRO registry
- Submit your first five CRE isolates to IDPH labs for validation testing (by 7/31/15)
- Submit any unusual CRE (e.g. NDM) to IDPH labs to send to CDC for confirmatory testing*

*Coordinate with your Local Health Department

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What happens after CRE cases are reported to the XDRO registry?

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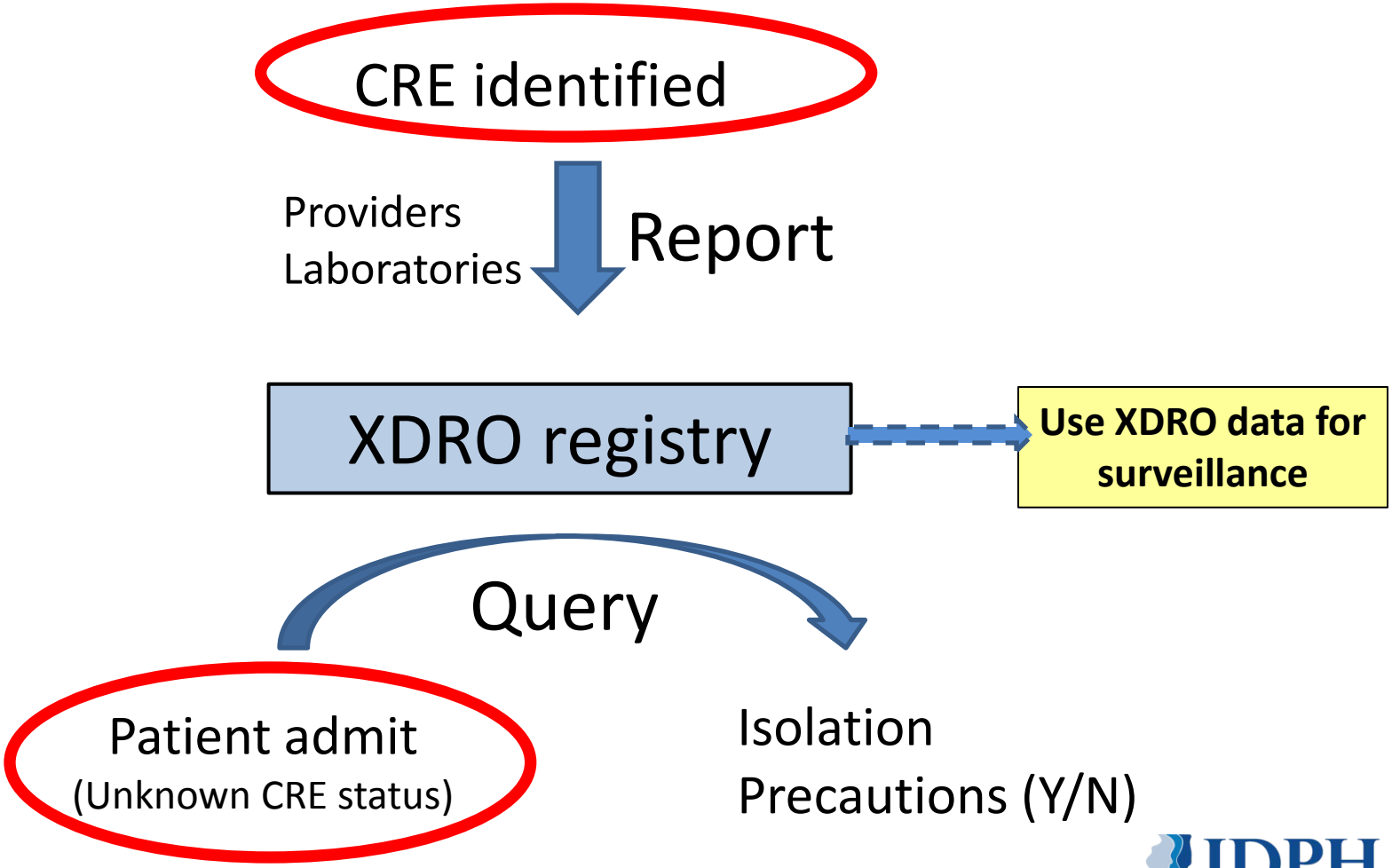
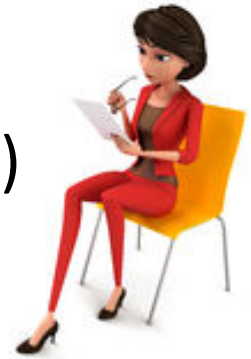

CRE identified
Providers
Laboratories
Report
XDRO registry
Use XDRO data for surveillance
Query
Patient admit
(Unknown CRE status)
Isolation
Precautions (Y/N)

Once CRE cases are in the XDRO registry…

- Health Departments review the cases
  - Look for anything unusual (e.g. NDM, clusters)
  - Follow-up as necessary



- IDPH does not publicly report CRE cases by facility

- For now, CRE cases are in the XDRO registry indefinitely

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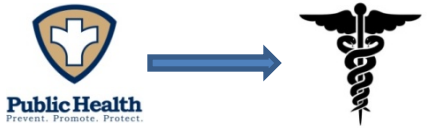
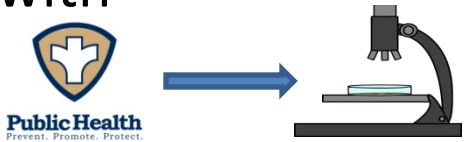
What happens if there is an unusual CRE or potential cluster?

1. IDPH will contact the local health department with jurisdiction over the involved facility

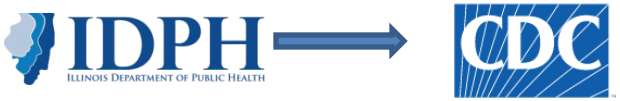
2. Local health department (or IDPH) will follow up with the healthcare facility to gather more information



3. Local health department (or IDPH) may follow up with the laboratory that identified the CRE



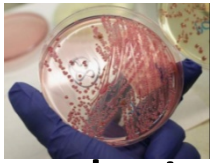
4. IDPH will notify CDC (as necessary)



More information for a CRE case

- Foreign travel
- Foreign healthcare exposure
- Invasive procedures
- Past medical history

- Dates and locations of previous healthcare facility exposure
- Surveillance cultures



- Adherence to CDC CRE Toolkit recommendations

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Closing up a CRE case

- Make sure facilities know what to do to prevent spread of CRE
- Summary report to local health departments, IDPH, and CDC, as necessary

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Who do I call for questions about CRE?

If you're a **Health Care Facility** or **Laboratory**, start with your Local Health Department

If you're a **Local Health Department**, contact IDPH CRE Team:

Mary Alice Lavin, Hektoen (MaryAlice.Lavin@illinois.gov)

Jodi Morgan (Jodi.Morgan@illinois.gov)

Angela Tang, Hektoen (Angela.Tang@illinois.gov)

Robynn Cheng Leidig (Robynn.Leidig@illinois.gov)

When in doubt, call IDPH Division of Infectious Diseases at 217-785-7165 or email dph.xdroregistry@illinois.gov

Websites: www.xdro.org; www.idph.state.il.us/patientsafety/cre/

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Recognizing Carbapenem-Resistant *Enterobacteriaceae*: Crash Course for Non-Microbiologists

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Department of Medical Laboratory Science
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Disclosures

- Research support through the CDC Chicago Prevention Intervention Epicenter (C-PIE), RA Weinstein, PI and MK Hayden, Co-I
- Industry sponsored grants/contracts (Cepheid)
- Unpaid research (AdvanDx)

Objectives

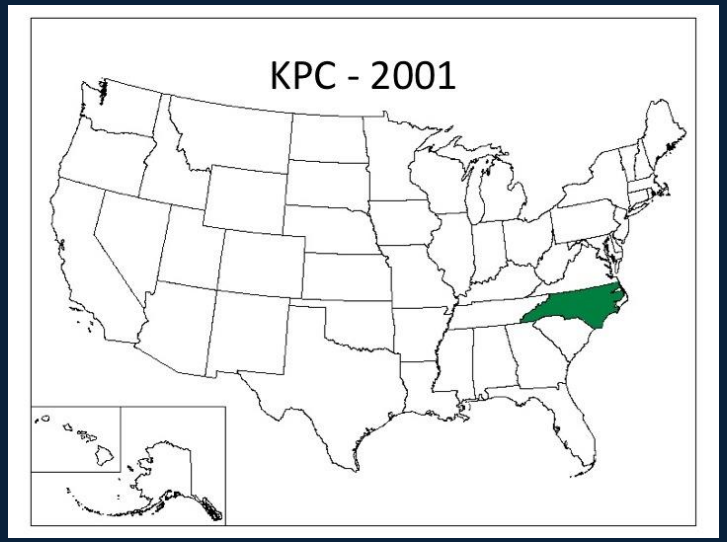
By the end of this presentation, the learner will be able to:

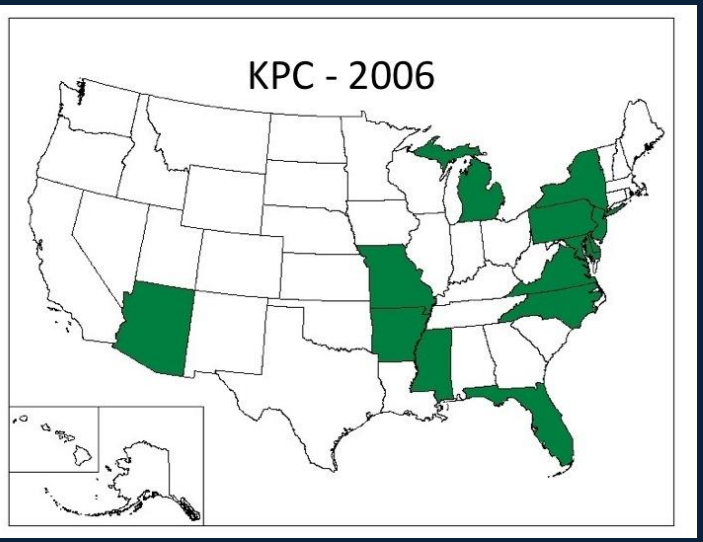
1. Define Carbapenem-Resistant *Enterobacteriaceae* (CRE)
2. Discuss laboratory techniques used to identify CRE
3. Distinguish between different mechanisms of carbapenem resistance

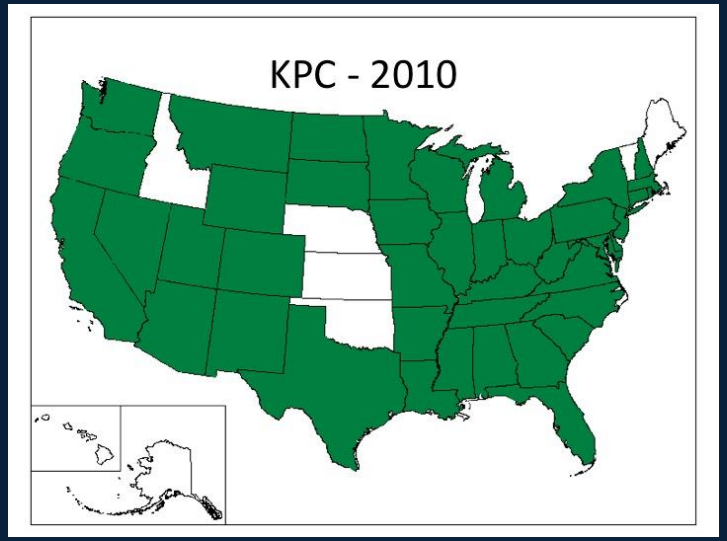
Carbapenem-Resistant *Enterobacteriaceae*

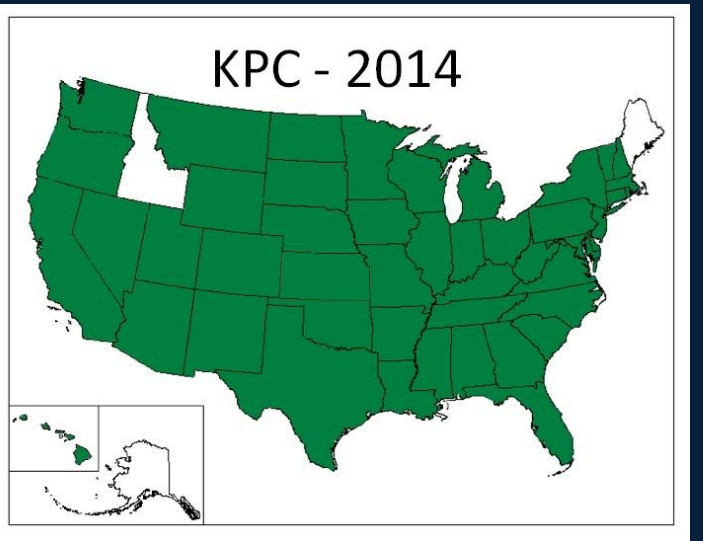
- CRE are serious public health threat
  - *Klebsiella pneumoniae* carbapenemase (KPC) is the most common worldwide

http://www.cdc.gov/drugresistance/biggest_threats.html


KPC - 2001

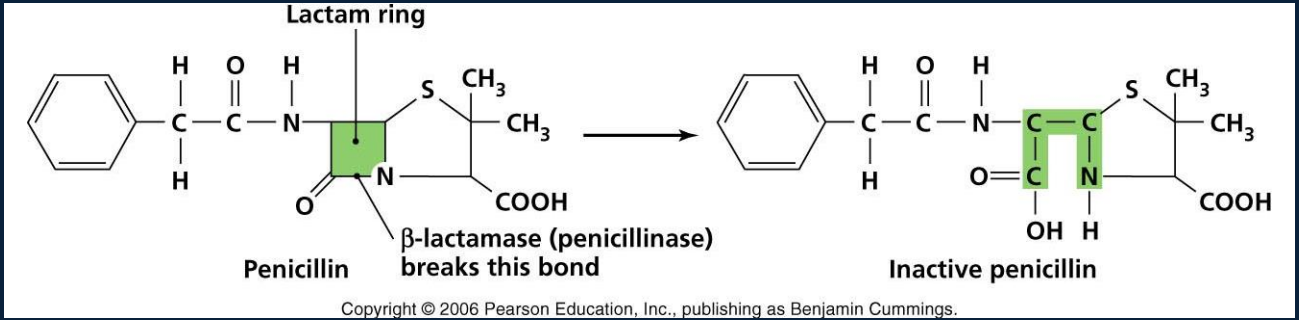

KPC - 2006


KPC - 2010


KPC - 2014

Carbapenems

- Imipenem
- Meropenem
- Ertapenem
- Doripenem

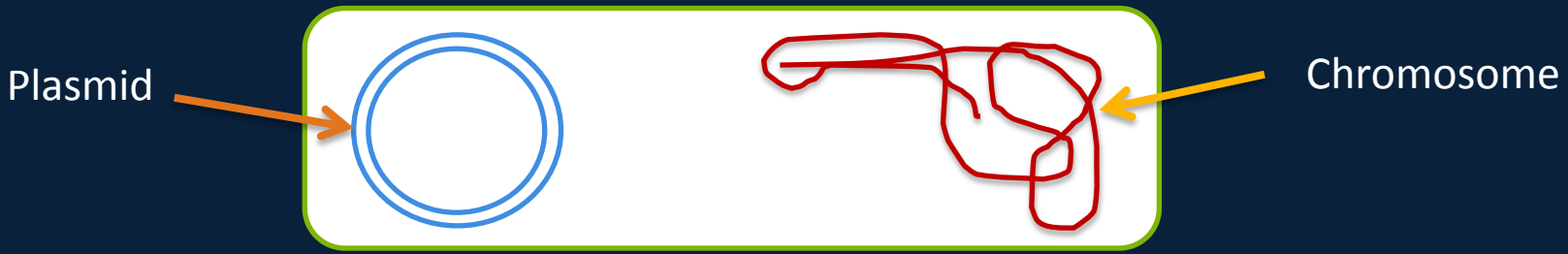


Carbapenemases

- Carbapenem-hydrolyzing beta-lactamases that confer carbapenem resistance
- The carbapenemases have been organized based on amino acid homology into the Ambler molecular classification schema
  - Class A, C, and D share a serine residue in the active site
  - Class B enzymes require the presence of zinc for activity

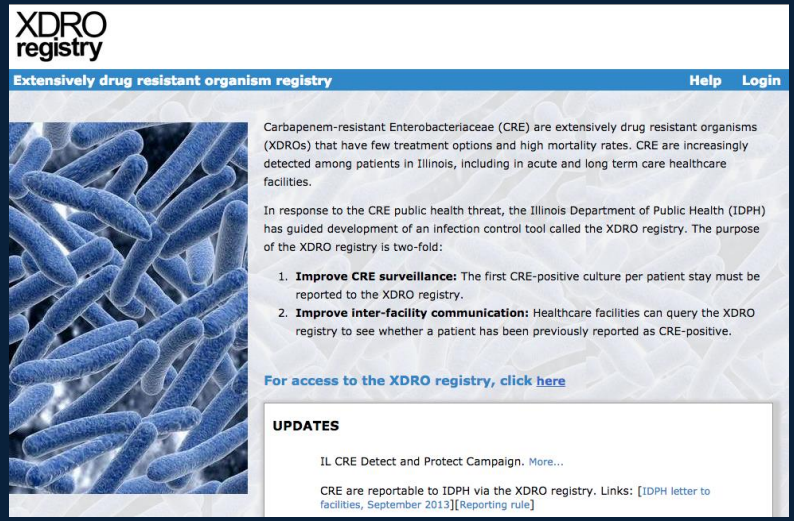
Carbapenemases

Ambler Class	Carbapenemase	Location of gene	Dissemination potential	Activity	Predominant Species
A	KPC	Plasmid	High	All β-lactams	*K. pneumoniae*
B	NDM-1	Plasmid	High	All β-lactams except aztreonam	*K. pneumoniae, E. coli*
D	OXA-48	Plasmid	High	Carbapenems, except 3rd gen cephalosporins	*K. pneumoniae, E. coli, E. cloacae*



Mandated Reporting in Illinois

- IDPH amended the Control of Communicable Diseases Code (77 Ill. Adm. Code 690) Rules to require reporting of CRE
- Began November 1, 2013
- XDRO Registry for CRE



Enterobacteriaceae

- *Enterobacteriaceae* are a large family of enteric Gram-negative bacilli

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Citrobacter* spp.
- *Enterobacter* spp.

- Other genera: *Proteus, Providencia, Serratia*

Defining CRE for the XDRO Registry

1. Molecular test (e.g. PCR) specific for a carbapenemase gene (e.g. *bla*$_{KPC}$, *bla*$_{NDM}$)

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

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

What is PCR?

- Polymerase chain reaction
- Laboratory method developed to rapidly generate copies of nucleic acids (DNA or RNA)
- Bacterial colony provides the template (DNA)
- Series of primers and probes specific for carbapenemase gene will bind to and recognize complementary sequence in bacterial DNA, if present
- Rapid cycles of denaturing, annealing, and extending will generate exponential copies of region of interest
- Fluorescent threshold → positive result

PCR

Pros

- Quick turn-around time
- Specific for carbapenemase
- Definitive
- Can multiplex targets into single assay (e.g. KPC/NDM)
- Does not require viable organisms

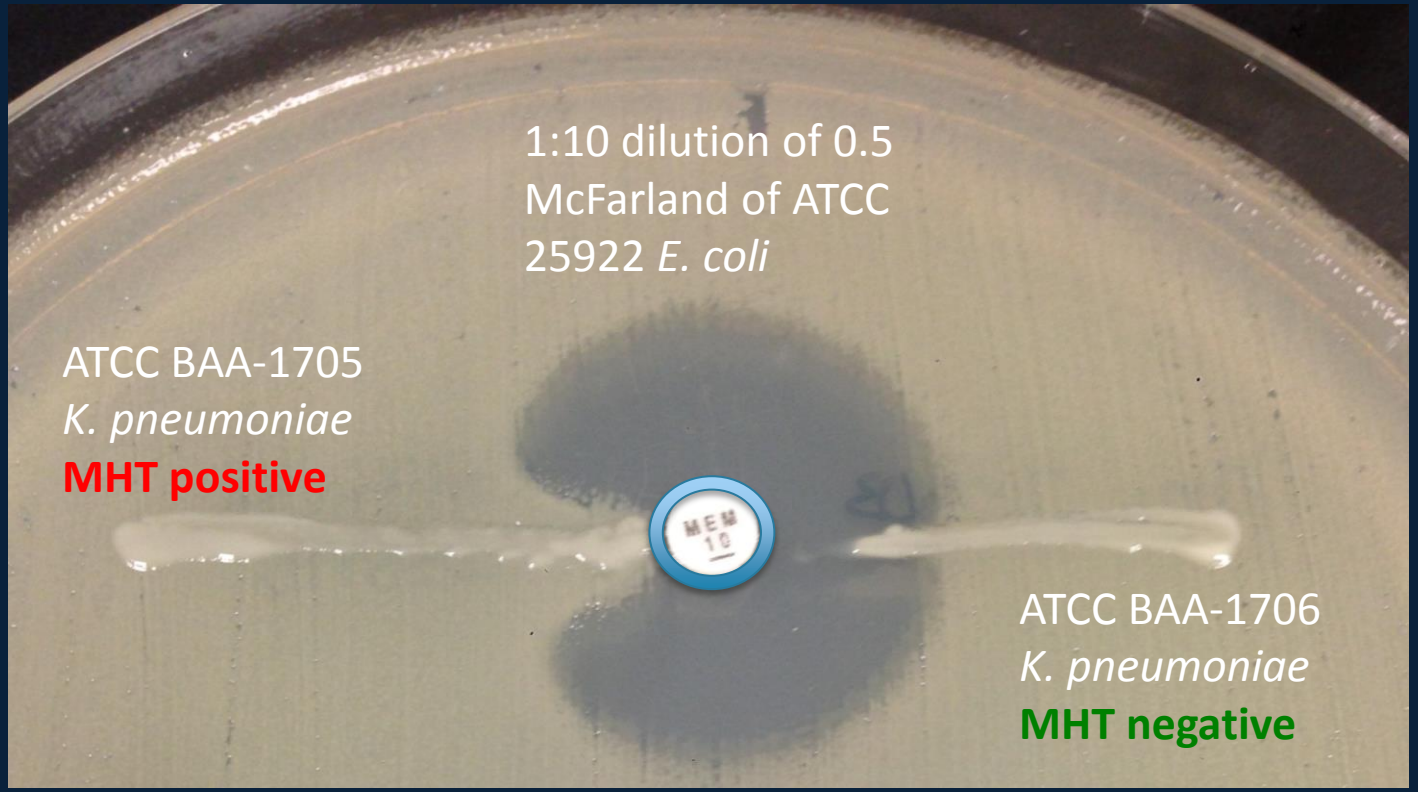
Cons

- Expensive
- High-complexity testing
- Organisms not available for additional testing, epidemiologic studies

Phenotypic Test: Modified Hodge

- Uses a pan-susceptible *E. coli* (indicator) to create a lawn of confluent growth on a Mueller Hinton agar plate
- Carbapenem disk applied to center of plate (meropenem or ertapenem)
- Suspicious isolates struck from center of disk to edge of plate
- Examine after 18-24 hour incubation for a growth of *E. coli* around the isolate streak

Modified Hodge Test



Modified Hodge Test

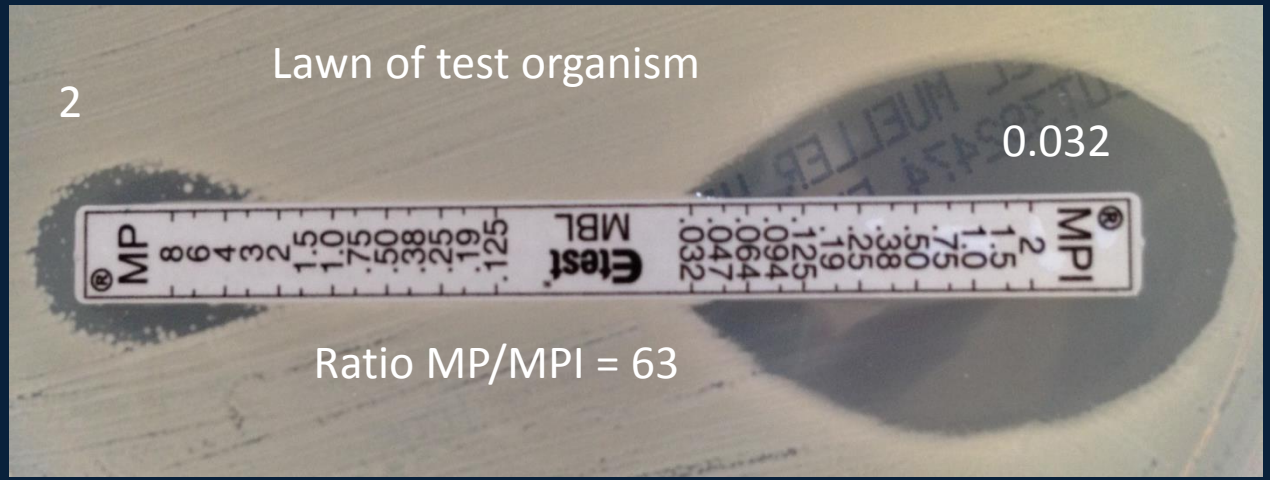
Pros

- Inexpensive
- Easy to perform
- Organisms available for additional testing

Cons

- Requires additional overnight incubation
- Not specific
- Lacks sensitivity for MBLs (e.g. NDM)

MβL Etest® Phenotypic Screening

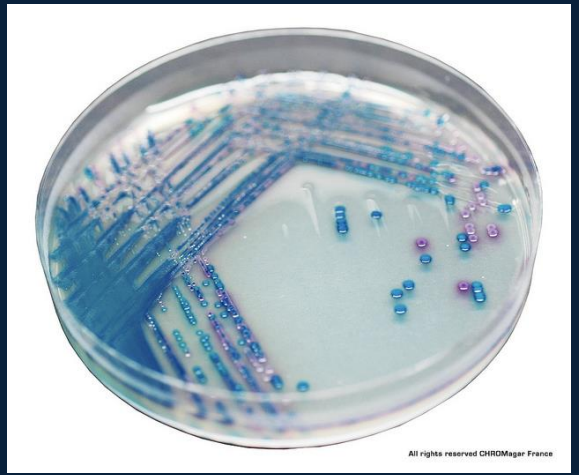


- Presence of MβL indicated by a reduction of the MP MIC by ≥ 3 doubling dilutions in the presence of EDTA
- Phenotypic method requires confirmation

Chromogenic Media

- CHROMagar™ KPC – research use only
- Brilliance™ CRE agar – not for sale in US
- chromID® CARBA agar
- HardyCHROM™ CRE agar

- Inexpensive and convenient
- No definitive ID
- Does not provide mechanism
- Studies with various sensitivity, specificity



Suspect KPC from a Micro Report

1 Klebsiella pneumoniae

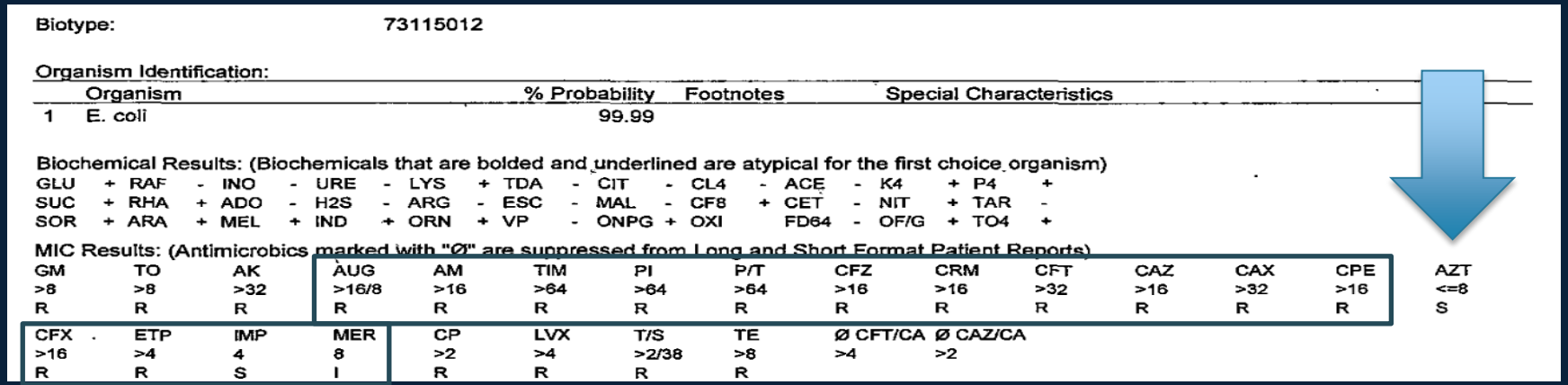
1 K. pneumoniae

Drug	MIC	Interps	Origin
Gentamicin	<=4	S	
Tobramycin	>8	R	
Amikacin	>32	R	
Amox/K Clav	>16/8	R	
Ampicillin	>16	R	
Ticar/K Clav	>64	R	
Piperacillin	>64	R	
Pip/Tazo	>64	R	
Cefazolin	>16	R	
Cefuroxime	>16	R	
Cefotaxime	>32	R	
Ceftazidime	>16	R	
Ceftriaxone	>32	R	
Cefepime	>16	R	
Aztreonam	>16	R	
Cefoxitin	>16	R	
Ertapenem	>4	R	
Imipenem	>8	R	IMP ENT R
Meropenem	>8	R	
Ciprofloxacin	>2	R	
Levofloxacin	>4	R	
Trimeth/Sulfa	>2/38	R	
Tetracycline	8	I	

- *Enterobacteriaceae*
- Non-susceptible to all β-lactam antibiotics
  - Penicillins
  - Cephalosporins
  - Cephamycins
  - Monobactams
  - Carbapenems

bla$_{KPC}$ PCR = POSITIVE

Suspect NDM from a Micro Report



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)

GM	TO	AK	AUG	AM	TIM	PI	P/T	CFZ	CRM	CFT	CAZ	CAX	CPE	AZT
>8	>8	>32	>16/8	>16	>64	>64	>64	>16	>16	>32	>16	>32	>16	<=8
R	R	R	R	R	R	R	R	R	R	R	R	R	R	S

CFX	ETP	IMP	MER	CP	LVX	T/S	TE	Ø CFT/CA	Ø CAZ/CA
>16	>4	4	8	>2	>4	>2/38	>8	>4	>2
R	R	S	I	R	R	R	R		

- *Enterobacteriaceae*
- Non-susceptible to all β-lactam antibiotics
  - except aztreonam

$bla_{\text{NDM-1}}$ PCR = POSITIVE

Suspect OXA-48 from a Micro Report

01 Klebsiella pneumoniae

01 K. pneumoniae

Drug	MIC	Interps
Gentamicin	>8	R
Tobramycin	<=4	S
Amikacin	>32	R
Amox/K Clav	>16/8	R
Ampicillin	>16	R
Amp/Sulbactam	>16/8	R
Pip/Tazo	>64	R
Cefazolin	>4	R
Cefuroxime	>16	R
Cefotaxime	8	R
Ceftriaxone	8	R
Cefepime	<=4	S
Ertapenem	>2	R
Imipenem	2	I
Meropenem	8	R
Ciprofloxacin	>2	R
Levofloxacin	>4	R
Trimeth/Sulfa	<=2/38	S
Tetracycline	>8	R
Tigecycline	<=2	S

- *Enterobacteriaceae*
- Non-susceptible to β-lactam antibiotics
- Remains susceptible to 4th generation cephalosporin

bla$_{\text{OXA-48}}$ PCR = POSITIVE

Summary

- XDRO Registry is tracking Carbapenem-resistant *Enterobacteriaceae* (CRE)
- Report isolates based off molecular, phenotypic or susceptibility test results
  - Reporting using only AST data is valid only if isolate is *E. coli* or *Klebsiella* spp.
- Some patterns in susceptibility profiles may suggest a particular mechanism, but must to be confirmed

Questions

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Robert Weinstein

Contact Information

- Questions? Comments? Troubleshooting?

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Carbapenem-Resistant Enterobacteriaceae (CRE) in Illinois: A Situational Update

Allison Arwady, MD, MPH

Southern Illinois Infection Prevention and CRE Workshop

July 23, 2015

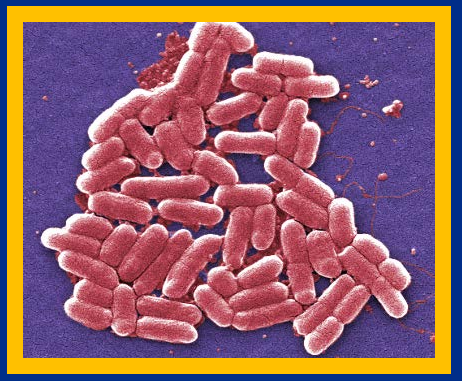
Conflict of Interest and Disclaimer

No conflicts of interest to report.

The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Illinois Department of Public Health.

Carbapenem-Resistant Enterobacteriaceae (CRE)

- **Enterobacteriaceae: Large family of bacteria**
  - *Escherichia coli, Klebsiella sp., Enterobacter sp….*



- **Carbapenem Resistance**
  - CRE can have an enzyme (*-ase*) that breaks down carbapenem antibiotics and makes them ineffective
    - *Klebsiella pneumoniae* carbapenemase (KPC)
    - New Delhi Metallo-beta-lactamase (NDM)

- **Patients who develop invasive infections with CRE have few antibiotic options and a high mortality rate**

Recommendations: Keep It Simple

- **Examples: *E. coli* and urinary tract infections**
- **Communication between labs and care facilities**
- **Original susceptibility reports**

BLOOD CULTURE (PERIPHERAL) (Abnormal):
PROCEDURE: BLOOD CULTURE (PERIPHERAL)
SOURCE: BLOOD
COLLECTED: [redacted]

---------- FINAL REPORT ----------

FINAL REPORT [redacted]
GROWTH OF GRAM NEGATIVE RODS
FINAL IDENTIFICATION: KLEBSIELLA PNEUMONIAE
This isolate demonstrates carbapenemase production.
Carbapenems, cephalosporins, and penicillins are
unlikely to be effective in treatment of serious
infections. Contact precautions required.

---------- SUSCEPTIBILITY TESTING ----------

	K PNEUMO			
	MIC mcg/ml	MIC INTERP	MIC mcg/ml	ET INTERP
TRIMETH/SULFA	>2/38	RESISTNT		
CEFAZOLIN	>16	RESISTNT		
TIGECYCLINE			1.00	SUSCEPT
LEVOFLOXACIN	>4	RESISTNT		
CEFOXITIN	16	INTERMED		
PIP/TAZOBACTAM	>64	RESISTNT		
TICARCIL/K CLAV	>64	RESISTNT		
CEFTRIAXONE	>32	RESISTNT		
GENTAMICIN	<=4	SUSCEPT		
TOBRAMYCIN	>8	RESISTNT		
AMIKACIN	16	SUSCEPT		
IMIPENEM	8	RESISTNT		
MEROPENEM	>8	RESISTNT		
CEFEPIME	16	RESISTNT		
COLISTIN			.38	SUSCEPT
A ERTAPENEM	>4	RESISTNT		

Antibiotic Use: Key Driver of Resistance

In 2010 alone

- 73 billion units of antibiotics used in humans
  - 10 antibiotic units for every man, woman, and child on earth; 36% increase from 2000
  - India and China were largest consumers by country
    - However, half of per-capita use compared to US (22 units/person)
- 63,151 tons of antibiotics used in livestock

- Van Boeckel et al. The Lancet 2014
- Van Boeckel et al. PNAS 2015

Slides: Trick, Lin (CDC Prevention Epicenter)

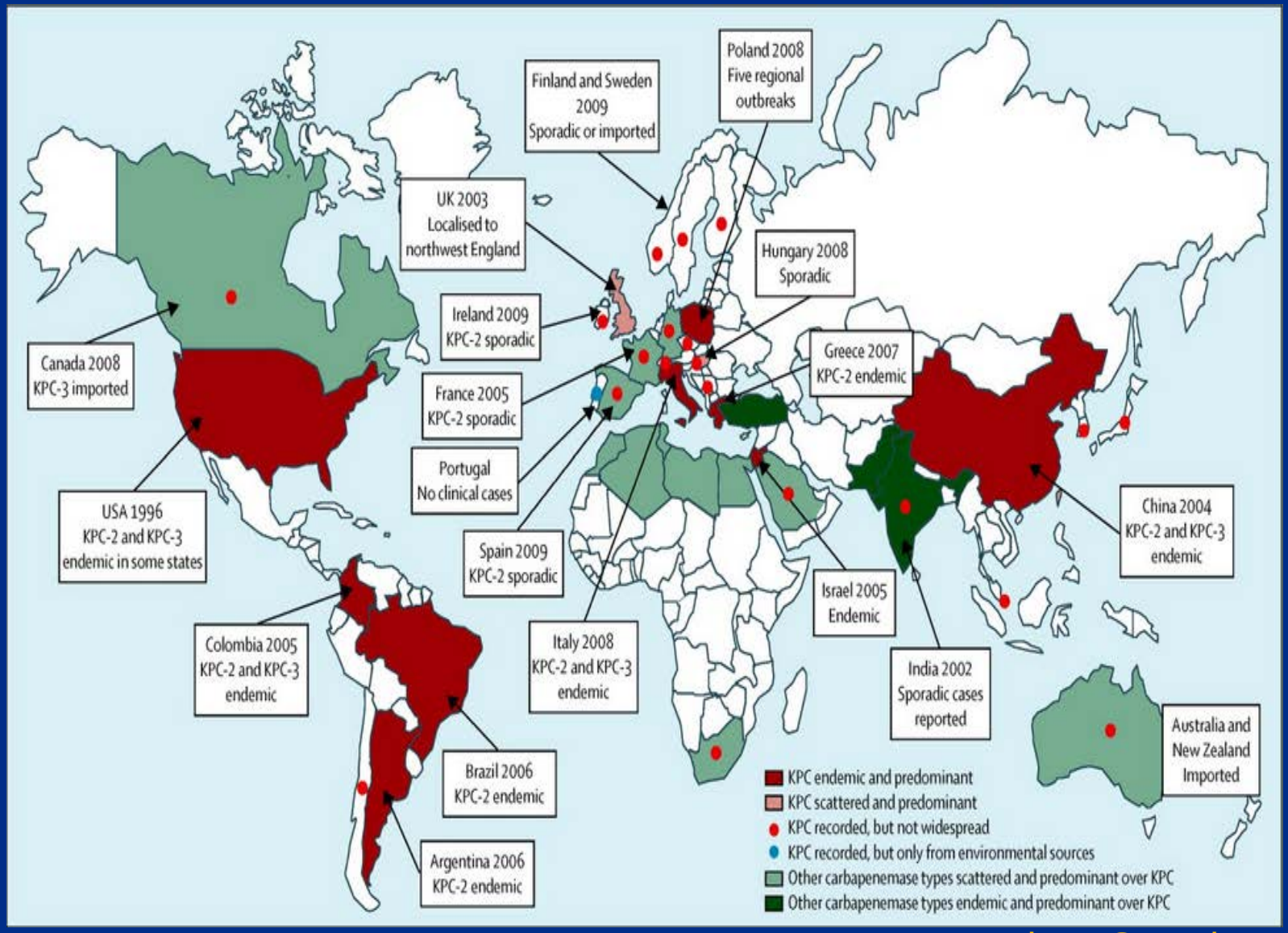
The ABCs of CRE

Class	Enzyme
A	KPC
B (metallo-β-lactamases)	NDM-1, VIM, IMP
D	OXA

KPC – Quick Facts

- *"Klebsiella pneumoniae* carbapenemase"
- Origin: USA
- First identified: 1996
- Associated bacteria:
  - *Klebsiella pneumoniae >>> E. coli > Enterobacter*
- Primarily found in debilitated hospitalized patients (not community)

KPC Global Spread

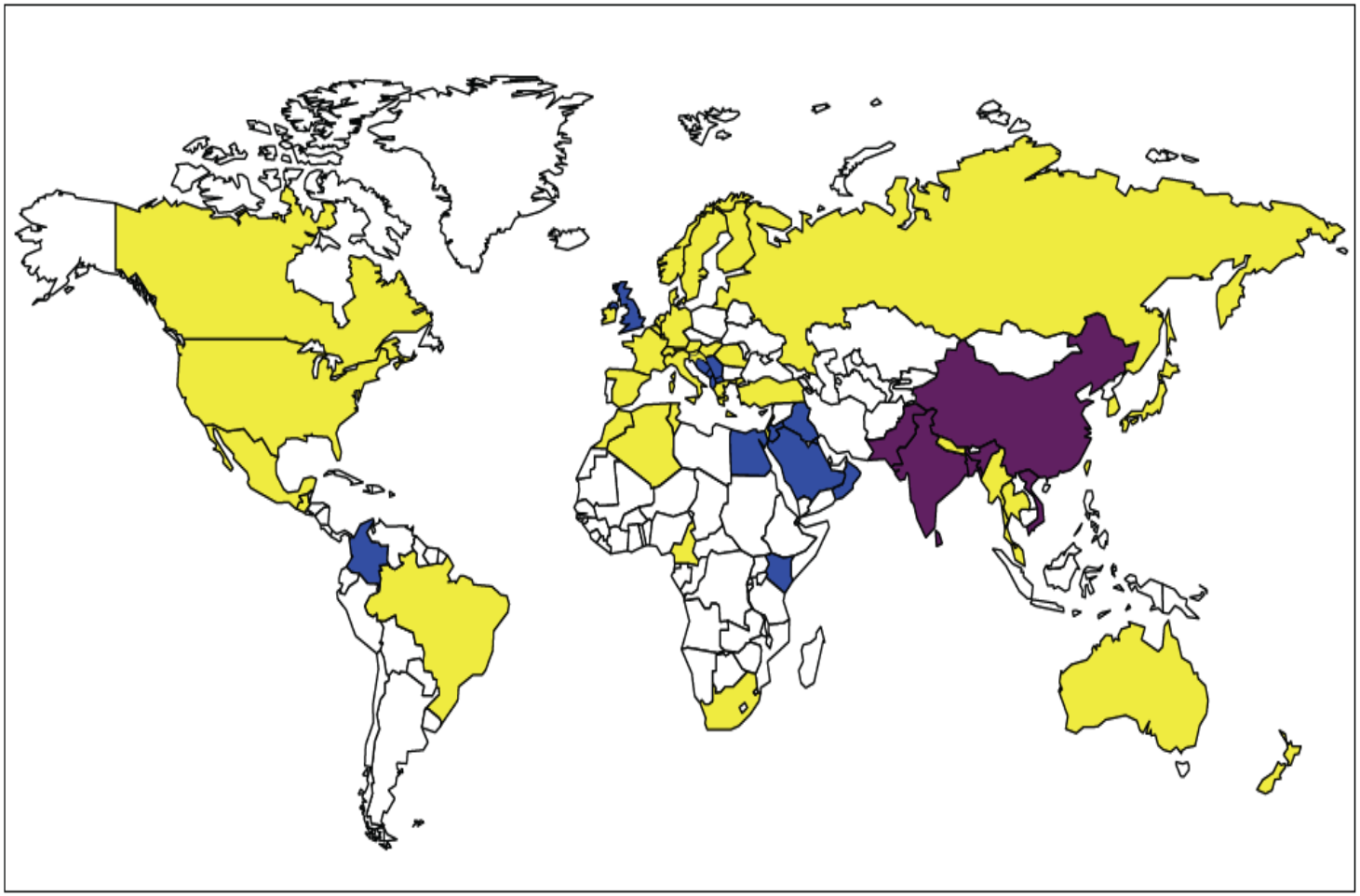


Munoz-Price LS et al.
Lancet ID. 2013

NDM – Quick Facts

- “New Delhi metallo-β-lactamase”
- Origin: South Asian continent
- First identified: 2008
- Species: *Klebsiella pneumoniae* = *E. coli*, others (*Enterobacter*, *Citrobacter*, *Proteus*, *Salmonella*, *Providentia*, *Acinetobacter*, *Pseudomonas*)
- Found in both in hospitalized pts and in the community

NDM Global Distribution

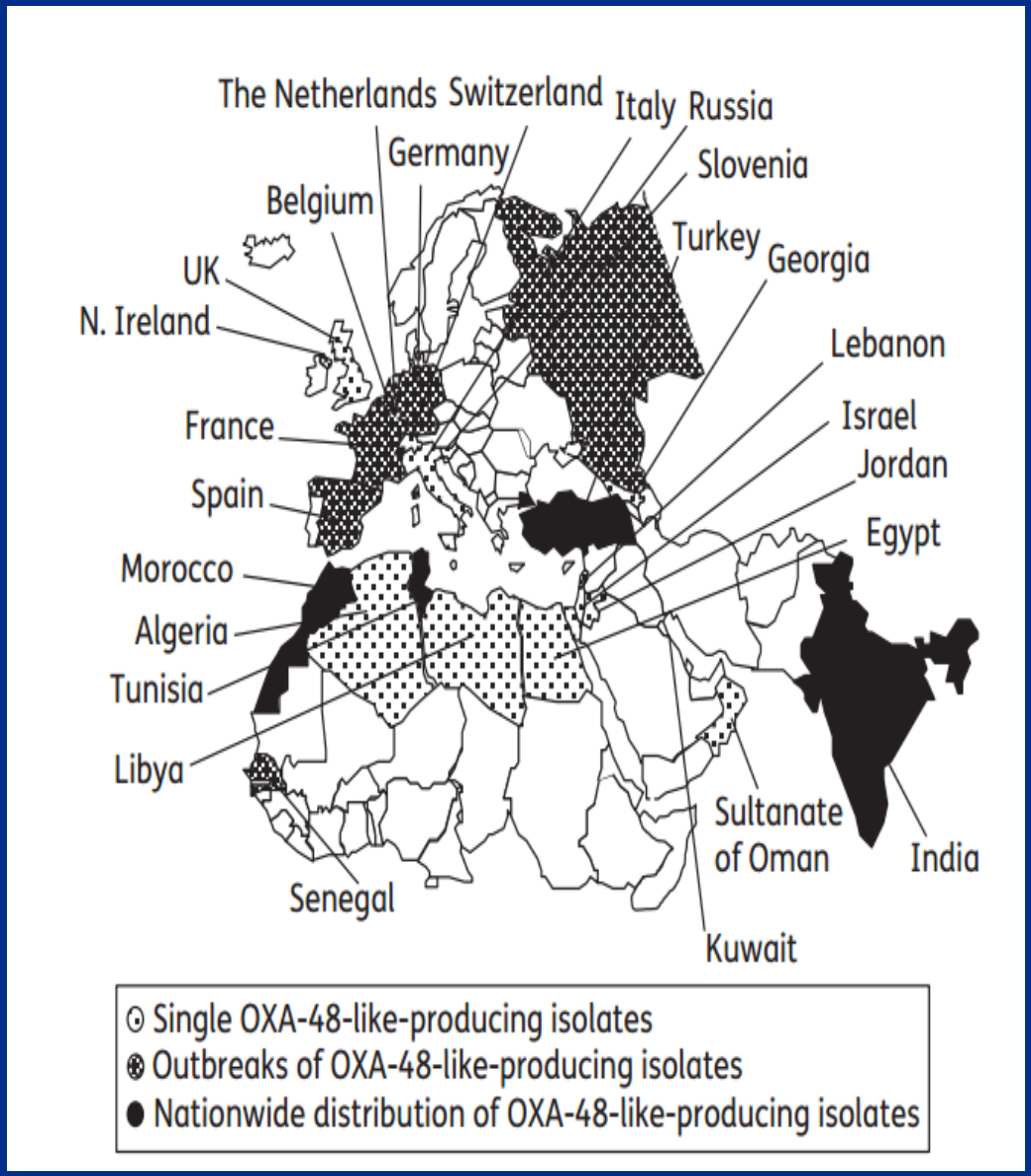


Dortet et al. BioMed Res Int. 2014

OXA-48 Quick Facts

- OXA = “Oxacillinase”
- Origin: Turkey
- First identified: 2001
- Claim to fame: is a weak carbapenemase, and does not have cephalosporin resistance.
- Species: *Klebsiella pneumoniae* >>> *E. coli*, others

OXA-48 Global



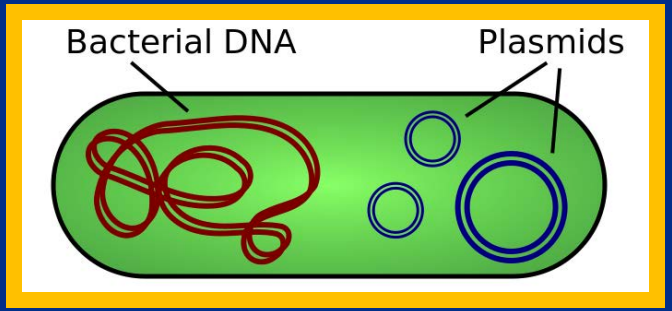
Poirel et al. J Antimicrob Chemo 2012; 67: 1597-1606

An Illinois Outbreak of NDM: First Steps

- **Suspected NDM-producing CRE isolates identified by clinical laboratory in Illinois (first in March 2013)**
  - Screened for metallo-β-lactamase (MBL) production by using carbapenem disks with and without inhibitors (Rosco Diagnostica)
  - MBL-positive isolates submitted to CDC for confirmation using polymerase chain reaction
- **August 2013 on-site investigation at Hospital A**
  - At that time, 9 confirmed NDM-producing *E. coli* cases

Background: New Delhi Metallo-β-Lactamase-Producing CRE (NDM)

- **First reported in U.S. in 2009, in international travelers**



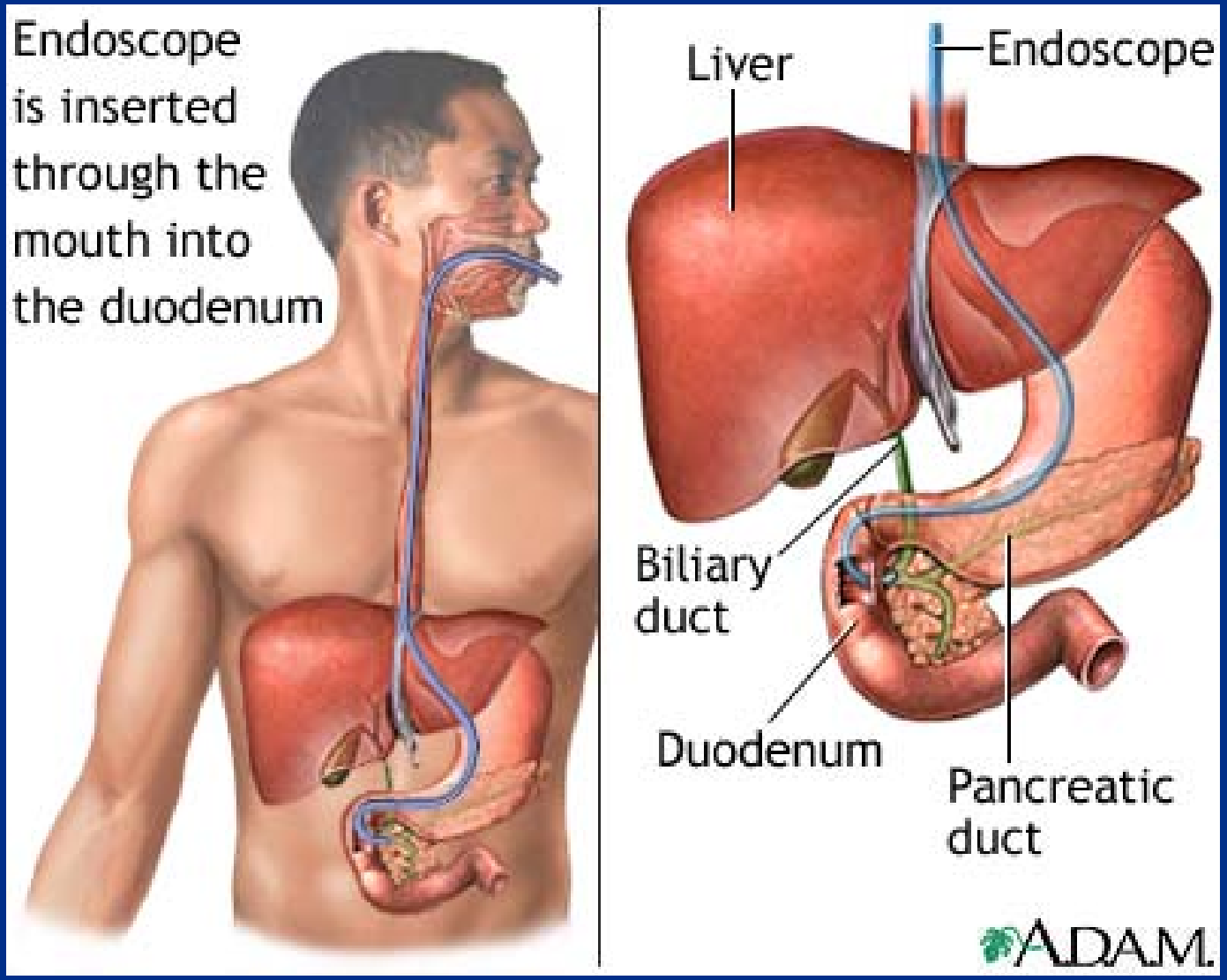
- **Gene encoding NDM-1: bla_{NDM-1}**
  - On plasmids, transferable between species and genera (can replicate independently from chromosomal DNA)

- **Between 2009 and 2012, 27 NDM isolates nationwide had been confirmed by CDC**

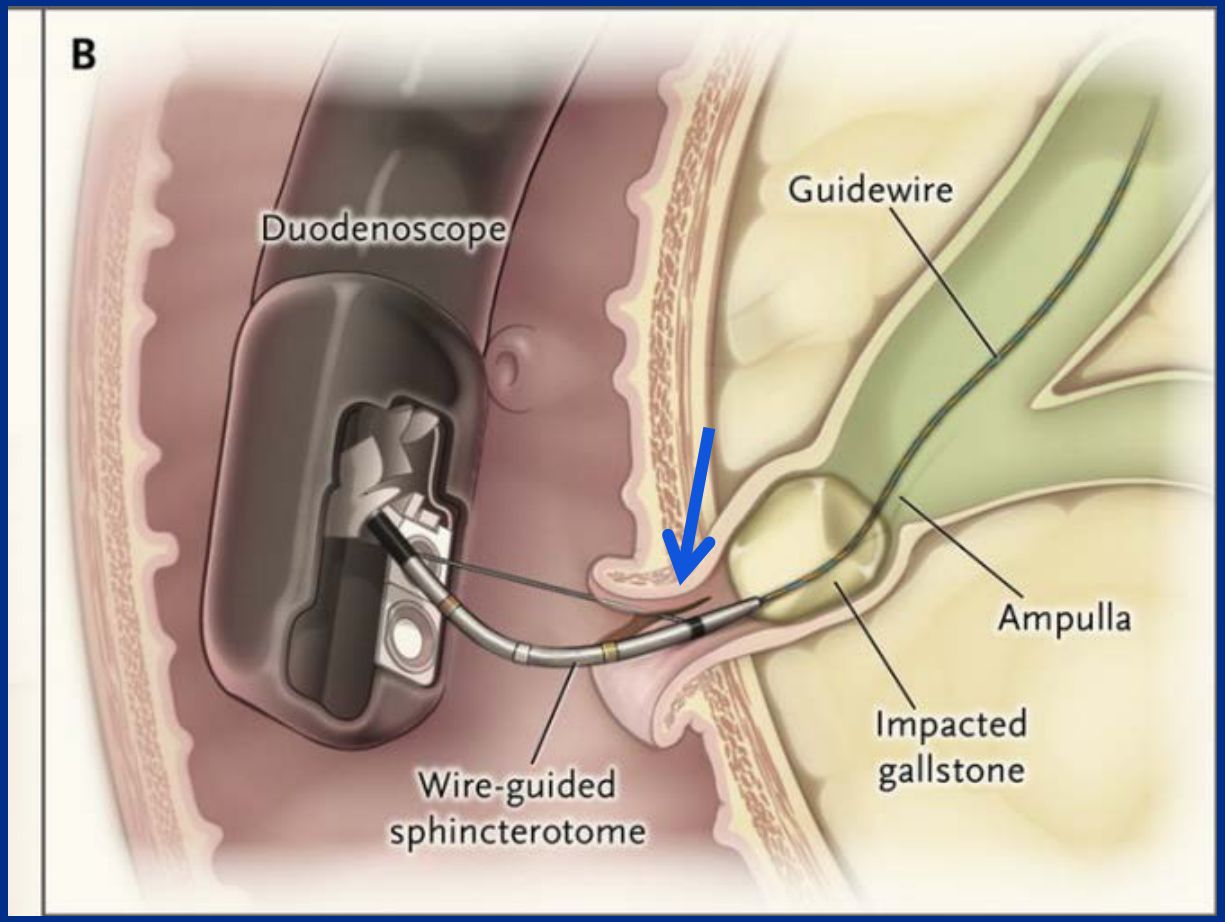
Initial Case Description (n=9)

	Mean (Range) or n (%)
Age, years	70 (45-88)
History of international travel	0/9 (0%)
History of admission to hospital A	8/9 (89%)
History of admission to long-term care facility	4/9 (44%)
History of Endoscopic Retrograde Cholangiopancreatography (ERCP)	6/9 (67%)

Background: Endoscopic retrograde cholangiopancreatography (ERCP)



Background: ERCP and Duodenoscopes



To access the ducts:

Needs to make sharp angle

Requires additional mechanical lever (elevator)

Fogel EL, Sherman S. N Engl J Med 2014;370:150-157

Background: Duodenoscopes

- **Previous outbreaks of CRE epidemiologically linked to gastrointestinal procedures, and to duodenoscopes**
  - Inadequate cleaning of elevator mechanism/channel
  - Manual cleaning required

Elevator Mechanism

Methods: On-site Investigation

- **Case definition**
  - NDM-producing *E. coli* isolate
  - Recovered from a patient in northeastern Illinois
  - With >85% similarity by pulsed field gel electrophoresis (PFGE) to the outbreak strain
  - Confirmed by CDC in 2013

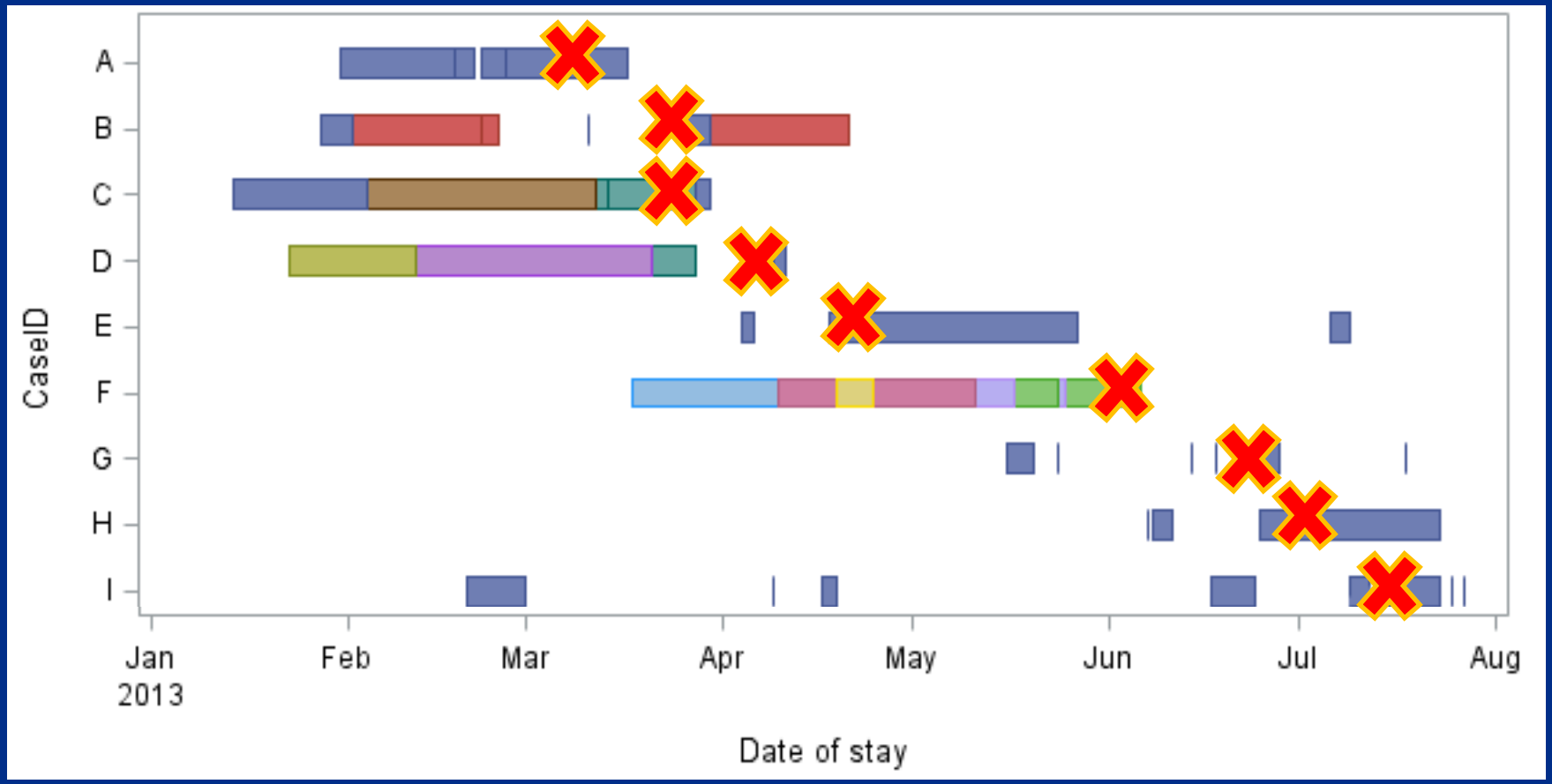
- **Epidemiologic investigation**
  - Characterized known cases
  - Hospital and local health departments screened patient roommates, including at other facilities
  - Reviewed duodenoscope cleaning and reprocessing procedures, took environmental samples

Methods: Case Control Study

- **Identify exposures that may contribute to NDM transmission**

- **Controls randomly selected from among 131 patients with negative surveillance cultures**
  - Hospital A rehabilitation unit

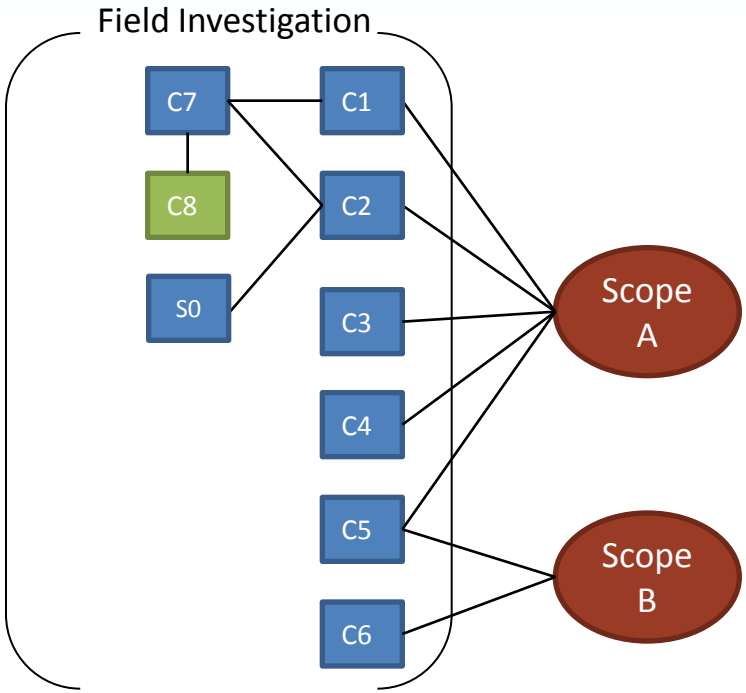
Initial Patients' (n=9) Facility Admissions



= Dates of admission to Hospital A

All other colors = Dates of admission to other area care facilities

= Date of NDM positive culture



Case from hospital

Case, not from hospital

Results: Case Control Study

Case-Control Analysis[a]	No. (%)		Odds Ratio (95% CI)[b]	*P* Value
	Case Patients (n = 8)	Control Patients (n = 27)		
Procedures				
ERCP[c]	6 (75.0)	1 (3.7)	78 (6.0-1008)	<.001
Other endoscopy[d]	2 (25.0)	3 (11.1)	2.7 (0.4-19.7)	.34
Operating room (any surgical procedure)	5 (62.5)	11 (40.7)	2.4 (0.5-12.3)	.29
Radiology				
CT	7 (87.5)	20 (74.1)	2.5 (0.3-23.6)	.44
MRI[e,f]	1 (12.5)	0	6.0 (0.1-308.6)	.34
MRCP	5 (62.5)	1 (3.7)	43.3 (3.7-505.8)	.003
Unit of stay				
Interventional radiology	2 (25.0)	8 (29.6)	0.8 (0.1-4.8)	.80
Medical ICU	3 (37.5)	8 (29.6)	1.4 (0.3-7.4)	.67
Surgical ICU	3 (37.5)	10 (37.0)	1.0 (0.2-5.2)	.98
Oncology	2 (25.0)	3 (11.1)	2.7 (0.4-19.7)	.34
Neurology	2 (25.0)	7 (25.9)	0.95 (0.2-5.9)	.96
Surgical care	3 (37.5)	4 (14.8)	3.5 (0.6-20.5)	.17
Other exposures				
Antibiotics[f,g,h]	8 (100.0)	15 (55.6)	9.5 (1.0-304.4)	.05
Anesthesia	7 (87.5)	12 (44.4)	8.8 (0.9-81.2)	.06

Results: Duodenoscope Reprocessing

- **Observation of duodenoscope reprocessing**
  - Pre-cleaning
  - Leak testing
  - Manual cleaning
  - High-level disinfection

- **Duodenoscope and AER manufacturers also on-site**

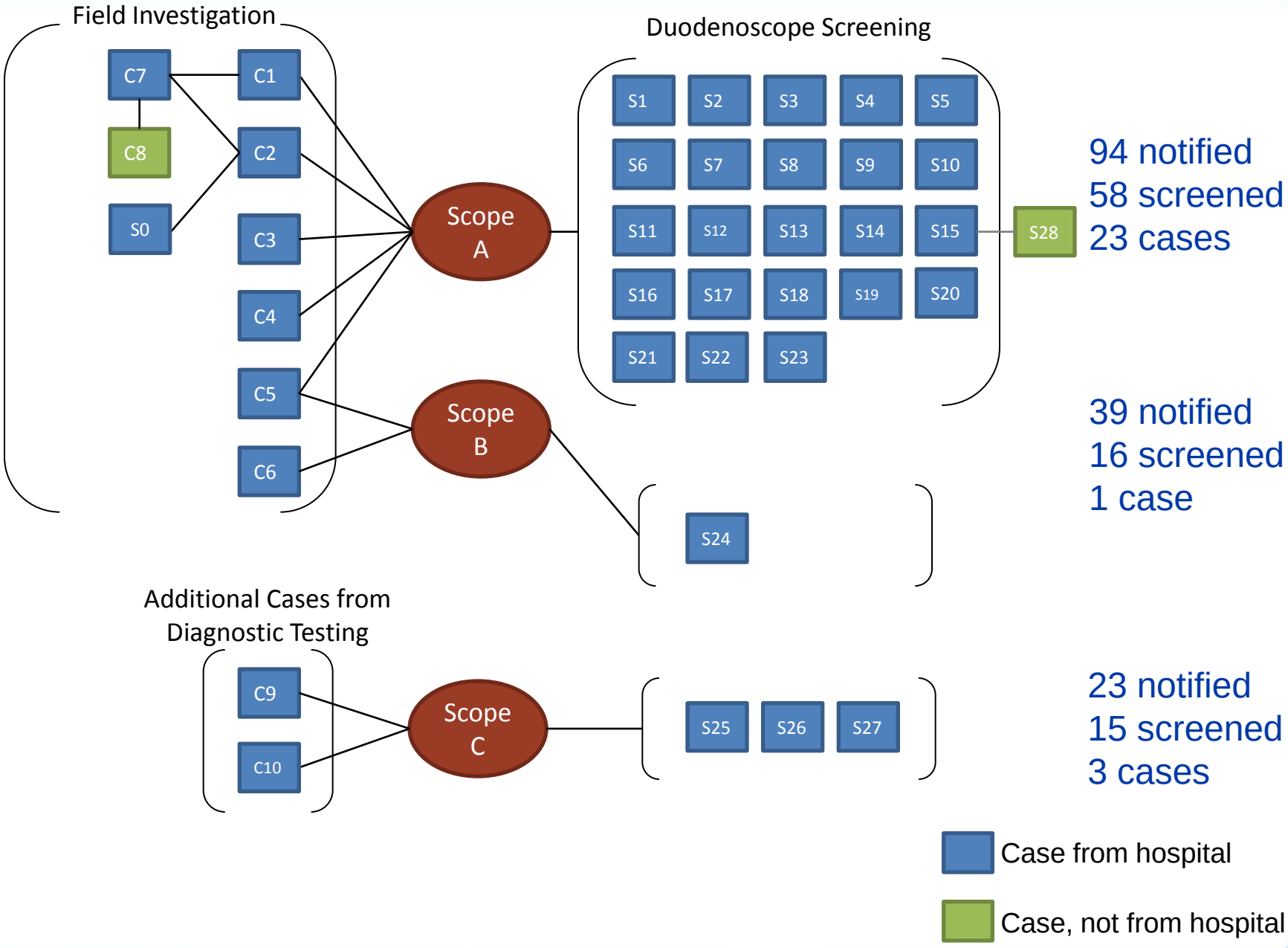
- **No lapses identified**

Results: NDM-producing *E. coli* Recovered From Duodendoscope

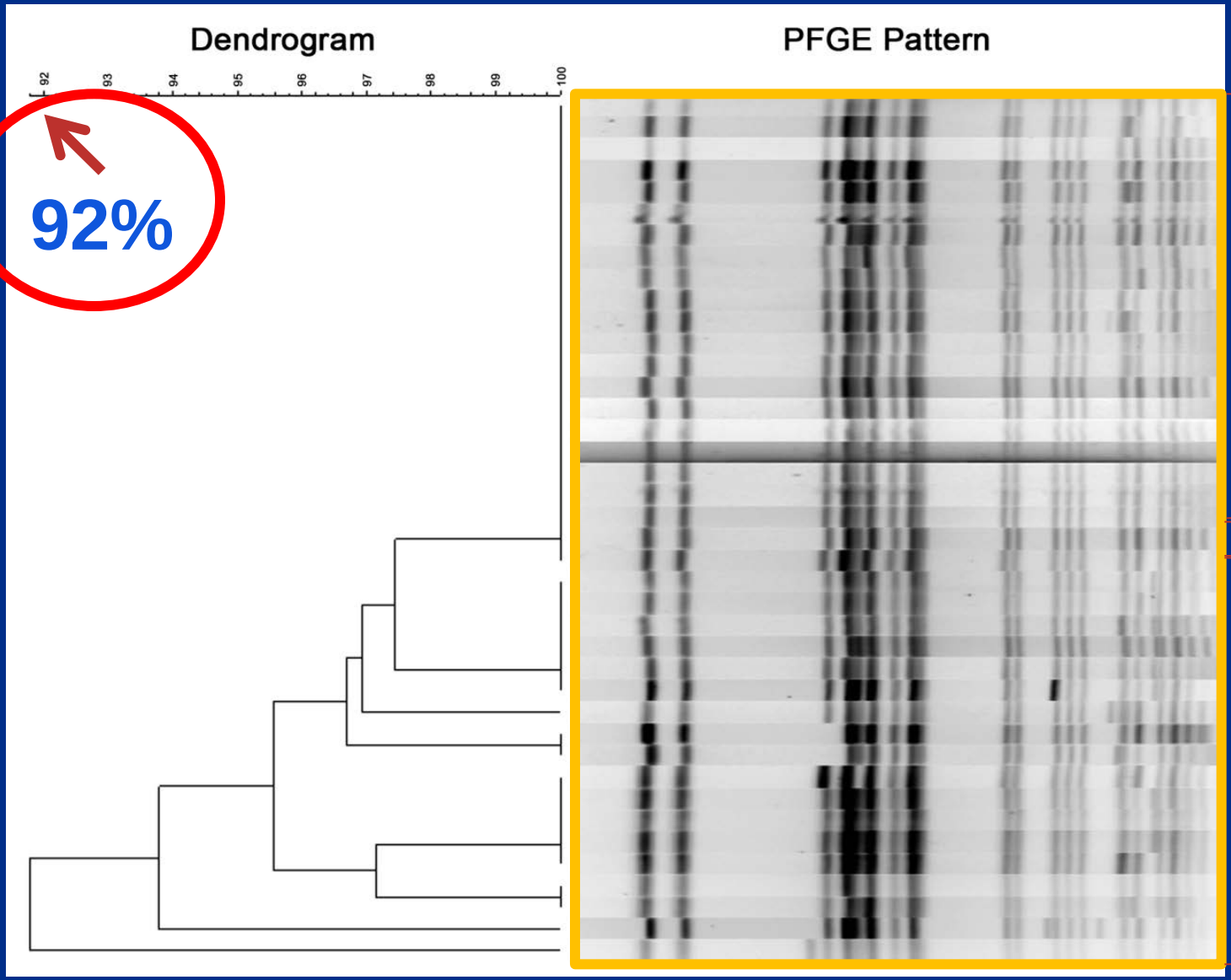
- **Duodendoscope A, used on 5 of the 6 original case-patients, was sent to CDC**
  - Had undergone manual and high level disinfection using an AER
  - Had been out of service for two months
- **NDM-producing *E. coli* and KPC-producing *K. pneumoniae* were recovered from the terminal section (the elevator channel) of the device**
- **Manufacturer did not identify structural defect in duodenoscope**

Next steps: Expanded CRE Screening

- **Hospital notified the 226 living patients who were exposed to any duodenoscope Jan.-Sept. 2013**
  - Offered CRE (rectal swab) and blood-borne pathogen screening
  - 102 (45%) returned for screening
  - NDM-producing *E. coli* were recovered from 27 (26%)
  - All blood-borne pathogen testing was negative


Field Investigation
Duodenoscope Screening
C7
C1
C8
C2
S0
C3
C4
C5
C6
Scope A
Scope B
S1
S2
S3
S4
S5
S6
S7
S8
S9
S10
S11
S12
S13
S14
S15
S28
S16
S17
S18
S19
S20
S21
S22
S23
S24
94 notified
58 screened
23 cases
39 notified
16 screened
1 case
Additional Cases from Diagnostic Testing
C9
C10
Scope C
S25
S26
S27
23 notified
15 screened
3 cases
Case from hospital
Case, not from hospital

Results: PFGE to Assess Relatedness



Conclusion

- Largest known cluster of NDM-producing *E. coli* in the U.S.
  - In total, 39 case patients identified, 35 with duodenoscope exposure in one hospital
  - Appears duodenoscopes can be an efficient source of transmission

- No reprocessing breaches or scope defects identified
  - However, NDM-producing *E. coli* recovered from a reprocessed duodenoscope and shared more than 92% similarity to all case patient isolates by PFGE
  - Appears duodenoscopes can remain contaminated with pathogenic bacteria even after recommended reprocessing

Conclusions for Facilities

- Be aware of the potential for transmission of bacteria, including antimicrobial-resistant organisms, via this route
  - If CRE identified, consider possibility of ERCP-related transmission
  - Conduct regular reviews of duodenoscope reprocessing procedures to ensure optimal manual cleaning and disinfection


Original Investigation

New Delhi Metallo-β-Lactamase–Producing Carbapenem-Resistant *Escherichia coli* Associated With Exposure to Duodenoscopes

Priorities: Identify and Control Spread of Novel Carbapenemases

- **Improve identification of novel carbapenemases by enhancing laboratory capacity**
  - Few laboratories regularly perform CRE resistance mechanism testing
  - Many cannot differentiate organisms producing novel carbapenemases from those producing KPC

- **Control spread of carbapenemases**
  - CRE reporting and facility intercommunication has historically been poor, limiting effective infection control
    - CRE became reportable in Illinois in November, 2013
    - New eXtensively Drug Resistant Organism (XDRO) registry
    - Acute- and long-term care facilities can access registry directly, to implement appropriate infection control measures when patients are admitted
  - Antimicrobial stewardship
    - Recent antibiotic use was a risk factor for case status

Illinois: REALM project

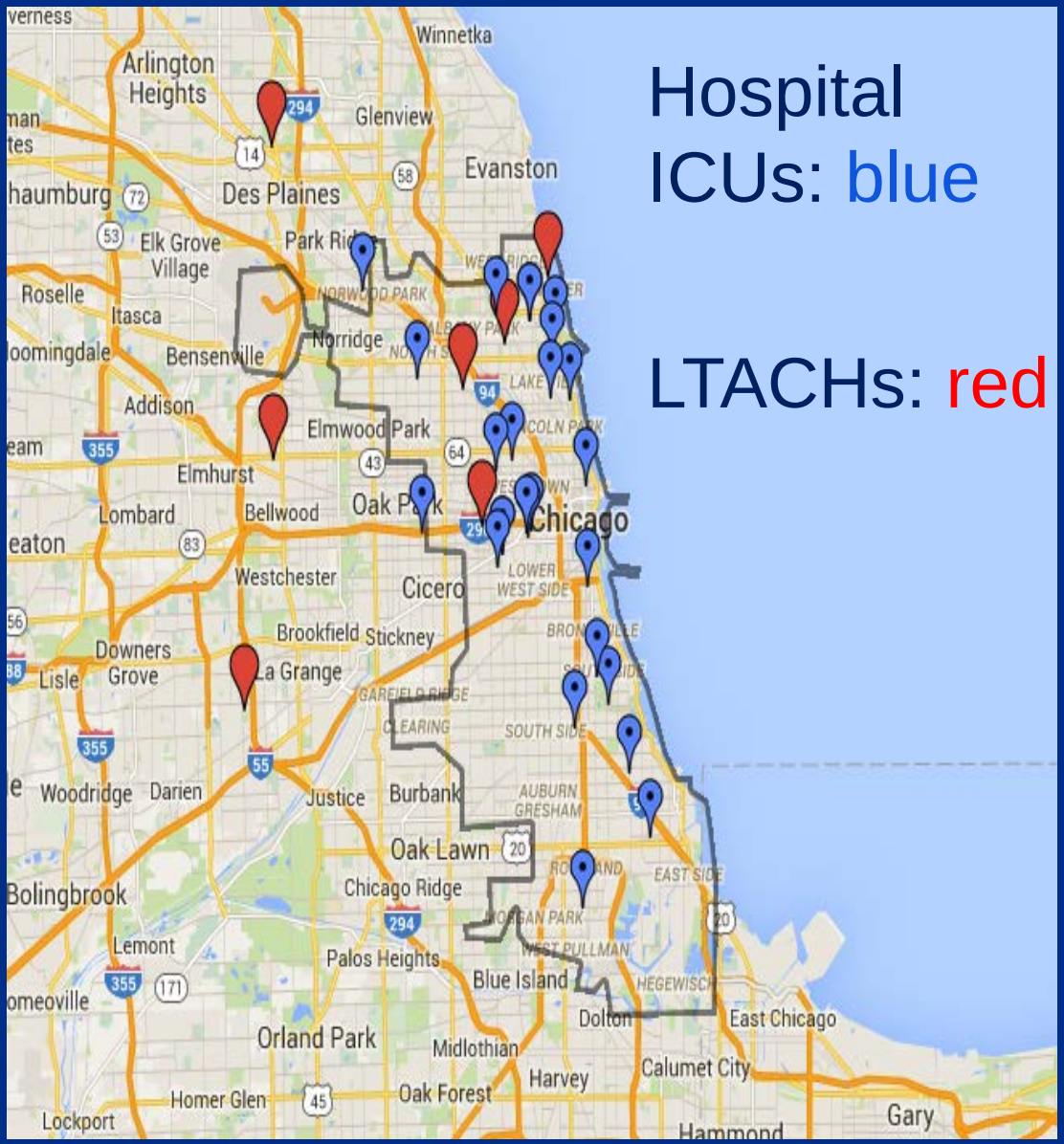
CDC-sponsored

Twice-yearly point prevalence surveys

- CRE, since 2010

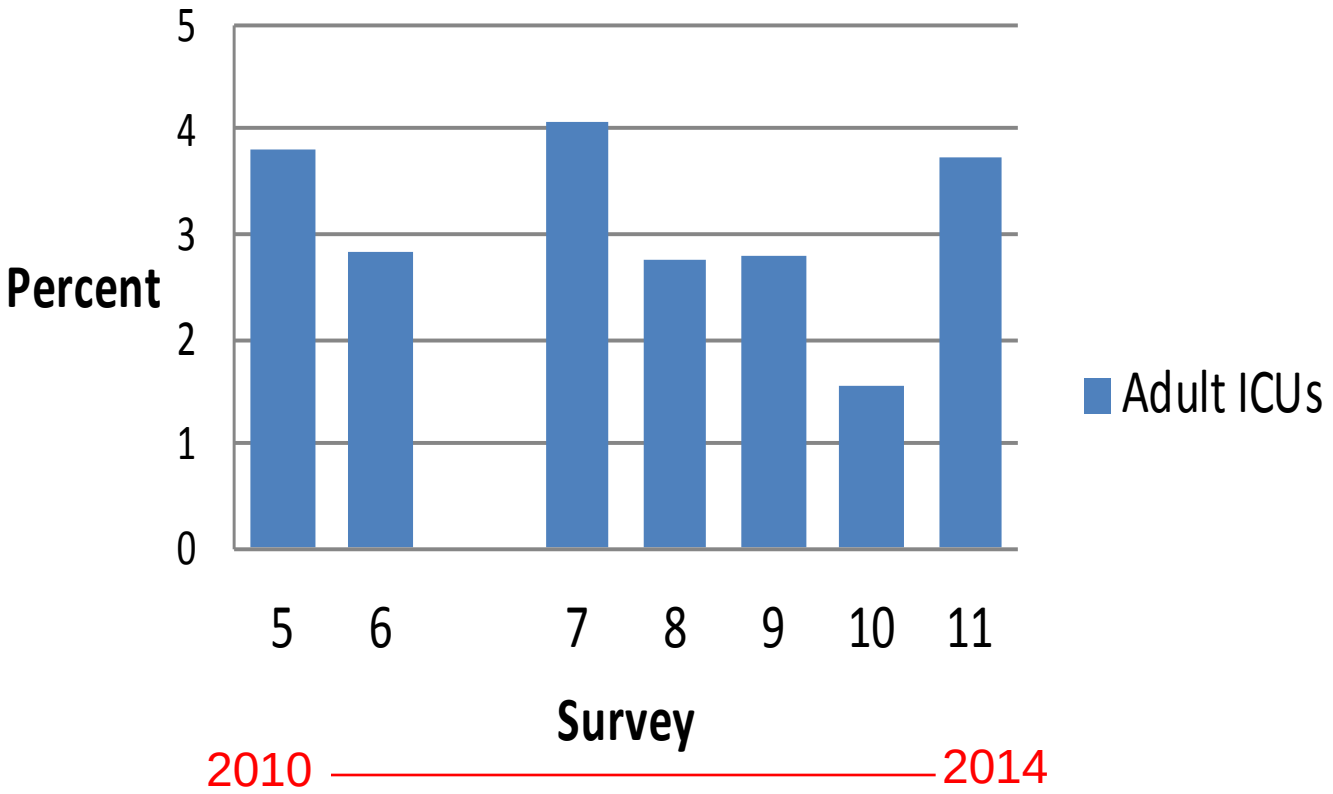
Slide: Trick, Lin (CDC Prevention Epicenter)

REALM project - KPC



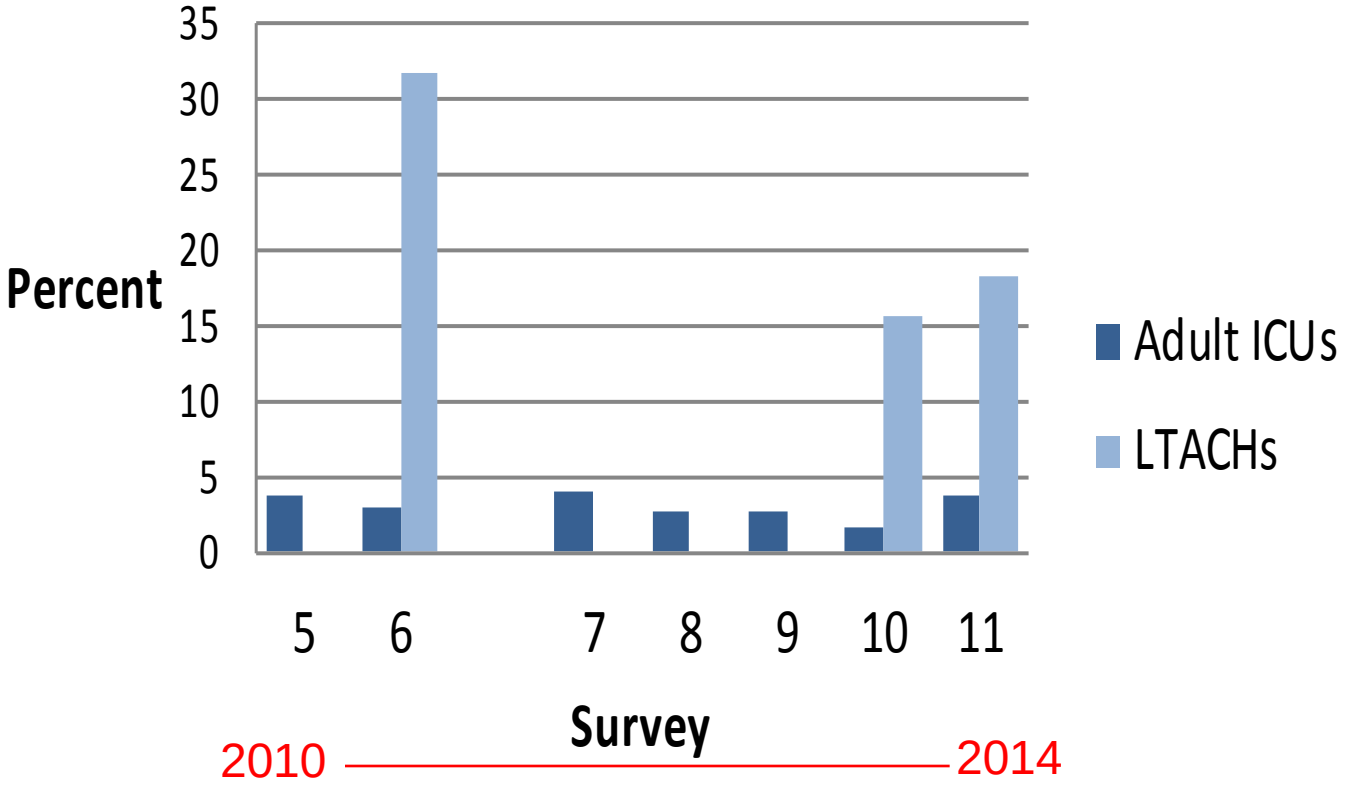
Slide: Trick, Lin (CDC Prevention Epicenter)

Prevalence of KPC colonization among adult ICU patients



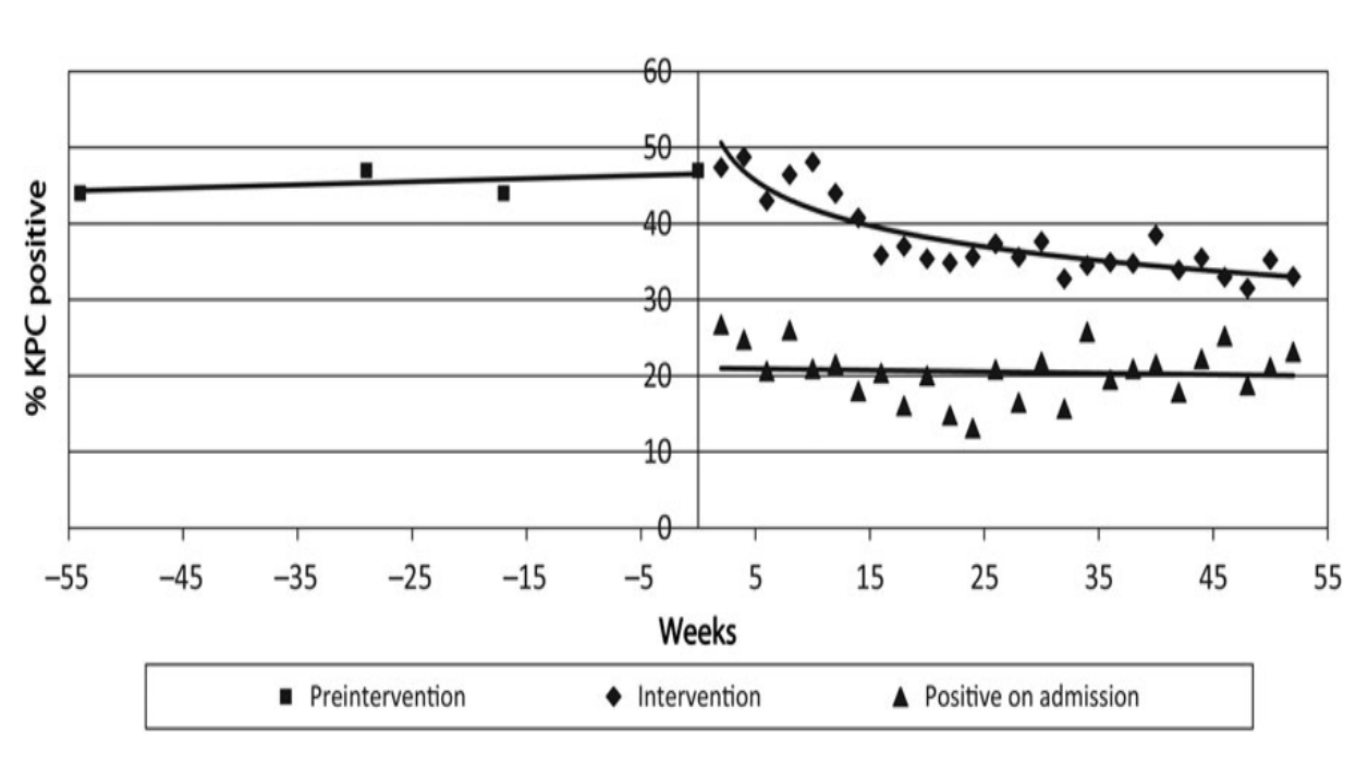
Slide: Trick, Lin (CDC Prevention Epicenter)

Prevalence of KPC colonization among ICU vs. LTACH patients



Slide: Trick, Lin (CDC Prevention Epicenter)

KPC Intervention for LTACHs



Hayden, Clin Infect Dis, 2014

REALM project 2015 update

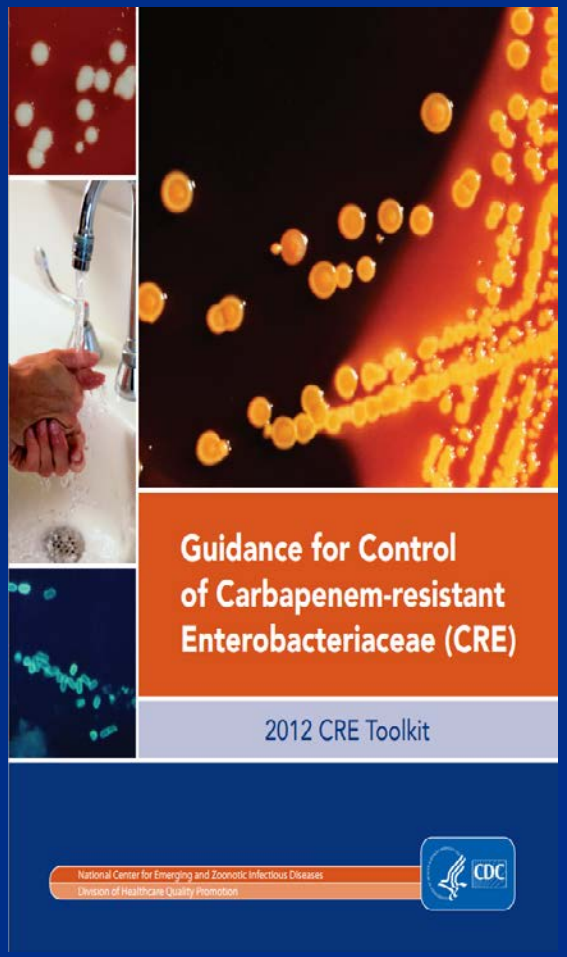
Survey #12 is underway

- Now testing for all 5 major carbapenemases (KPC, NDM, OXA-48, VIM, IMP)

Thank you to REALM hospitals for continued participation

Slide: Trick, Lin (CDC Prevention Epicenter)

“Detect and Protect”



- Detect: Identify all patients with CRE
- Protect: Maintain CRE-colonized patients in isolation precautions throughout the healthcare system

Challenges

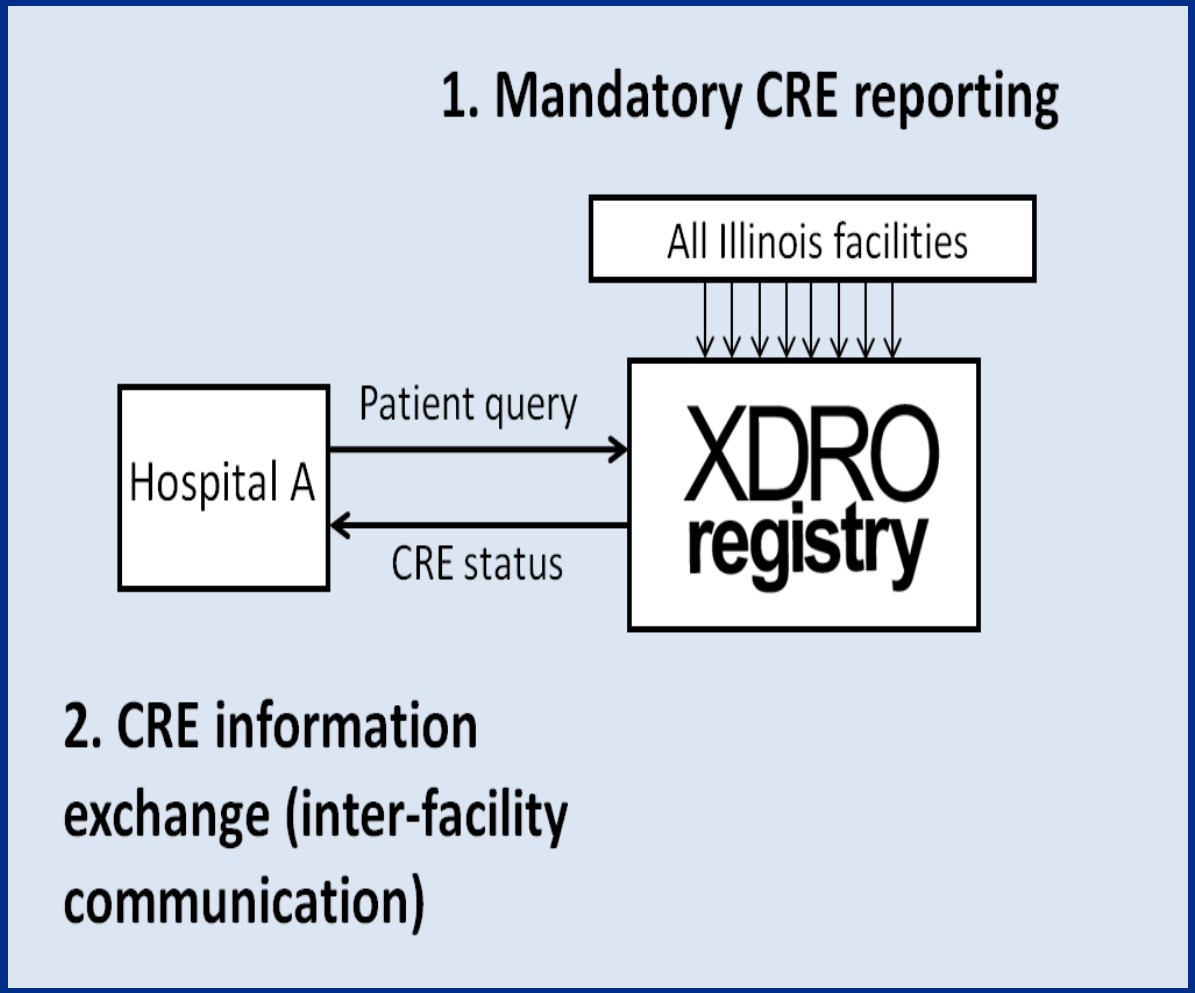
- Peripatetic Patients
  - Within 1 year of ICU discharge
    - Median 4 facility transitions
- Information lost between transfers
  - Patients may go home between facilities

Unroe, Annals Int Med, 2010; 153(3)

XDRO registry

- Facilitates the Detect and Protect strategy
- Partnership
  - Illinois Department of Public Health
  - Chicago CDC Prevention Epicenter
  - Medical Research Analytics and Informatics Alliance (MRAIA)

XDRO Registry Overview



Participants: Illinois hospitals including LTACHs (142), nursing homes (784), laboratories

Illinois CRE definition: Enterobacteriaceae with one of the following test results

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

OR

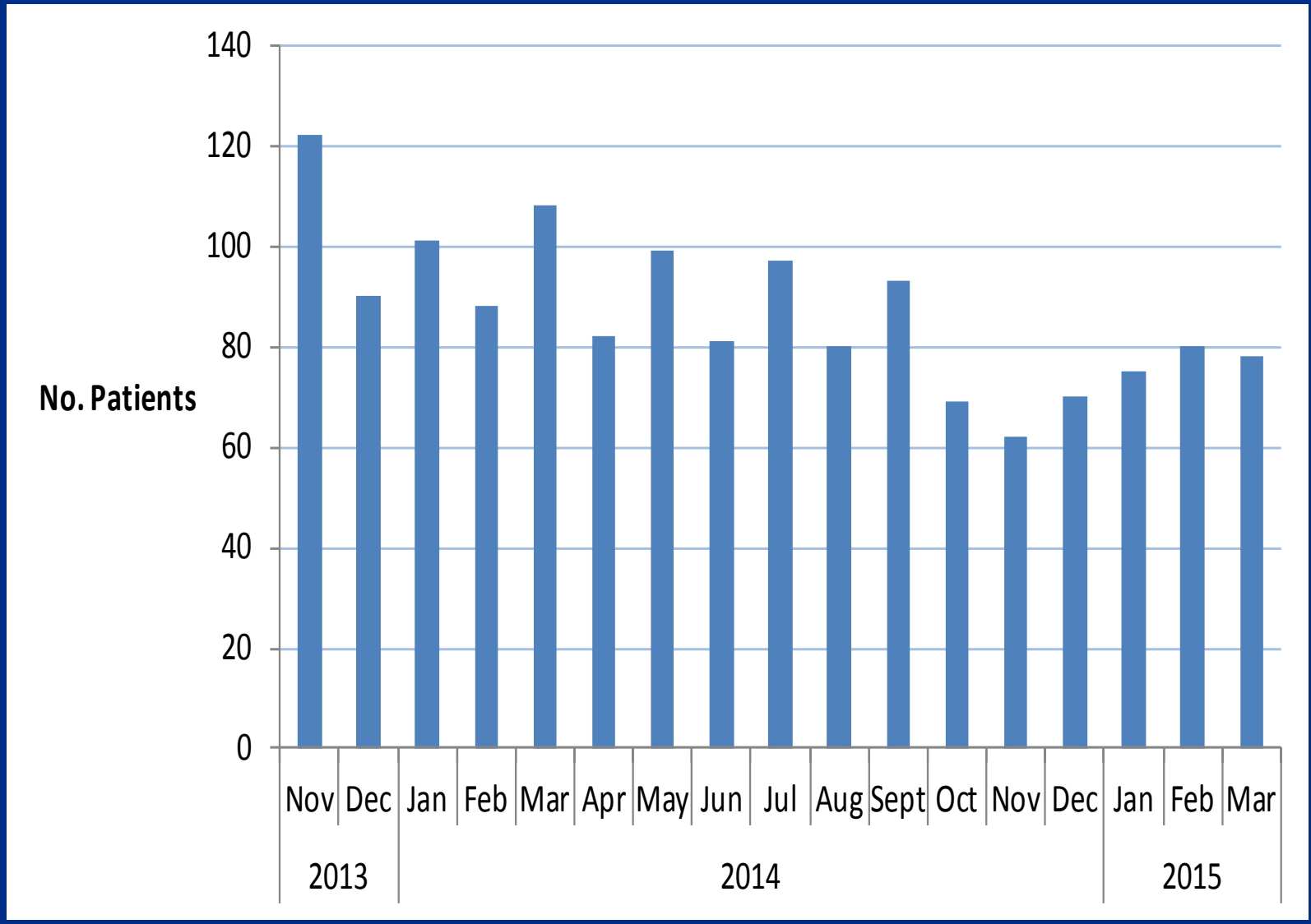
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production

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, ceftazidime).

Report 1st CRE event per patient per encounter

Unique patients reported to XDRO registry



Data courtesy of IDPH

XDRO registry, year 1

Reporting

- Unique reports: 1,557 reports
- Unique patients: 1,095
- Reporting facilities: 175

115	Acute hospitals
5	LTACHs
46	SNFs
7	reference labs
2	Outpatient clinics

Querying

- 30 unique facilities query the registry/month

XDRO registry summary, 2014

Characteristics of ALL submitted reports	N	%
Culture Type		
Clinical	1254	80
Screening	301	20
Organism		
Klebsiella spp.	1347	86
E. coli	103	7
Enterobacter spp.	77	5

Data and adapted slide from IDPH (A. Tang)

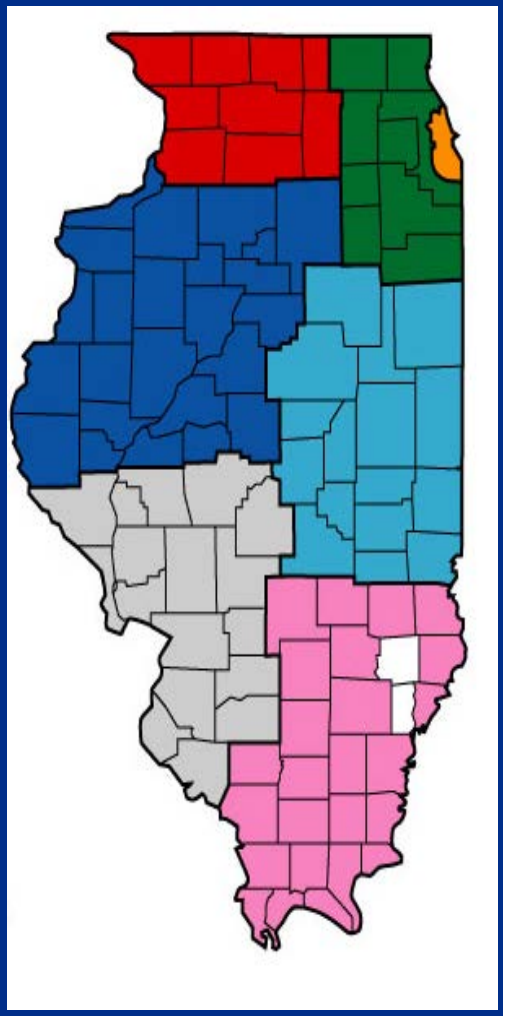
XDRO registry summary, 2014

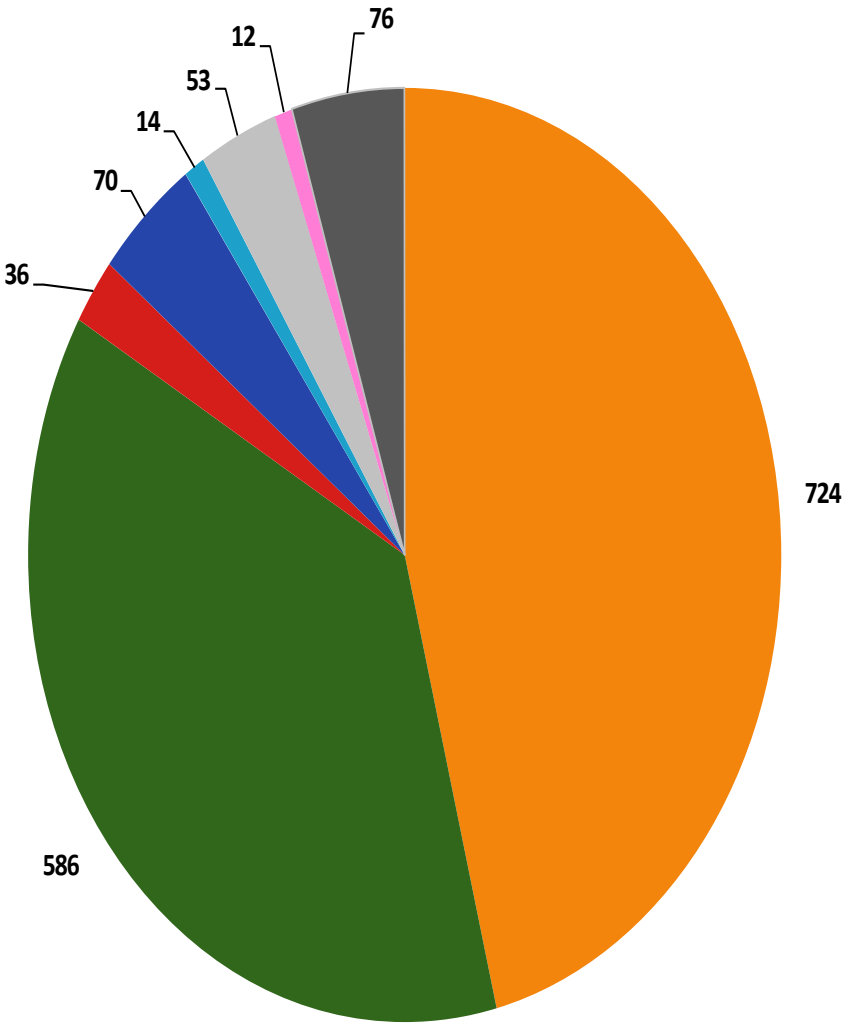
Characteristics of ALL submitted reports	N	%
Type of testing performed*		
1) Molecular test*	397	25
2) Phenotypic test*	751	48
3) Susceptibility test ONLY	449	29
Unknown	29	2
Mechanism of resistance (applies only to reports with molecular test)		
KPC	363	91
NDM	11	3
Other/Unknown	23	6

*≥1 response accepted per isolate

Data from IDPH (A. Tang)

All XDRO reports by region

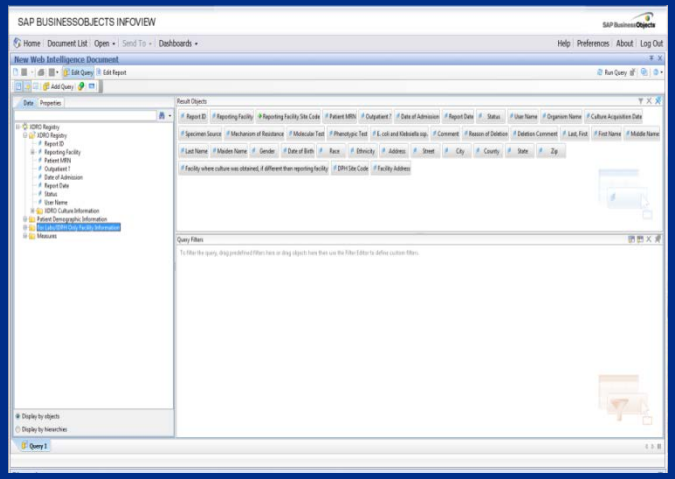




Data and adapted slide from IDPH (A. Tang)

XDRO data access for LHDs

- Local health departments can obtain access to XDRO data through I-NEDSS Business Objects
- Must fill out a user agreement form
- E-mail dph.xdroregistry@illinois.gov for the form or questions about XDRO data access



XDRO Registry: Future Directions

1. Laboratory validation
2. Automated CRE alerts
3. Cluster detection

Laboratory Validation

First 5 consecutive CRE isolates from each lab should be sent to IDPH (Jan 1, 2015 -)

- Identification to species
- Antibiotic susceptibility testing
- *bla*$_{KPC}$/$_{NDM}$ PCR
- Additional phenotypic and genotypic evaluation if necessary

Courtesy of M. Hayden

Validation Preliminary Results: 134 isolates (January-April, 2015)

- 115 (86%) carbapenemase-producing Enterobacteriaceae
  - 111 (97%) KPC PCR+
  - 2 (2%) NDM PCR+
  - 2 (2%) OXA-48-like

- 10 (8%) carbapenem-resistant Enterobacteriaceae
  - 9 *Enterobacter* spp, 1 *E. coli*

- 3 (2%) carbapenem-resistant *Acinetobacter*/*Pseudomonas*

- 6 (5%) carbapenem-susceptible *E. coli*

Courtesy of M. Hayden

Lab validation – moving forward

- Current protocol:
  - Labs should continue to send their first 5 consecutive CRE isolates of 2015 to IDPH until they meet their quota

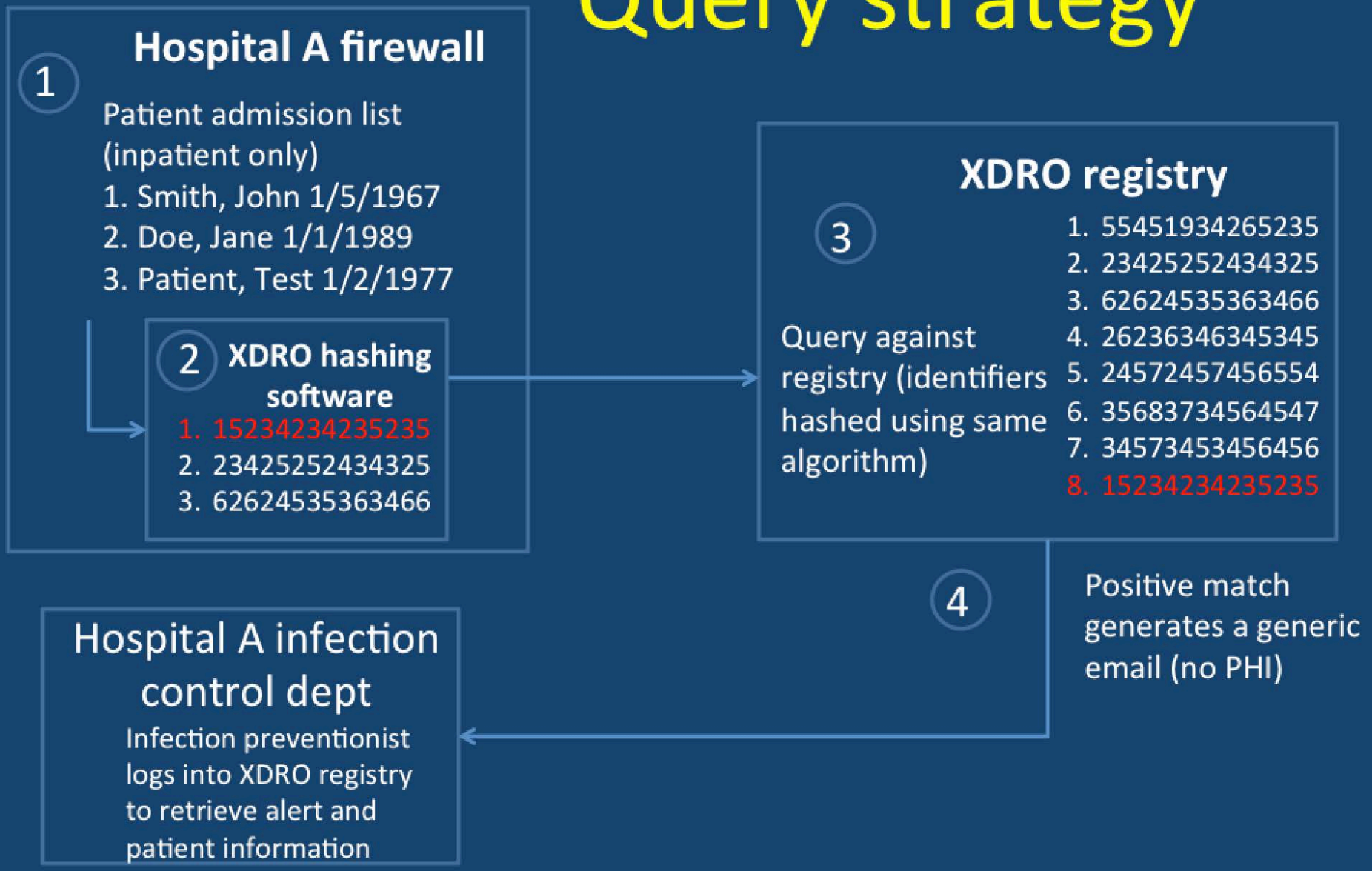
- Proposed protocol for next year (contingent on CDC support)
  - Every lab sends 5 consecutive CRE isolates for 2016
  - For confusing CRE isolates, every lab can send an additional 5 CRE isolates

CRE automated alerts

In a REALM survey, 96% of hospitals indicated interest in receiving automated CRE alerts from the XDRO registry

Slide: Trick, Lin (CDC Prevention Epicenter)

Query strategy



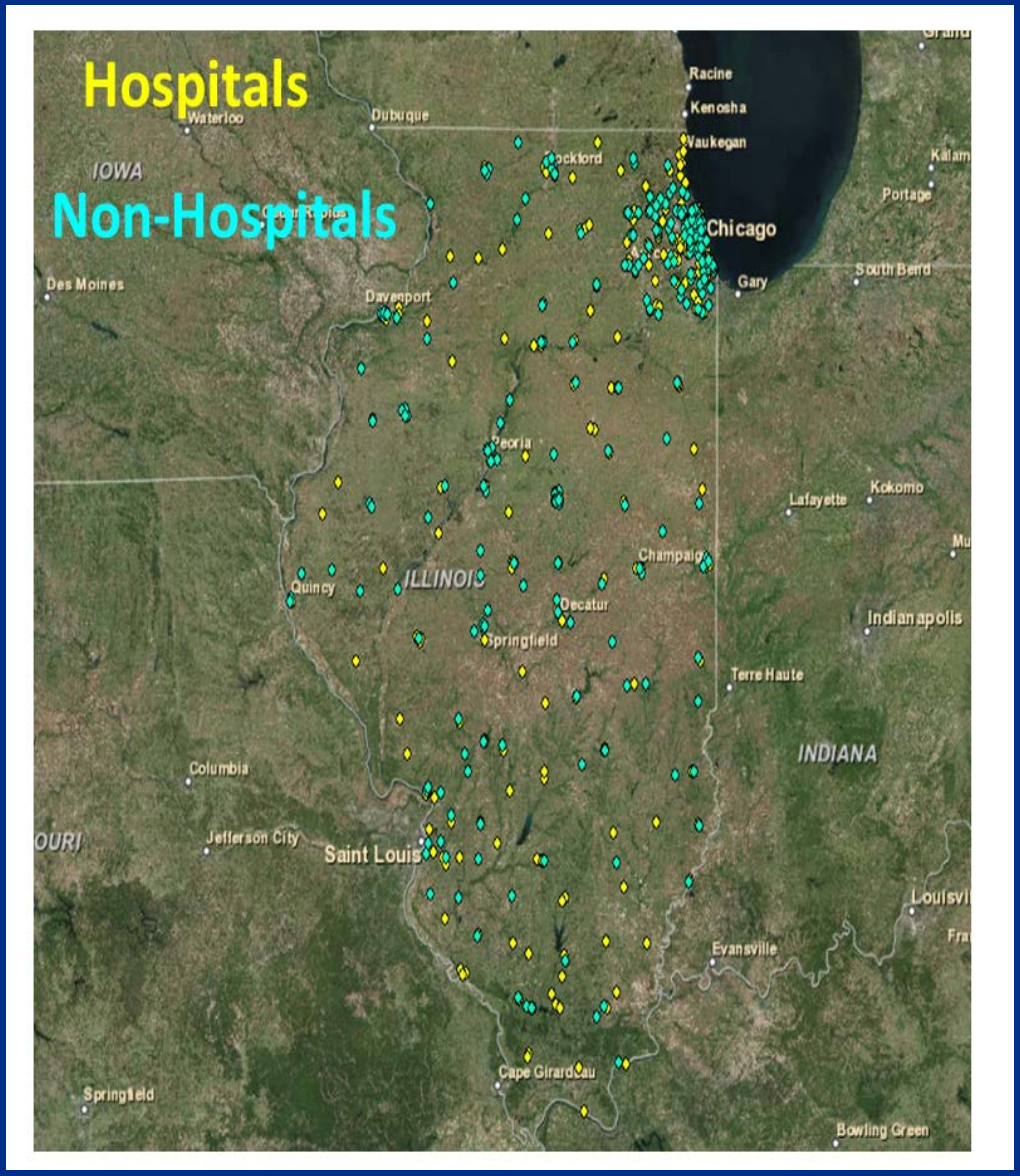
Piloting automated CRE alerts

- Pilot 1 (convenience sample)
  - 1 hospital (Stroger) active since Jan 2015
  - 2 hospitals in next month

- Pilot 2 (MedMined hospitals)
  - Plan for 2 hospitals to trial alerts
  - MedMined represents 60+ Illinois hospitals (~42% of hospital beds in state)

Slide: Trick, Lin (CDC Prevention Epicenter)

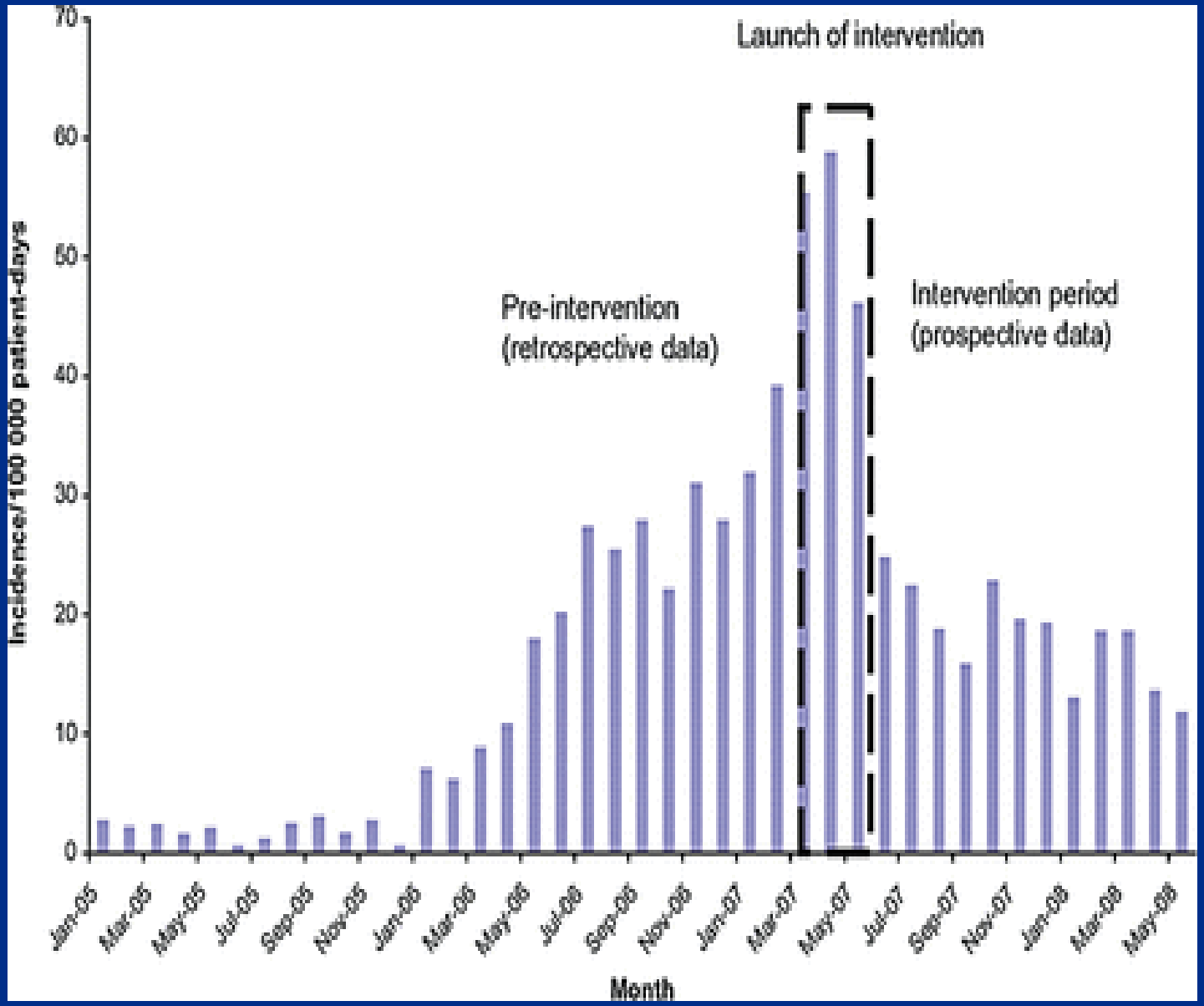
Detection of CRE Clusters in Illinois



Slide: Trick, Lin (CDC Prevention Epicenter)

National Intervention to Reduce CRE Incidence

Clinical Cultures at Acute Care Hospitals



Schwaber et al. Clin Infect Dis. 2014

TABLE 1. Compliance with Infection Control Guidelines in 13 Post-Acute Care Hospitals as Noted on 3 Site Visits

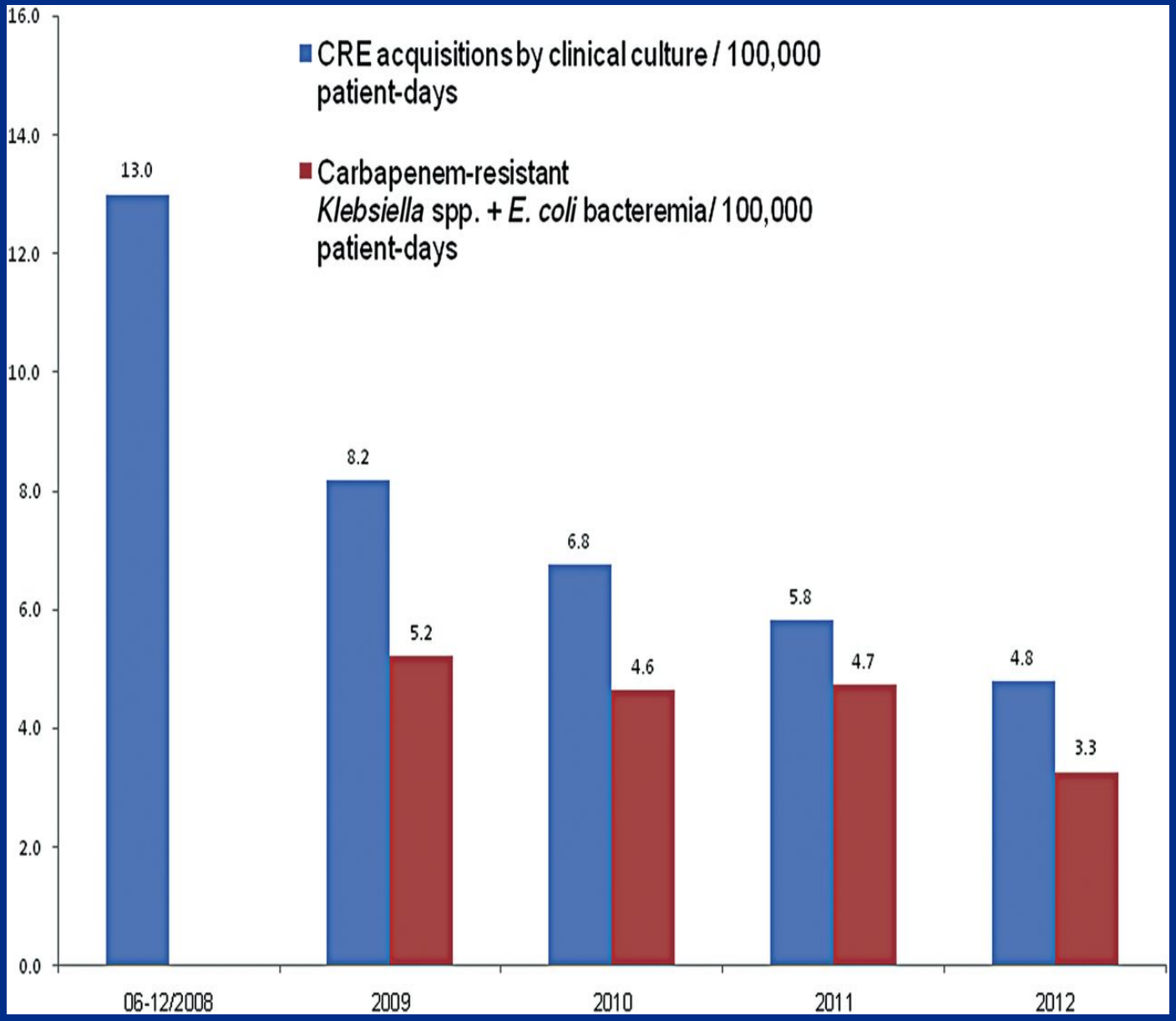
Variable	2008	2010	2011	*P*
Infection control consultant	62	85	92	.055
Hand hygiene[22]				
Presence of ABHR in each room	85	92	100	.146
ABHR at site of care	15	54	85	<.001
Presence of antiseptic soap	15	92	85	<.001
Presence of sink in each room	23	31	46	.164
Paper towel availability	69	85	100	.032
Compliance audits	0	46	77	<.001
Appropriate use of barrier precautions in context of standard precautions[23]				
Gloves	31	69	92	.001
Gowns	54	77	77	.208
Masks	38	62	69	.118
CRE prevention program				
Placement of colonized patients in single rooms or cohorting	77	85	100	.082
Use of gown and gloves in contact isolation	46	92	100	.001
Designated medical equipment	92	100	100	.221
Admission screening cultures	15	69	77	.002
Contact screening	38	77	100	.001
Discontinuation of isolation per standard protocol	15	46	100	<.001
Total infection control score (average, out of possible 16)	6.8	11.6	14.0	<.001

NOTE. Data are percentage of compliant hospitals ($n = 13$), unless otherwise indicated. ABHR, alcohol-based hand rub; CRE, carbapenem-resistant Enterobacteriaceae.

Schwaber et al. Clin Infect Dis. 2014

National Intervention to Reduce CRE Incidence:

Clinical Cultures & Bacteremia at Acute Care Hospitals



Schwaber et al. Clin Infect Dis. 2014

Summary

CRE control can be successful

- Coordinated approach
- Improve detection and inter-facility communication (XDRO registry)
- Antibiotic stewardship

Thank you

Illinois' Infection Control Community

Illinois Dept of Public Health
Craig Conover
Mary Driscoll
Robynn Leidig
Michael Ray
Erica Runningdeer

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Mary Alice Lavin
Angela Tang

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Sarah Kemble
Massimo Pacilli

Cook County Dept of Public Health
Mabel Frias
Michael Vernon

CDC Prevention Epicenter
Wei (Vicky) Gao
Mary Hayden
Michael Lin
William Trick
Robert Weinstein

ANTIBIOTIC STEWARDSHIP

And Carbapenem-Resistant Enterobacteriaceae (CRE) in the Acute Care Setting

HOLLY BROWER BSN, RN
INFECTION PREVENTION MANAGER
ST. JOSEPH MEMORIAL HOSPITAL

DISCLOSURE

- I have no relevant financial or nonfinancial relationships related to the *Southern Illinois Infection Prevention CRE Workshop* to disclose.

ANTIBIOTIC INFORMATION

- Have reduced illness and death since 1940's
- Once lethal infections are now treatable
- 30-50% of all Antibiotics prescribed in US hospitals are unnecessary or inappropriate
- Have serious side effects
- The infectious organisms the antibiotics were designed to kill have adapted to them and developed drug resistance


ANTIBIOTIC RESISTANCE INDENTIFIED
ANTIBIOTIC INTRODUCED
penicillin-R Staphylococcus 1940
1943 penicillin
1950 tetracycline
1953 erythromycin
tetracycline-R Shigella 1959
1960 methicillin
methicillin-R Staphylococcus 1962
penicillin-R pneumococcus 1965
1967 gentamicin
erythromycin-R Streptococcus 1968
1972 vancomycin
gentamicin-R Enterococcus 1979
1985 imipenem and ceftazidime
ceftazidime-R Enterobacteriaceae 1987
vancomycin-R Enterococcus 1988
levofloxacin-R pneumococcus 1996
1996 levofloxacin
imipenem-R Enterobacteriaceae 1998
XDR tuberculosis 2000
2000 linezolid
linezolid-R Staphylococcus 2001
vancomycin-R Staphylococcus 2002
PDR-Acinetobacter and Pseudomonas 2004/5
2003 daptomycin
ceftriaxone-R Neisseria gonorrhoeae 2009
PDR-Enterobacteriaceae
2010 ceftaroline
ceftaroline-R Staphylococcus 2011

ANTIBIOTIC INFO CONT…..

- CDC estimates more than two million are infected with Antibiotic-Resistant Organisms
- Approximately 23,000 deaths each year
- Antibiotic Stewardship Programs began to appear in the late 1990's
- 2009 CDC launched "Get Smart for Healthcare" campaign http://www.cdc.gov/getsmart/healthcare/

NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least **2,049,442** illnesses,

23,000 deaths

**bacteria and fungus included in this report*

+

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least **250,000** illnesses,

14,000 deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CS239559

EMPIRIC ANTIBIOTIC THERAPY

- When an antibiotic is prescribed based on “clinical judgment” or “best guess” related to patient’s symptoms
- Sensitivity returned and empiric is not always the best therapy
- Followed by Antimicrobial Stewardship Program

SIH AND ANTIBIOTIC STEWARDSHIP

- Began November 2014
- Deanna Olexia RPh, Antibiotic Stewardship Pharmacist for the System
  - Memorial Hospital of Carbondale
  - Herrin Hospital
  - St. Joseph Memorial Hospital

WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO AT SIH?

- Audit and give feedback to prescribers of Antimicrobial therapy at 48-72 hours
  - Match culture data to therapy.
  - Dose adjustments for renal insufficiency, site of infection, MIC, etc…
  - De-escalation of therapy (try to decrease number of patients on duplicate gram negative coverage or duplicate anaerobic coverage).

WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO CONT….

- Review Data from Computerized Surveillance system
  - Positive blood cultures
  - Drug-Bug mismatch
  - Identify patients on targeted antimicrobial agents for review (carbapenems, broad spectrum, MRSA agents etc.. for more than 48 hours)

WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO CONT….

- Developed an antimicrobial formulary
  - Restricted some agents to Infectious Disease physician only
  - Available to any physician for initial therapy (24-48 hrs)
  - Must be reviewed within 24 hours by a member of stewardship team for continuing therapy

WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO CONT….

- Created pathways for pneumonia
- Created pathway for sepsis
- Help guide antimicrobial therapy
- Meet with Infection Prevention and Infectious Disease Physician monthly to go over findings

SIH Antibiotic Stewardship Program 1st Quarter 2015

Month	Total Intervention	Total Recommend	REC Accept	REC Unaccept	Automatic	Accept Rate
January	126	90	82	8	36	91.1%
February	84	70	66	4	14	94.3%
March	113	88	83	5	25	94.3%
1st QTR	323	248	231	17	75	93.1%

ANTIBIOTIC STEWARDSHIP PROGRAMS IN THE HOSPITAL

- Optimize the treatment of infections
- Reduce adverse events
- Improve quality of patient care
- Improve patient safety
- Reduce treatment failures
- Increase frequency of correct prescribing therapy and prophylaxis
- Significantly reduce hospital rates of C-Diff and antibiotic resistance
- Save hospital money

CORE ELEMENTS OF HOSPITAL ANTIBIOTIC STEWARDSHIP PROGRAM

- Leadership commitment
- Accountability
- Drug expertise
- Action
- Tracking
- Reporting
- Education

LEADERSHIP

- CRITICAL TO SUCCESS OF PROGRAM
- CAN TAKE DIFFERENT FORMS:
  - Formal statements
  - Stewardship related duties in job descriptions
  - Ensure staff from relevant departments have time for stewardship duties
  - Support stewardship education
  - Ensure participation

ACCOUNTABILITY AND DRUG EXPERTISE

- STEWARDSHIP PROGRAM LEADER
  - Identify a single leader who will be responsible for program outcomes
- PHARMACY LEADER
  - Identify a single pharmacy leader who will co-lead the program

ACTIONS

- DEVELOP AND IMPLEMENT FACILITY SPECIFIC TREATMENT RECOMMENDATIONS
  - BASED ON NATIONAL GUIDELINES FOR ANTIBIOTIC USE IN:
    - Community acquired pneumonia
    - Urinary tract infection
    - Intra-abdominal infections
    - Skin and soft tissue infections
    - Surgical prophylaxis
- IMPLEMENT POLICIES THAT SUPPORT OPTIMAL ANTIBIOTIC USE
  - Document dose, duration, and indication

TRACKING & REPORTING

- MONITOR ANTIBIOTIC PRESCRIBING
  - Measure if policies and guidelines are being followed
  - Have interventions improved antibiotic use and patient outcomes?
- ANTIBIOTIC USE MEASURES
  - DETERMINE IF PRESCRIBERS HAVE:
    - Accurately applied diagnostic criteria for infections
    - Prescribed recommended antibiotics
    - Documented, indicated, and planned duration
    - Obtained cultures and relevant tests
    - Modified antibiotic findings to micro findings

EDUCATION

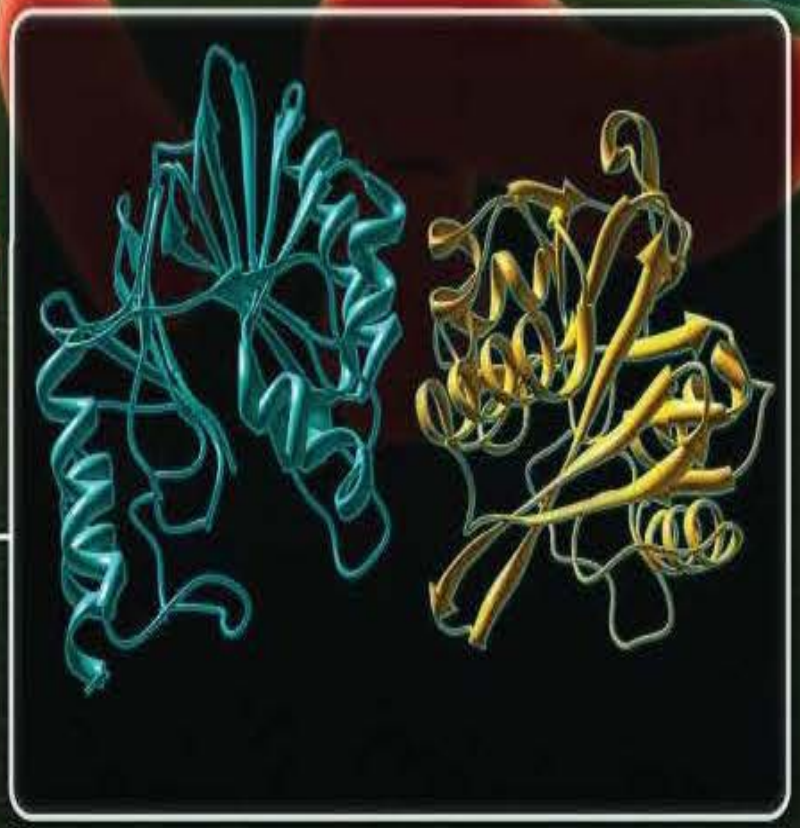
- ANTIBIOTIC STEWARDSHIP PROGRAM WILL PROVIDE REGULAR UPDATES:
  - Antibiotic prescribing
  - Antibiotic resistance
  - Infectious diseases

WHY IS THIS PROGRAM IMPORTANT?

- Promotes proper use of antibiotics
- Decrease C-diff
- Decrease drug resistant organisms
- Prevent NEW drug resistant organisms from forming
- Improves Patient Safety

Carbapenem-Resistant Enterobacteriaceae

An Emerging Threat



RECENT CRE OUTBREAKS

- Between October 2014 and January 2015, Two patients died from CRE at Ronald Reagan UCLA Medical Center after a duodenoscope procedure, 179 others were tested for the bacteria
- Between 2012 and 2014, 35 patients were infected with CRE and 11 died in a Seattle Hospital related to duodenoscope procedure

SIH RESPONSE TO CRE OUTBREAK

- Be Proactive
- Infection Prevention began investigation
  - Contact Operating Room Managers
    - What duodenscopes are being used
  - Contact all staff processing scopes
    - Are manufacturer's reprocessing recommendations present?
    - Are manufacturer's reprocessing recommendations being followed?
    - Infection Prevention staff observe disinfection process at all three SIH Hospitals

WHAT DOES THE SCOPE LOOK LIKE?

SIH RESPONSE TO CRE OUTBREAK CONT….

- Olympus 180 duodenscope involved
  - What SIH facilities use this scope?
  - What is recommended to improve cleaning process?
    - New Brush for properly cleaning extra channel
  - Is all staff properly trained?
    - Staff travel to all three facilities

PROBLEM AREA

SIH RESPONSE TO CRE OUTBREAK CONT….

- Each facilities cleaning, drying, and reprocessing is evaluated
  - Infection Prevention followed the process at each facility
  - Findings discussed with Operating Room Managers
  - Education planned and completed

IS IT CLEAN?

- Bacteria can not be sterilized or disinfected
- New product being used across the system
  - 3-in-1 Channel Check Residual Soil Test Strips
    - Hemoglobin
    - Protein
    - Carbohydrates

CHANNELCHECK STRIPS

- Duodenscope is cleaned per recommendations
- Small bag attached to end of duodenscope
- 10 cc syringe with sterile water obtained
- Sterile water injected through duodenscope
- Sterile water ends in small bag
- Small bag removed
- Dip stick placed into small bag of sterile water
- Wait 90 seconds
- Checks for any residual hemoglobin, protein, and/or carbohydrate
- Negative results allow duodenscope to move on to reprocessing stage
- A positive result would indicate more cleaning needed

MICRO, LAB, AND CRE

- What role does Microbiology and Lab have with CRE?
  - Calls the nurse caring for patient with any positive culture results
    - Blood
    - Sputum
    - Urine
    - Wound

MICRO, LAB, AND CRE CONT….

- Why is the positive culture called to the nurse?
  - No delay in diagnosis
    - Consult Infectious Disease Physician if needed
  - Treatment can begin sooner
    - Proper antibiotics
  - Move patient to private room without further delay
  - Use of proper PPE
  - Improve patient outcome

WOUND CULTURE Final

Organism 1	KLEBSIELLA PEUMONIAE			
Organism 2	PROTEUS MIRABILIS			
TRIMETHOPRIM/SULFAMETHOXAZOLE	R	>=320	R	>=320
AMOXACILLIN/CLAVULANATE	R	>=32	S	<=2
AMPICILLIN	R	>=32	R	>=32
AMPICILLIN/SULBACTAM	R	>=32	S	<=2
CEFAZOLIN	R	>=64	S	8
CEFTAZIDIME	R	>=64	S	<=1
CEFTRIAXONE	R	>=64	S	<=1
* CEFEPIME	R	16	S	<=1
CIPROFLOXACIN	R	>=4	R	>=4
LEVOFLOXACIN	R	>=8	R	>=8
GENTAMICIN	S	<=1	S	<=1
ERTAPENEM	R	<=0.5		
EXTENDED SPECTRUM B LACTAMASE	-	NEG		
TOBRAMYCIN	I	8	S	<=1
PIPERACILLIN/TAZOBACTAM	R	>=128	S	<=4

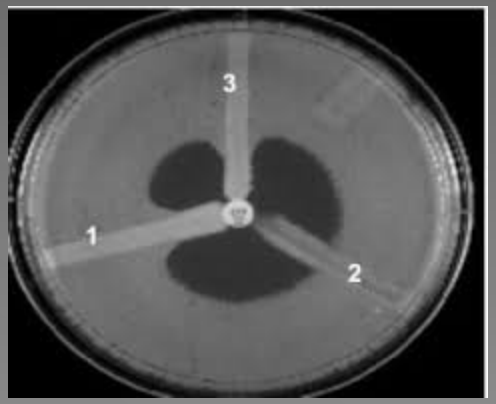
5/3/15-KLEBSIELLA PNEUMONIAE & PROTEUS MIRABILIS BOTH SENT TO ARUP FOR HODGE TEST.

KLEBSIELLA PNEUMONIAE IS POSITIVE FOR HODGE TEST.
PROTEUS MIRABILIS IS NEGATIVE FOR HODGE TEST.

MODIFIED HODGE TEST

(MHT) detects carbapenemase production in isolates of Enterobacteriaceae. In the United States, the most common carbapenemase found in Enterobacteriaceae is the Klebsiella pneumoniae carbapenemase (KPC).

Carbapenemase production is detected when the test isolate produces the enzyme and allows growth of a carbapenem susceptible strain. The result is a characteristic cloverleaf-like indentation.



SOME CARBAPENEM EXAMPLES

Generic	Brand Name
Imipenem	Primaxin
Doripenem	Doribax
Meropenem	Merrem
Ertapenem	Invanz

HOW ARE WE WORKING TO DECREASE THE SPREAD OF CRE INFECTION?

- Infection Prevention makes daily rounds
  - Hand washing
  - Proper PPE
  - Dedicated equipment in room
  - Contact Precautions sign present
  - Documented Education
  - Private Room
- Infection Prevention reviews Data from Computerized Surveillance system
- Evaluate devices used
  - Central line
  - Foley Catheter

HOW DO WE TREAT CRE?

- Consult Infectious Disease Physician
  - Often resistant to many prescribed antibiotics
  - Decisions to treat made on a case by case assessment
  - Someone may be colonized but not infected and not need treatment

WHAT DO WE DO TO PREVENT THE SPREAD OF CRE?

- Early recognition
  - Nursing called with positive Drug Resistant Organism
- Placing colonized and infected patients on contact precautions
- Use proper PPE & Contact Precautions
- Using medical devices and antimicrobials wisely
  - Nurse driven protocols to review need for Catheters
  - Antibiotic Stewardship Program
  - Infectious Disease Physician to ensure proper antibiotics prescribed
- Education
  - Infection Prevention rounding

DO WE EVER DISCONTINUE CONTACT PRECAUTIONS FOR THE CRE PATIENT?

- There is not enough data for the CDC to make a recommendation
- It is known that patients can be colonized for long periods of time
- Do not base on a single negative culture, patients can be intermittently positive on serial surveillance cultures
- We do not discontinue CRE contact precautions during hospital stay

Questions?

CONTACT INFORMATION

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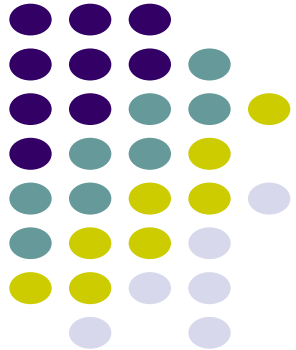
CRE

Carbapenem Resistant Enterobacteriaceae

Jenny Pierce
Executive Nursing Director with RDK Management Services, Inc.

Disclosure Statement: None



What is CRE?

- A gram-negative bacteria that is nearly resistant to all antibiotics that are listed in the Carbapenem class
- It is considered the new drug resistant “super bug”
- The mortality rate is greater than two of the other known health care infections:
  - MRSA
  - C-Diff
- Statistics show that the death rate is between 40% and 50% of patients infected

Who is at risk?

- Patients in Long-Term Care health settings are the most vulnerable
- Patients in Acute Care settings
- Patients who have had excessive use of certain antibiotics
- Patients who have had certain medical procedures

How does it spread?

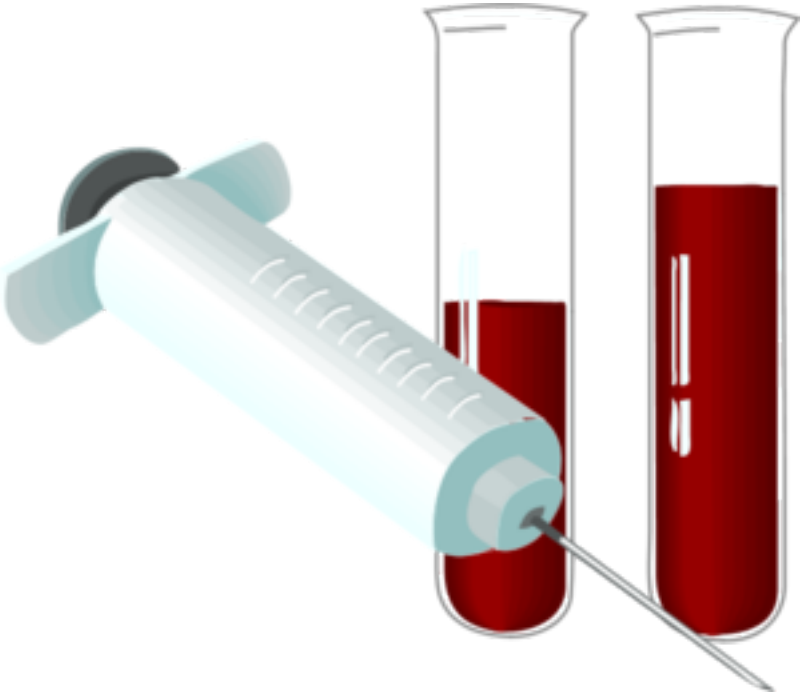
- Transmitted person to person
- A person must come in contact or be exposed to the bacteria in order to become infected
- Can be transmitted by direct contact with contaminated skin, feces, or wounds
- By patients who are colonized
- Contaminated medical devices such as:
  - Intravenous Catheters
  - Urinary Catheters

Symptoms

- NO specific symptoms
- Problems that can alert physicians:
  - Severe Pneumonia
  - Sepsis
  - Severe UTI
  - Resistance to Antibiotic Therapy

Diagnosis

- Blood Tests
  - Blood Cultures
  - Drug Sensitivity

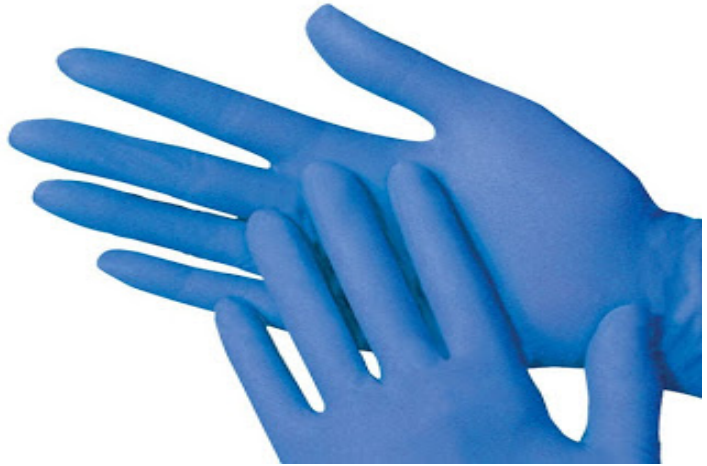


Treatment

- A combination of antibiotics can be prescribed to inhibit the growth of the bacteria
- Contact Infectious Disease Expert
  - This bacteria is very difficult to treat and not many treatments have been successful
  - There are currently no new antibiotics in development that show any promise to kill the bacteria

Prevention

- Education
- Hand Hygiene
- Isolating Infected Patients
- Wearing Gowns & Gloves
- Limit Antibiotic Usage
- Limit Usage of Invasive Medical Devices



Conclusion

- Infection Control is **KEY**
- Updated Infection Control Log
- Good Communication
- Education & Knowledge
- Documentation

Contact Information

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  - jenny@rdkmgnt.com

Laboratory Detection of Carbapenem Resistant Enterobacteriaceae

Thomas Kirn MD PhD
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Evanston, IL

Disclosures

- I have nothing relevant to this presentation to disclose

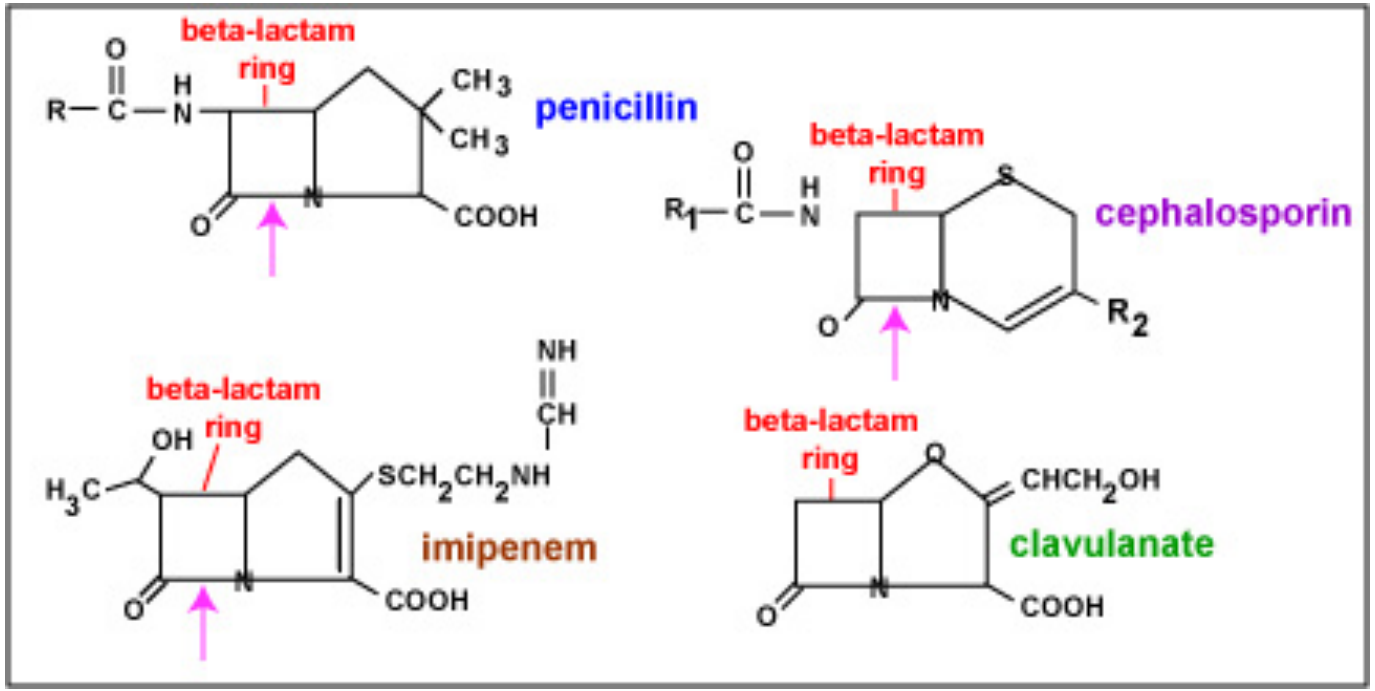
Objectives

- Participants will be able to:
  - Describe the general structure, mechanism of action and clinical utility of the β lactam class of antibiotics
  - Describe mechanisms of resistance to β lactam antibiotics in Enterobacteriaceae with emphasis on carbapenem resistance
  - Compare/contrast laboratory methods that may be employed to detect and/or characterize carbapenemase producing organisms
  - Critically evaluate (and improve if necessary) current procedures employed in their own laboratories for the detection of carbapenem resistant organisms

Nomenclature

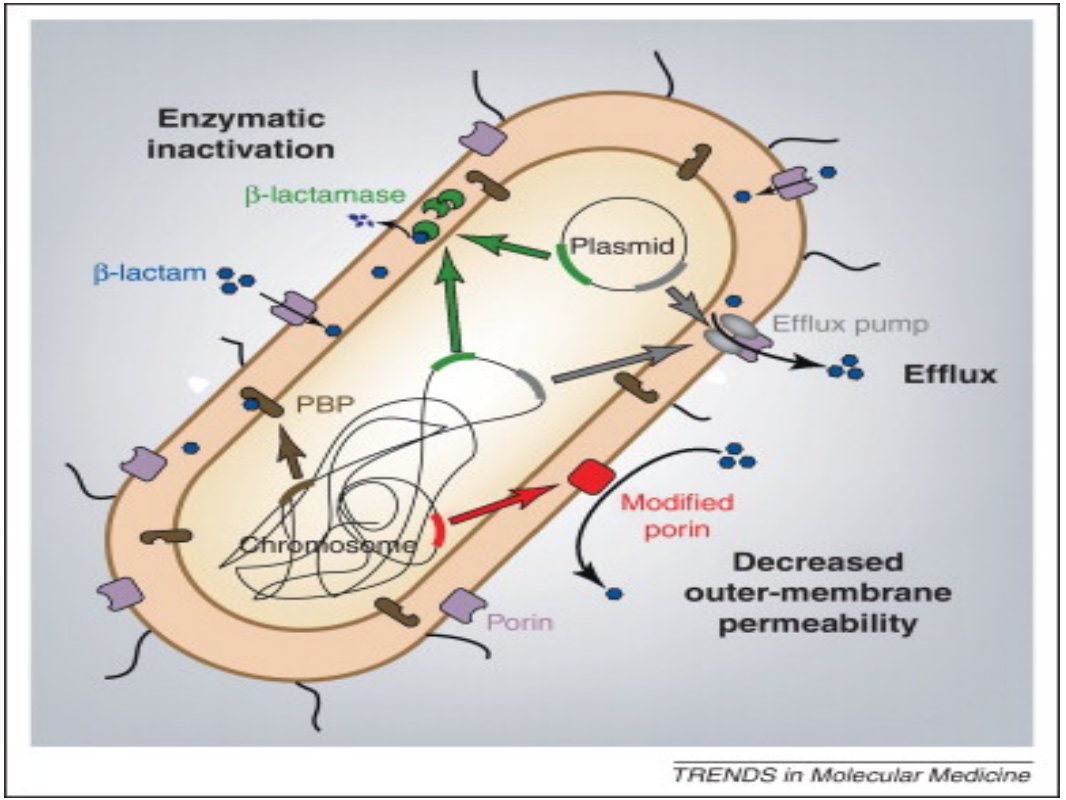
- MDRO
  - Multi drug resistant organism
- CRE
  - Carbapenem resistant Enterobacteriaceae
- CP-CRE
  - Carbapenemase producing CRE

β-Lactams

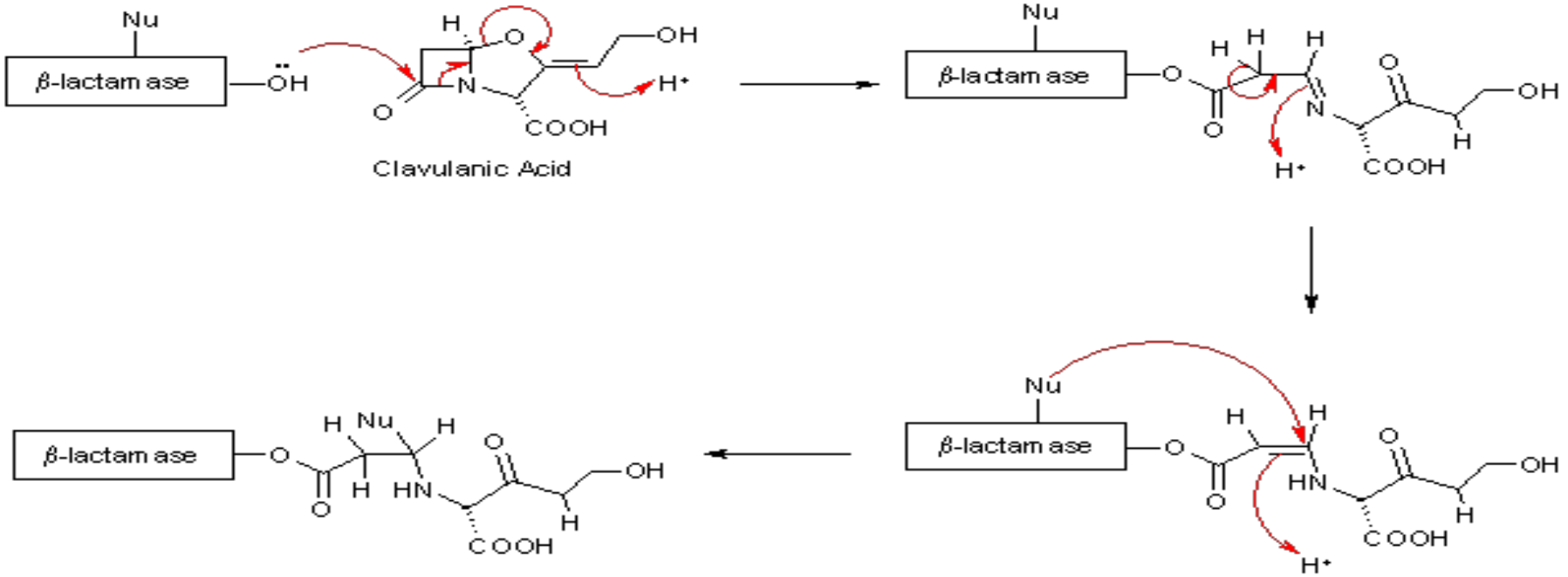


http://faculty.ccbcmd.edu/courses/bio141/lecguide/unit2/control/blactam.html

Mechanisms of Resistance to β Lactam Antibiotics



β Lactamase Inhibitors

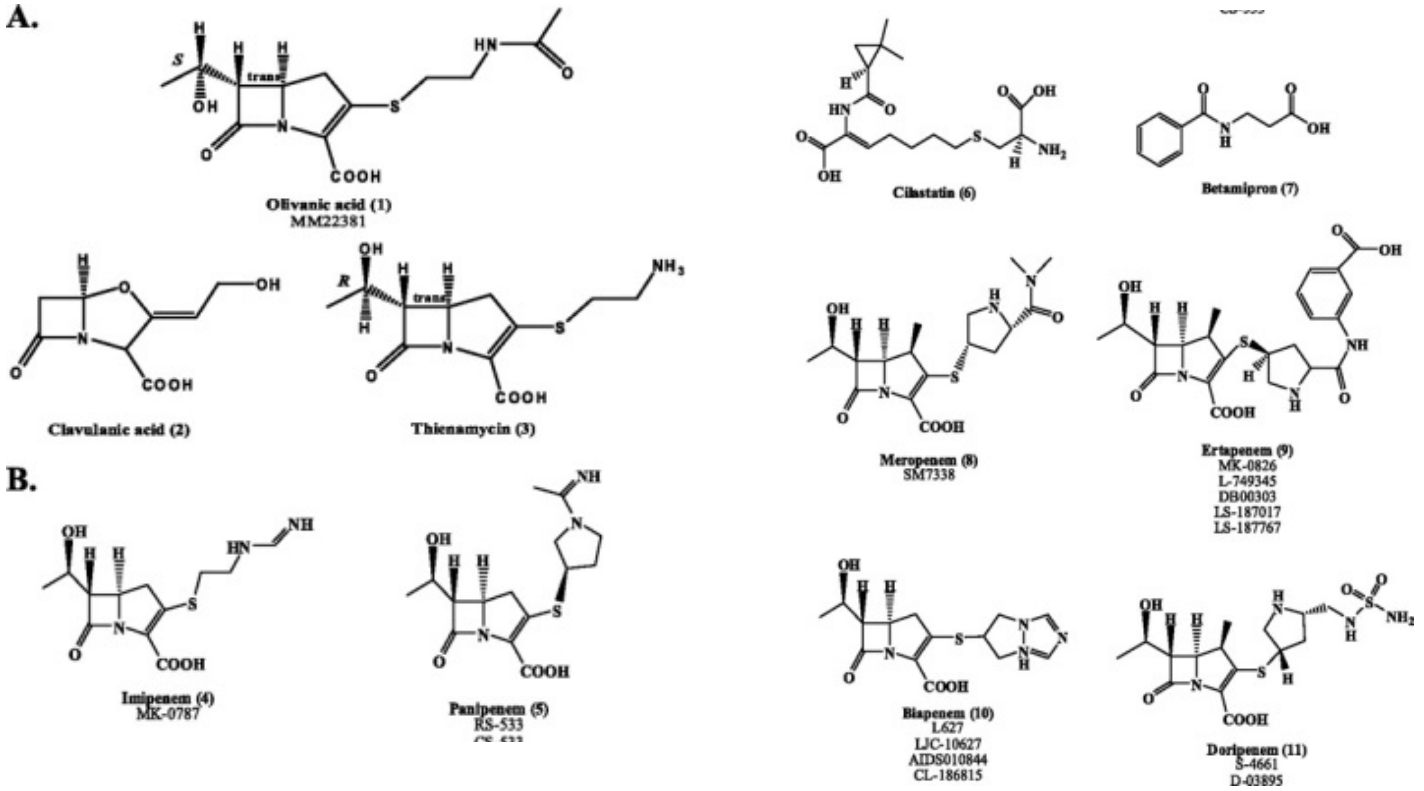


http://homepage.ntlworld.com/diamonddove/08_BLInhibitors/BLInhi30.gif

β-Lactam Antibiotics

Penicillins	Cephalosporins	Cephamycins	Monobactams
Penicillin Methicillin Ampicillin Ticaricillin	1st Generation (narrow, G+) Cephalothin Cefazolin 2nd Generation (expanded, G-) Cefamandole Cefuroxime 3rd Generation (broad, more G-) Cefotaxime Ceftazidime Ceftriaxone 4th Generation (extended, G-) Cefepime 5th Generation(G+ incl MRSA) Ceftaroline	(2nd Gen + Anaerobes) Cefoxitin Cefotetan Cefmetazole	Aztreonam

Evolution of Carbapenems



Carbapenems

- 4:5 fused ring lactam of penicillins with a double bond between C-2 and C-3 but with substitution of carbon for sulfur at C-1
- First stable carbapenem was imipenem
- Mechanism of action
  - Do not diffuse easily across OM
  - Must be transported by OMPs (porins)
  - Permanently acylate PBPs, inhibiting cell wall synthesis
- Activity
  - Broader spectrum than penicillins/cephalosporins and combinations
  - Imipenem/doripenem – better gram + coverage
  - Meropenem/ertapenem/doripenem – Better gram – coverage
  - Erta less active against *Pseudomonas aeruginosa*
  - Mero less active against *A. baumanii*
  - Dori exhibits lower MICs against Pa and Ab
  - Dori is the most stable in the face of beta-lactamases

β-lactam Antibiotics

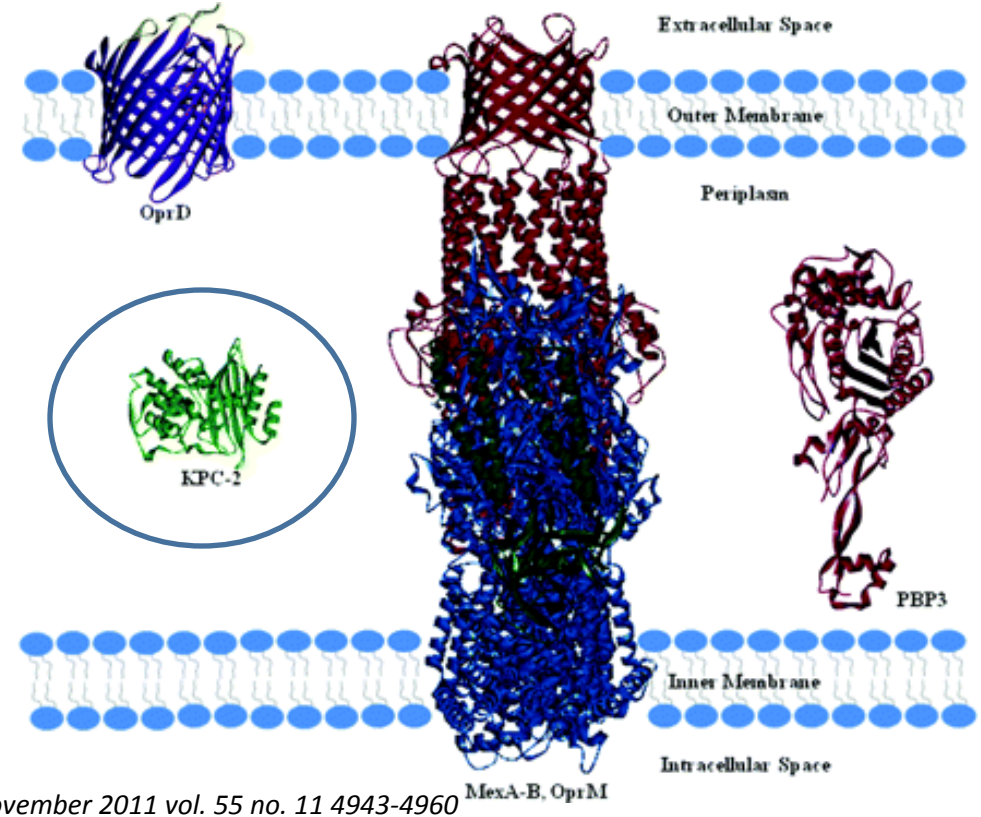
Penicillins	Cephalosporins	Cephamycins	Monobactams	Carbapenems
Penicillin Methicillin Ampicillin Ticaricillin	1st Generation (narrow, G+) Cephalothin Cefazolin 2nd Generation (expanded, G-) Cefamandole Cefuroxime 3rd Generation (broad, more G-) Cefotaxime Ceftazidime Ceftriaxone 4th Generation (extended, G-) Cefepime 5th Generation(G+ incl MRSA) Ceftaroline	(2nd Gen + Anaerobes) Cefoxitin Cefotetan Cefmetazole	Aztreonam	Imipenem Meropenem Ertapenem Doripenem

Carbapenem resistance is a public health problem

- Increased length of stay
- Increased mortality
  - Limited treatment options for serious infections
- Few new drugs for resistant GNRs
- Mobile genetic elements transmit resistance
- Infection control practices are essential to limit spread of colonization and infection

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

Mechanisms of Carbapenem Resistance



Antimicrob. Agents Chemother. November 2011 vol. 55 no. 11 4943-4960

Carbapenemases

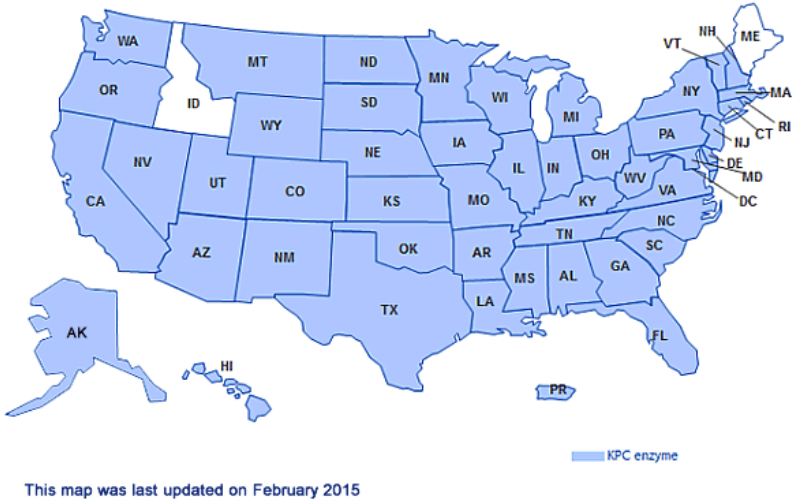
Carbapenemase Classes

β lactamase Molecular Class	Enzymes	Common Bacteria	Features
A	KPC SME IMI, NMCA, GES	*K. pneumoniae*, others *S. marscenses* Enterobacteriaceae	Chromosomal or Plasmid encoded, partially inhibited by clavulanate and boronic acid
B - MBLs	IMP, VIM, GIM, SPM, NDM-1	*S. maltophilia* *P. aeruginosa* Enterobacteriaceae *Acinteobacter spp.*	Do not hydrolyze aztreonam, inhibited by EDTA
C	AmpC	Enterobacteriaceae	Some activity against carbapenems, resistance associated with porin mutations/efflux
D	OXA	*A. baumanii* Enterobacteriaceae	Not inhibited by EDTA, boronic acid or clavulanate

Clin Microbiol Rev. 2007 Jul; 20(3): 440–458.

KPC

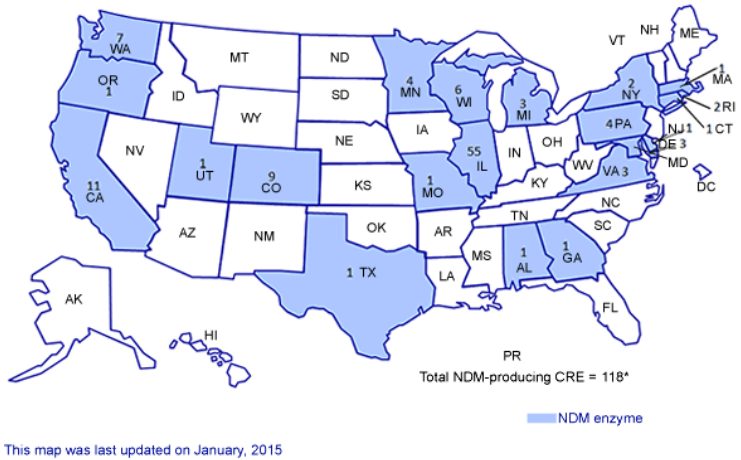
- Most prevalent carbapenemase in USA
- At least 22 types of KPC identified
- Encoded by the bla_{KPC} gene which is present on a plasmid
- Plasmid often encodes resistance to other drug classes
- Enterobacteriaceae
- Inhibited by boronic acid compounds



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

MBLs

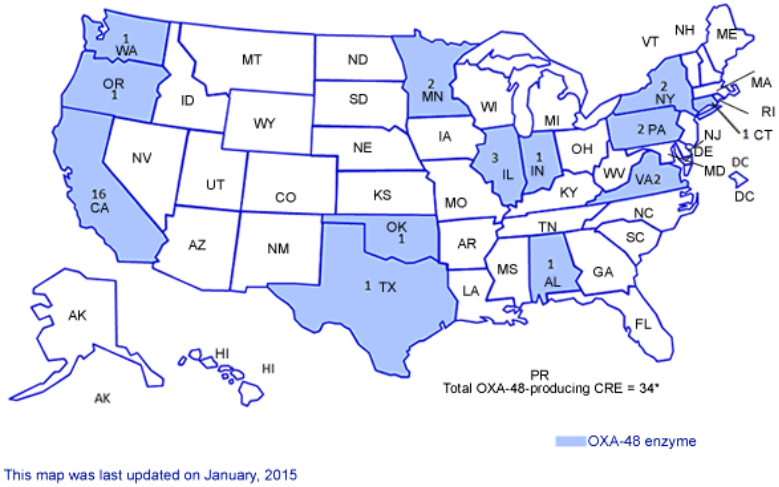
- Require zinc for activity (inhibited by zinc chelators)
- NDM most common example in US
- Carried on a mobile genetic element with additional resistance genes
- Highly transmissible
- Environmental reservoirs in Indian subcontinent, Middle East and Balkan countries
- Enterobacteriaceae, *P. aeruginosa*, *Acinetobacter*



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

OXA

- Nearly 500 types
- Most plasmid encoded
- Enterobacteriaceae
- *A. baumanii*
- Most challenging to detect using current phenotypic methods



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

Other Mechanisms of Carbapenem Resistance

- Cephalosporinase combined with altered permeability
  - AmpC, CTX-M may have low-level carbapenemase activity
  - Porin loss limits entry of the carbapenem into the periplasm
  - When combined, these two traits can mediate resistance to carbapenems (organisms will test I or R *in vitro*)
  - *Enterobacter spp.,* other Enterobacteriaceae
- Intrinsic non-suscpetibility
  - *Proteus spp., Morganella morganii, Providenica spp.* VS imipenem for example

β-lactam Antibiotics

Penicillins	Cephalosporins	Cephamycins	Monobactams	Carbapenems
Penicillin Methicillin Ampicillin Ticaricillin	1st Generation (narrow, G+) Cephalothin Cefazolin 2nd Generation (expanded, G-) Cefamandole Cefuroxime 3rd Generation (broad, more G-) Cefotaxime Ceftazidime Ceftriaxone 4th Generation (extended, G-) Cefepime 5th Generation(G+ incl MRSA) Ceftaroline	(2nd Gen + Anaerobes) Cefoxitin Cefotetan Cefmetazole	Aztreonam	Imipenem Meropenem Ertapenem Doripenem

β-lactam Antibiotics

Penicillins | Cephalosporins | Cephamycins | Monobactams | Carbapenems

(2nd Gen + Anaerobes)
Cefoxitin
Cefotetan
Cefmetazole

Imipenem
Meropenem
Ertapenem
Doripenem

ESBL

CTX-M, SHV, TEM

β-lactam Antibiotics

Penicillins | Cephalosporins | Cephamycins | Monobactams | Carbapenems

Imipenem
Meropenem
Ertapenem
Doripenem

4th Generation (extended, G-)
Cefepime

AmpC

β-lactam Antibiotics

Penicillins | Cephalosporins | Cephamycins | Monobactams | Carbapenems

Aztreonam

MBL

β-lactam Antibiotics

Penicillins Cephalosporins Cephamycins Monobactams Carbapenems

KPC

CDC Definition of CRE

- As of January 2015:
  - **Resistant** to imipenem, meropenem, doripenem, or ertapenem OR documentation that the isolate possesses a carbapenemase
- The previous CDC CRE definition (nonsusceptible to imipenem, meropenem, or doripenem, AND resistant to all third generation cephalosporins tested) was designed to be more specific for CP-CRE; however, it has proven to be complicated, difficult to implement, and has been found to miss some CP-CRE

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

Distinguishing CP-CRE from other CRE

- Why?
  - Identify isolates resistant to all carbapenems and other β-lactams
  - May need to modify antibiogram (2010 and earlier CLSI carbapenem breakpoints)
  - Infection control
    - CP-CRE are the greatest public health/infection control threat
  - Contribute to national surveillance efforts

Distinguishing CP-CRE from other CRE

- How?
  - Methods that detect carbapenemases
  - Methods that characterize carbapenemases
  - Combinations

CLSI Carbapenem Breakpoints

	CLSI M100-S19 (2009) MIC (µg/mL)			Updated CLSI M100-S23 (2013) MIC (µg/mL)		
Antimicrobial	**S**	**I**	**R**	**S**	**I**	**R**
Imipenem	≤ 4	8	≥ 16	≤ 1	2	≥ 4
Meropenem	≤ 4	8	≥ 16	≤ 1	2	≥ 4
Ertapenem	≤ 2	4	≥ 8	≤ 0.5	1	≥ 2
Doripenem	N/A	N/A	N/A	≤ 1	2	≥ 4

	CLSI M100-S19 (2009) disk zones (mm)			Updated CLSI M100-S23 (2013) disk zones (mm)		
Antimicrobial	**S**	**I**	**R**	**S**	**I**	**R**
Imipenem	≥ 16	14-15	≤ 13	≥ 23	20-22	≤ 19
Meropenem	≥ 16	14-15	≤ 13	≥ 23	20-22	≤ 19
Ertapenem	≥ 19	16-18	≤ 15	≥ 22	19-21	≤ 18
Doripenem	N/A	N/A	N/A	≥ 23	20-22	≤ 19

Detection of Carbapenemases - CLSI

Introduction to Tables 3B and 3C. Tests for Carbapenemases in *Enterobacteriaceae, Pseudomonas aeruginosa,* and *Acinetobacter* spp.

Institutional infection control procedures or epidemiological investigations may require identification of carbapenemase-producing *Enterobacteriaceae, P. aeruginosa,* and *Acinetobacter* spp. Such testing is not currently recommended for routine use.

Carbapenemase-producing isolates of *Enterobacteriaceae* usually test intermediate or resistant to one or more carbapenems using the current interpretive criteria as listed in Table 2A (NOTE: Ertapenem nonsusceptibility is the most sensitive indicator of carbapenemase production), and usually test resistant to one or more agents in cephalosporin subclass III (eg, cefoperazone, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone). However, some isolates that produce carbapenemases such as SME or IMI often test susceptible to these cephalosporins.

Laboratories using *Enterobacteriaceae* minimal inhibitory concentration (MIC) interpretive criteria for carbapenems described in M100-S20 (January 2010) should perform the modified Hodge test (MHT), the Carba NP test, and/or a molecular assay as described below when isolates of *Enterobacteriaceae* are suspicious for carbapenemase production based on imipenem or meropenem MICs of 2–4 µg/mL or ertapenem MIC of 2 µg/mL. Refer to Tables 3B-1 or 3C-1 for specific steps to use with interpretive criteria for carbapenems listed in M100-S20 (January 2010).

	Tests Used for Epidemiological or Infection Control–Related Testing		
	MHT	Carba NP	Other (eg, molecular assays)
Organisms	*Enterobacteriaceae* that are nonsusceptible to one or more carbapenems	*Enterobacteriaceae, P. aeruginosa,* and *Acinetobacter* spp. that are nonsusceptible to one or more carbapenems	*Enterobacteriaceae, P. aeruginosa,* and *Acinetobacter* spp. that are nonsusceptible to one or more carbapenems to determine the presence of a carbapenemase, or to determine carbapenemase type in isolates positive by MHT or Carba NP
Strengths	Simple to perform No special reagents or media required	Rapid	Determines type of carbapenemase in addition to absence or presence of the enzyme
Limitations	False-positive results can occur in isolates that produce ESBL or AmpC enzymes coupled with porin loss. False-negative results are occasionally noted (eg, some isolates producing NDM carbapenemase). Only applies to *Enterobacteriaceae.*	Special reagents are required, some of which require in-house preparation (and have a short shelf life). Invalid results occur with some isolates. Certain carbapenemase types (eg, OXA-type, chromosomally encoded) are not consistently detected.	Special reagents and equipment required Specific to targeted genes; false-negative result if specific carbapenemase gene present is not targeted

Abbreviations: ESBL, extended-spectrum β-lactamase; MHT, modified Hodge test; NDM, New Delhi metallo-β-lactamase.

Detection of Carbapenemases - CLSI

Table 3B-1. Modifications of Table 3B When Using Interpretive Criteria for Carbapenems Described in M100-S20 (January 2010)

Test	Confirmatory Test
When to Do This Test:	**Until laboratories can implement the current carbapenem MIC interpretive criteria, this test (or an alternative confirmatory test for carbapenemases) should be performed when isolates of *Enterobacteriaceae* are suspicious for carbapenemase production based on imipenem or meropenem MICs of 2–4 µg/mL or ertapenem MIC of 2 µg/mL.**
Reporting	For isolates that are MHT positive and have an ertapenem MIC of 2–4 µg/mL, imipenem MIC of 2–8 µg/mL, or meropenem MIC of 2–8 µg/mL, report all carbapenems as resistant. If the MHT is negative, interpret the carbapenem MICs using CLSI interpretive criteria as listed in Table 2A in M100-S20 (January 2010). **NOTE:** Not all carbapenemase-producing isolates of *Enterobacteriaceae* are MHT positive and MHT-positive results may be encountered in isolates with carbapenem resistance mechanisms other than carbapenemase production.

Abbreviations: MHT, modified Hodge test; MIC, minimal inhibitory concentration.

Modified Hodge Test

- Not specific for carbapenemases
- AmpC with porin loss/efflux could be positive
- May miss NDM producing isolates

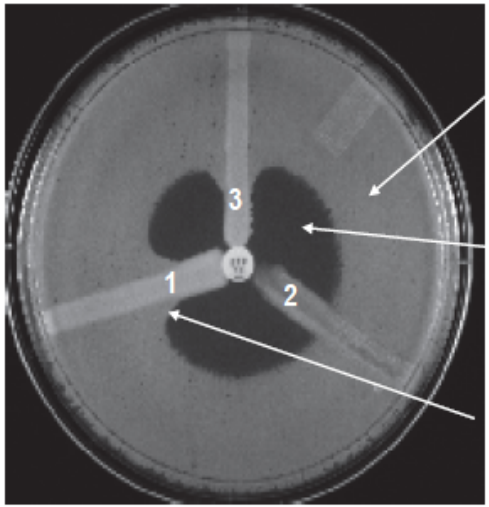
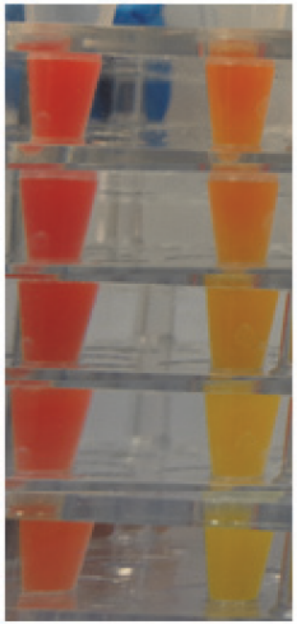


Figure 1. The MHT Performed on a Small MHA Plate.
(1) *K. pneumoniae* ATCC® BAA-1705, positive result;
(2) *K. pneumoniae* ATCC® BAA-1706, negative result;
and (3) a clinical isolate, positive result.

Carba NP

Solution A		Solution B
Red		Orange
Red		Light Orange
Red		Dark Yellow
Red-orange		Yellow
Red-orange		Yellow

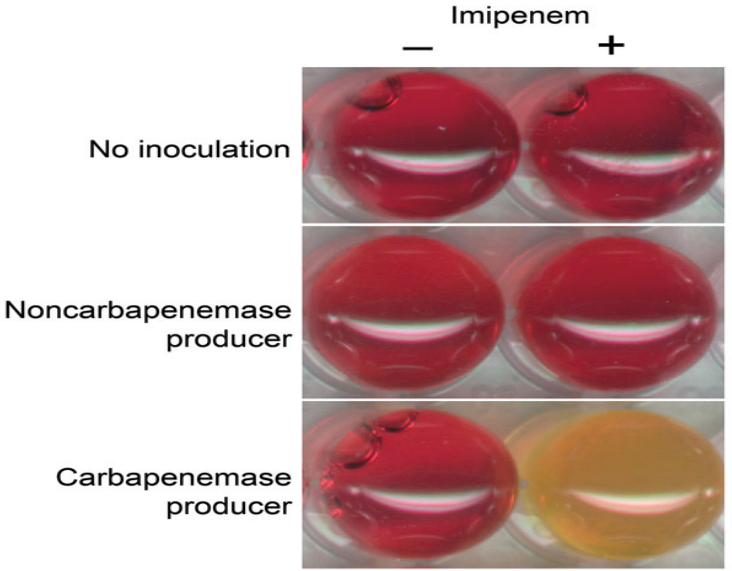
Results for Patient and QC Tubes		
Tube "a": Solution A (serves as internal control)	Tube "b": Solution B	Interpretation
Red or red-orange	Red or red-orange	Negative, no carbapenemase detected
Red or red-orange	Light-orange, dark yellow, or yellow	Positive, carbapenemase producer
Red or red-orange	Orange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

- Nordmann and Poirel
- Enterobacteriaceae, *P. aeruginosa* and *Acinetobacter*
- Imipenem is hydrolyzed, producing a color change

EID Volume 18, Number 9—September 2012

Carba NP

- Sometimes difficult to interpret results
- Reagents must be made fresh
- Not great for detection of OXA-48



EID Volume 18, Number 9—September 2012

Carbapenem Inactivation Method

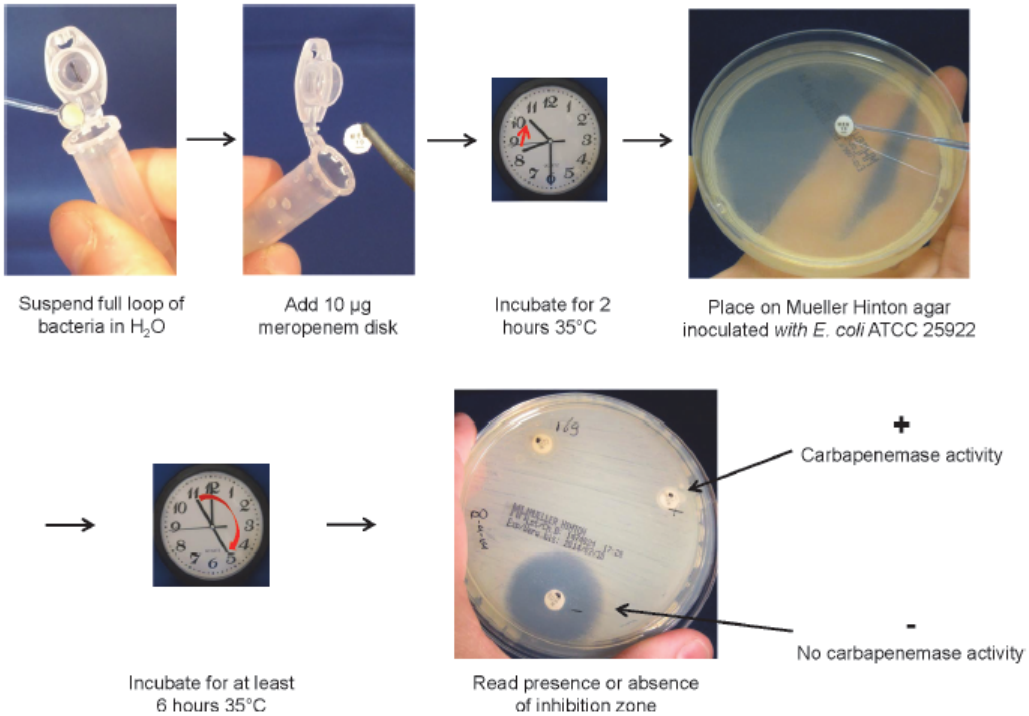


Fig 1. Schematic of the CIM.

PLOS ONE | DOI:10.1371/journal.pone.0123690 March 23, 2015

CIM

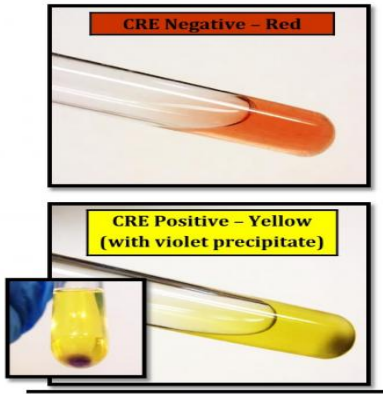
Table 1. Isolates used for validation of the CIM.

Species	carbapenemase gene	CIM	CarbaNP
Klebsiella pneumoniae[1]	KPC-2	+	+
Klebsiella pneumoniae[1]	NDM-1	+	+
Klebsiella pneumoniae[1]	OXA-48	+	+
Klebsiella pneumonia	OXA-48	+	+
Klebsiella pneumonia		-	-
Klebsiella pneumonia		-	-
Klebsiella pneumonia		-	-
Escherichia coli		-	-
Escherichia coli		-	-
Escherichia coli		-	-
Escherichia coli		-	-
Escherichia coli		-	-
Escherichia coli ATCC25922[1]		-	-
Enterobacter cloacae		-	-
Enterobacter cloacae		-	-
Salmonella Bareilly		-	-
Salmonella Heidelberg		-	-
Pseudomonas aeruginosa[1]	VIM-2	+	+
Pseudomonas aeruginosa	VIM-2	+	+
Pseudomonas aeruginosa[1]	IMP-1	+	+
Pseudomonas aeruginosa[1]	GIM-1	+	+
Pseudomonas aeruginosa[1]	SPM-1	+	+
Pseudomonas aeruginosa	AIM-1	+	+
Pseudomonas fluorescens	BIC-1	+	-
Pseudomonas stutzeri[1]	DIM-1	+	+
Acinetobacter baumannii	OXA-23	+	+
Acinetobacter baumannii	OXA-40	+	+
Acinetobacter baumannii	OXA-58	+	+
Acinetobacter baumannii	OXA-143	+	+
Acinetobacter baumannii[1]	SIM-1	+	+

EPI-CRE

Carbapenem-Resistant *Enterobacteriaceae* (CRE)

It's Easy to See...



Specifications

Time to Results:	**Positive** – as soon as the sample changes from red to yellow.
	Negative – after 24 hours if no color change from red 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.

Distributed by:

EPI-CRE® is intended to be used as an epidemiological surveillance tool. It is not an antibiotic susceptibility test.

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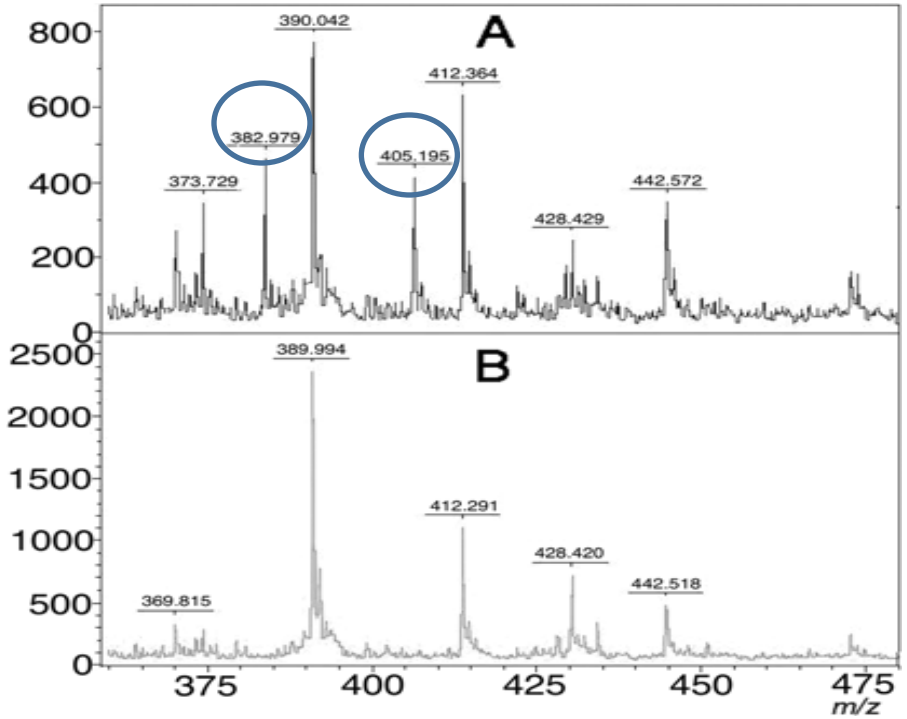
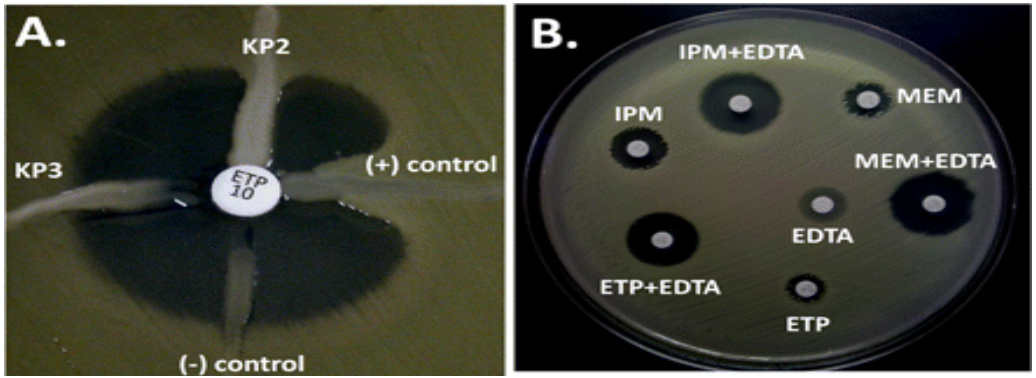
MALDI



J. Clin. Microbiol. September 2011 vol. 49 no. 9 3222-3227

Characterization of Carbapenemases

MBL Disk Test/MBL Etest



- EDTA, dipicolinic acid, mercaptopropionic acid all may be used as inhibitors of MBLs
- EDTA may permeabilize cells

Different growth-inhibition patterns:

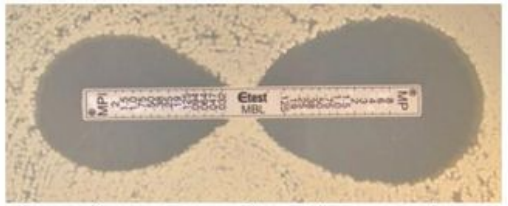


Figure 2. Clear cut MBL negative: MP/MPI IC <0.125/<0.032

Figure 3. Clear cut MBL positive: MP/MPI IC >8/0.19 = >42

Figure 4. Phantom zone between MP/MPI is indicative of MBL

J. Clin. Microbiol. April 2011 vol. 49 no. 4 1667-1670

Boronic Acid Methods

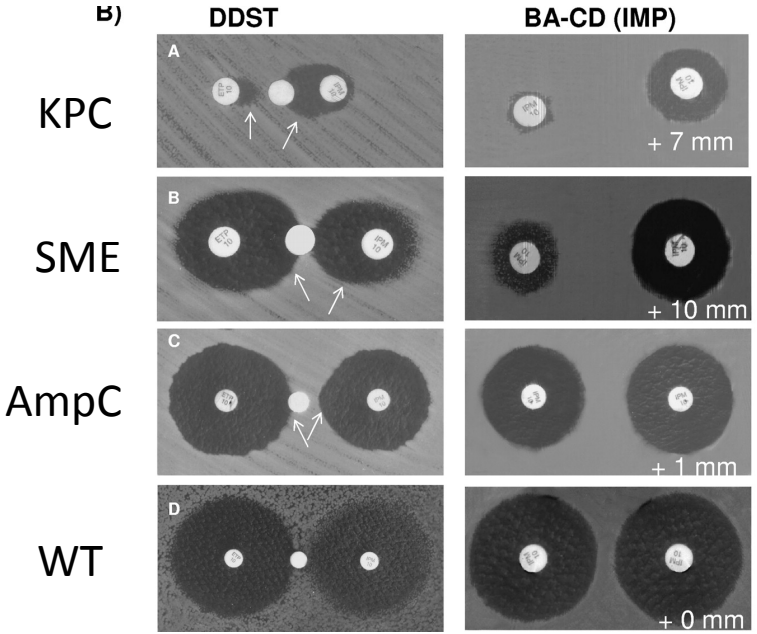


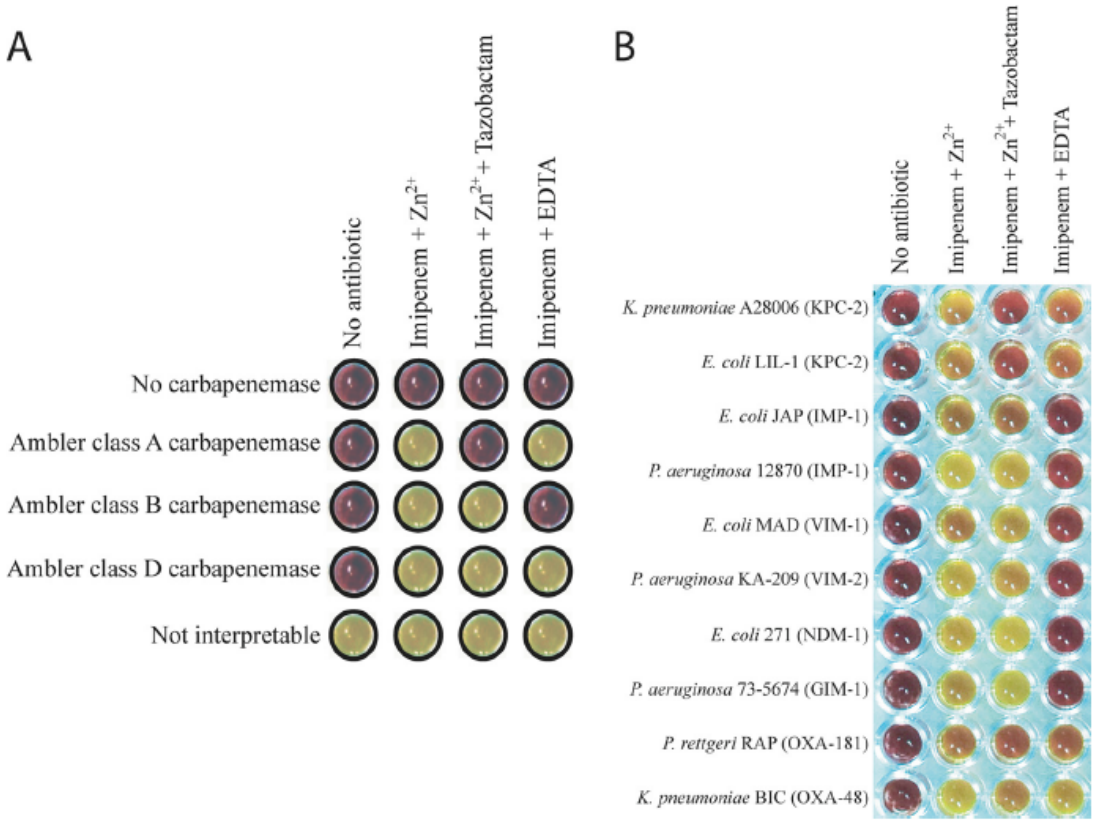
TABLE 5. Summary of sensitivities, specificities, positive predictive values, and negative predictive values of the combined-disk tests using different boronic acid compounds and different antibiotic substrates in the phenotypic detection of KPC-producing isolates

Antibiotic substrate and boronic acid	Sensitivity (%)	Specificity (%)	PPV[a] (%)	NPV[b] (%)
Imipenem				
APBA, 300 μg	64.3	97.6	96.0	75.6
APBA, 600 μg	82.1	97.6	96.8	86.1
PBA, 400 μg	100	97.6	97.4	100
Meropenem				
APBA, 300 μg	77.7	97.6	96.7	83.2
APBA, 600 μg	96.4	97.6	97.3	96.9
PBA, 400 μg	100	97.6	97.4	100

[a] PPV, positive predictive value.
[b] NPV, negative predictive value.

J. Clin. Microbiol. June 2009 vol. 47 no. 6 1631-1639
J. Clin. Microbiol. August 2011 vol. 49 no. 8 2804-2809

Carba NP Test II



Antimicrob Agents Chemother. 2012 Dec; 56(12): 6437–6440

Limitations of Inhibition Assays

- Interpretation can be subjective
- Requires overnight incubation in most cases
- Limitations in detecting OXAs
- Multiple methods may need to be used in combination to detect more than one enzyme (AmpC plus KPC for example)

NAATs

- Single PCR reactions vs multiplex panels
- Target driven:
  - KPC, NDM, VIM, IMP, OXA, etc…
- FDA cleared assays for signal positive BC panels exist (Biofire, Verigene)
- BD MAX CRE assay (KPC, NDM, OXA48)
- Check Points (KPC, VIM, NDM, OXA48, OXA181)
- Others, LDTs
- Time consuming, technically complex, validation

CRE Surveillance Cultures

- Active surveillance allows for detection of patients colonized with CRE in the intestinal tract
- Patients who are found to be colonized or infected with CRE should be placed on Contact Precautions in order to prevent transmission of the resistant bacteria
- Additionally, it allows additional opportunities for recovery of organisms
- Who to screen?
  - Everyone, critically ill
- When to screen?
  - Admission, at defined intervals
- How to screen
  - Broth enrichment followed by selective culture
  - Direct KB disk test
  - Chromogenic Agar
  - NAATs
  - Combinations

MDRO Surveillance at NorthShore

- Screen all ICU admissions
- Weekly sampling from patients in the ICU (rotating among 4 hospitals)
- Respiratory (sputum/throat), axillae, rectum
- Pooled specimens inoculated to VACC agar
- Pooled specimen PCR (CTX-M, KPC, NDM)
- Quarterly point prevalence screening

IDPH Guidance/Recommendations

- For *E. coli* and *Klebsiella* spp. non-susceptible to any carbapenem and resistant to all 3rd generation cephalosporins, test for carbapenemases. Testing should include a method for detection of metallo-beta-lactamase (MBL). Examples of acceptable testing methods are shown below.
  - Modified Hodge Test (MHT)
  - MBL Etest[3]*
  - MBL Screen test[3]*
  - Tablet/disc diffusion detection of KPC/MBL resistance mechanisms[4]*
  - Boronic Acid Inhibition Test for KPC and AmpC[5]
  - Broth microdilution-BMD MBL screen[6,7]*
  - CarbaNP test to detect carbapenemase[8]*
  - MALDI-TOF detection of carbapenemases[9]*

  *These tests have the potential to detect MBL production

- 1.Perform Modified Hodge Test (MHT) for carbapenemase detection AND
- Perform MBL Etest3.
- 2.If MBL Etest positive, regardless of MHT results, report results as follows:

- **"Carbapenem resistant Enterobacteriaceae (CRE) detected by EDTA Inhibition Test –probable MBLtype. Implement infection control measures according to facility policy."**
- **Isolates that are MBL positive should be forwarded to IDPH lab for confirmation and further characterization. Prior to sending specimens, laboratories should contact local health department for approval. The authorization number provided by the LHD must be printed on the laboratory test requisition form in order for the specimen to be tested.**

- If MHT positive, but MBL Etest negative report results as follows:

- **"Carbapenem resistant Enterobacteriaceae (CRE) detected by Modified Hodge Test –probable KPC type. Implement infection control measures according to facility policy."**

IDPH **Reporting** Requirements

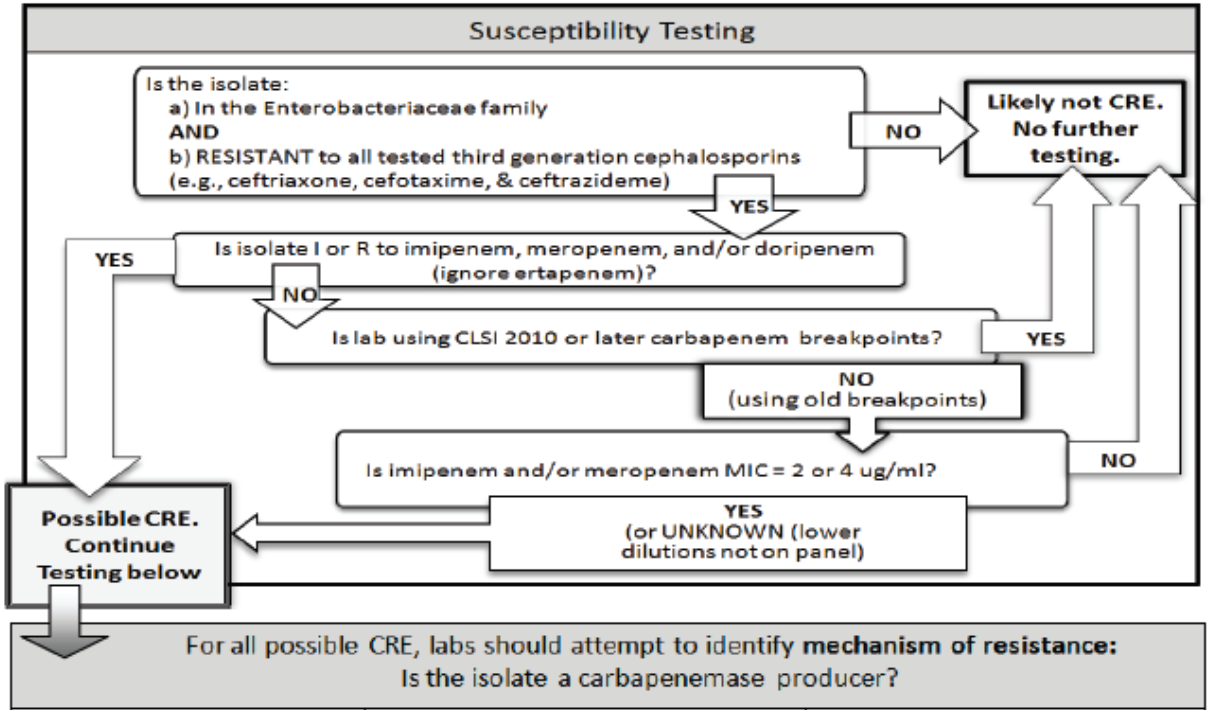
CRE surveillance criteria

Enterobacteriaceae (e.g., *E. coli, Klebsiella* spp, *Enterobacter* spp, *Proteus* spp, *Citrobacter* spp, *Serratia* spp, *Morganella* spp, *or Providentia* spp) with one of the following laboratory test results:

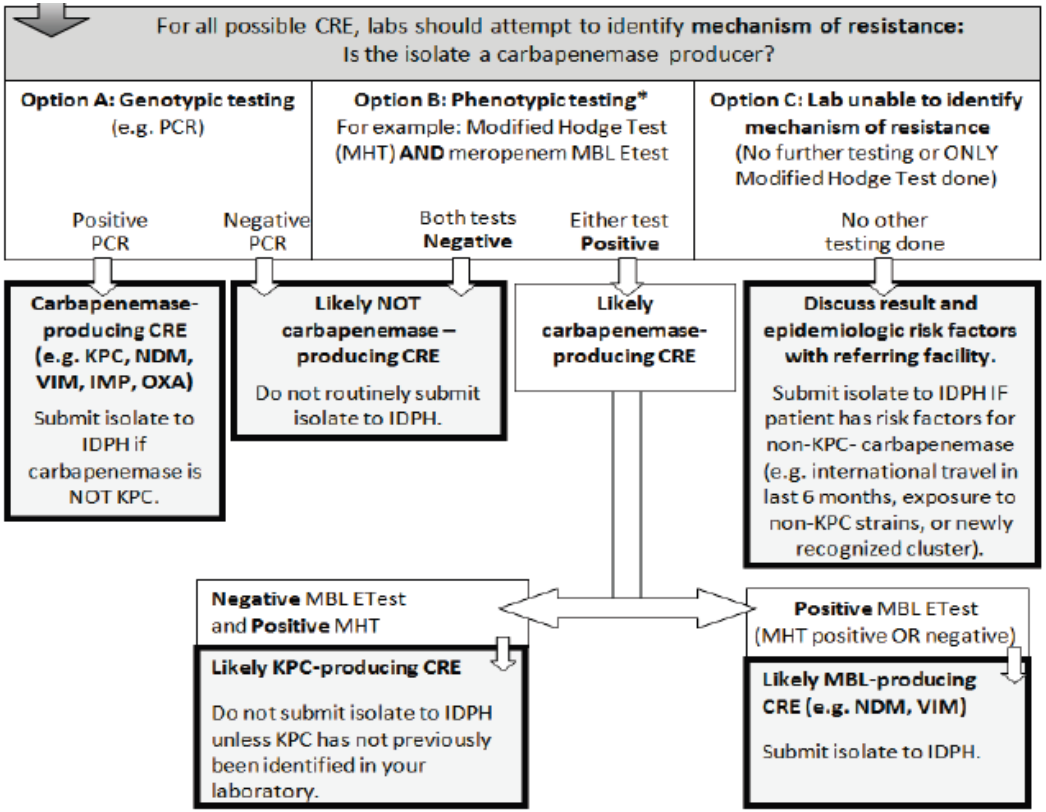
1. Molecular test (e.g., polymerase chain reaction [PCR]) specific for carbapenemase;
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production;
3. Susceptibility test (**for *E. coli* and *Klebsiella* spp only**): non-susceptible (intermediate or resistant) to ONE of the following carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL of the following third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime). *Note: ignore ertapenem for this definition.*

Report 1st CRE event per patient per encounter

Submission of Isolates to IDPH (1)



Submission of Isolates to IDPH (2)



*Other phenotypic tests are available and may be used; this two-step process is most common.

What about new drugs?

-	Gram +	Gram –	AmpC	ESBL	KPC	Metallo
Ceftolozane/ Tazobactam	–	++	+/–	++	–	–
Ceftazidime/ Avibactam	+/–	+++	++	++	++	–

Summary

- CRE are an important cause of serious infections and of infection control/epidemiologic importance
- Detecting and/or characterizing CP-CRE is important for epidemiologic purposes and may have therapeutic decision making utility
- A perfect method for CP-CRE detection/ characterization does not yet exist