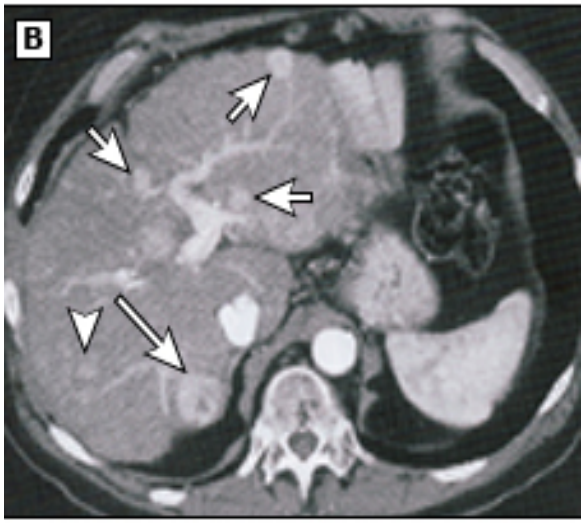
CASE 3

Case 3

- 61 yr old presenting to ED in septic shock
  - Fever 103°F
  - Tachycardic
- History of present illness:
  - Over several weeks worsening
    - Abdominal pain
    - Nausea/ vomiting
    - Fatigue/ fever
  - Multiple hepatic lesions seen on CT
- Past medical history:
  - Cholangiocarcinoma s/p resection and partial hepatectomy



www.uptodate.com

Case 3

- Microbiology Cultures
  - 2 sets of blood cx drawn
    - 2/2 *Enterobacter cloacae*

- Results Timeline
  - Day 1- Positive blood cx
    - GNR on GS
    - *Enterobacter* spp. by PCR
    - AR markers not detected
  - Day 2- Growth on culture plates
    - *Enterobacter cloacae*
  - Day 3- MIC available
    - Unusual resistance pattern
    - Discordant results
  - Day 4- Additional testing
    - mCIM
    - Ceftazidime-avibactam

Case 3

Molecular AR

From Positive Blood Cx	
bla_{CTX-M}	Not Detected
bla_{IMP}	Not Detected
bla_{KPC}	Not Detected
bla_{NDM}	Not Detected
bla_{OXA}	Not Detected
bla_{VIM}	Not Detected

From Colony Growth	
mCIM	Positive

Clinical Lab Results

MIC Testing

Antimicrobial	MIC µg/mL
Aztreonam	≥ 64 R
Cefepime	4 SDD
Ceftriaxone	≥ 64 R
Ertapenem	8 R
Gentamicin	≤ 1 S
Levofloxacin	4 I
Meropenem	4 R
Piperacillin-tazo	≥ 128 R

Antimicrobial	MIC µg/mL
Ceftazidime-avi	4 /4 S

CLSI

From a Lab Director's Perspective

3 Different Scenarios Encountered:

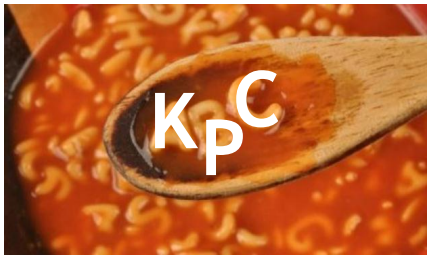
1. Genotype correlates with phenotype – Woohoo!

2. Detection of a AMR resistance marker with a susceptible AST profile

3. Lack of detection AMR resistance marker and a resistant AST profile

AMR & Gram-Negative Bacilli

- Heterogeneous resistance mechanisms
  - Absence of a gene does ≠ Susceptible
- Our example:
  - Negative for *bla*$_{CTX-M}$, *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{OXA}$, *bla*$_{VIM}$ & *bla*$_{IMP}$
  - Patient likely started empirically on cefepime and metronidazole
    - Inducible AmpC producer



SPACE Organisms with Inducible AmpC:

- *Serratia marcescens*
- *P. aeruginosa*
- *Acinetobacter* spp.
- *Citrobacter freundii*
- *Enterobacter* spp – including *Klebsiella* (formerly *Enterobacter*) *aerogenes*

(9) *Enterobacter, Citrobacter,* and *Serratia* may develop resistance during prolonged therapy with third-generation cephalosporins as a result of derepression of AmpC β-lactamase. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted.

Annavajhala et al, Front Microbiol, 2019; 10:44. CLSI, M100-S29, 2019. Tamma et al, CID, 2019.

CLSI

Likelihood of AmpC β-Lactamase Induction

	Enterobacter spp.	*Citrobacter spp.*	*Serratia marcescans*	*Morganella morganii*
Chow 1991	19%	--	--	--
Jacobson 1995	21%	--	--	--
Kaye 2001	19%	--	--	--
Lee 2002	3%	--	--	--
Choi 2007	--	--	7%	--
Choi 2008	8%	3%	0%	0%
Tamma 2013	38%	1%	15%	--
Hilty 2013	66%	--	--	--

Chow JW, et al. Ann Intern Med 1991;115:585. Kaye KS, et al. Antimicrob Ag Chemother 2001;45:2628. Choi SH, et al. Antimicrob Ag Chemother 2008;52:995. Tamma PD, et al. Clin Infect Dis 2013; 57:781. Slide courtesy of Pranita Tamma.

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What Are the Possibilities?

- Positive for an off target carbapenemase gene – *bla*$_{IMI}$, bla$_{FRI}$, bla$_{NMCA}$
- False-positive mCIM due AmpC hyperproduction (and/or acquisition of plasmid-mediated AmpC and/or ESBL genes) + changes in membrane permeability
- False-negative AMR molecular panel
- A mixed culture

Check Out M100 Appendix H3

Table H3. (Continued)

Indication	Target(s)	Method	Specimen Type	Results		Suggestions for Resolution	Report as:	Comments[a]
				Molecular Target Results	Observed Phenotype (if tested)			
Detection of carbapenem resistance in *Enterobacteriaceae* (Continued)	KPC, OXA-48-like, VIM, NDM, or IMP	NAAT, microarray	Colony, blood culture	No detection of tested carbapenemase targets	Resistance to any carbapenems except ertapenem (eg, meropenem R, imipenem R, doripenem R, ertapenem R or S)	Possible other carbapenemase. If blood culture, check for mixed culture. If mixed, test isolates individually and report as found; consider repeating molecular and AST and performing a phenotypic test for carbapenemase activity (eg, CarbaNP or mCIM).	If carbapenemase activity is detected, repeat AST should be performed using a reference method, and the conflicting genotypic and phenotypic testing results should both be reported along with a comment advising caution; current clinical and laboratory evidence is insufficient to conclude whether carbapenem monotherapy of carbapenemase-carrying strains with an MIC in the S range will be effective or whether the molecular assays are completely accurate. Otherwise report phenotypic results as found.	1–4, 12–16

"Phenotypic antimicrobial susceptibility testing results do not match the genotypic antimicrobial resistance gene results for carbapenems. Infectious diseases consult may be warranted."

To Report OR Not To Report, Here's Another Question…

Negative for AMR Markers

MICROBIOLOGY

Source: Blood, central line *Collected: 06/05/19 08:00 Received: 06/05/19 16:55 Order#: G20500064*

Site

BACTERIOLOGY

Bac Blood Cult *** PRELIM** **06/05/19 17:08** **J**

Gram stain positive for Gram Negative Bacilli
Critical action value called to and read back by
Dr. Carroll 06/05/2019 16:56

Enterobacter (non-cloacae complex) detected by Nucleic Acid Testing.

Gram-negative panel includes the following targets:
*Enterobacterales: Citrobacter species, Cronobacter sakazakii, Enterobacter cloacae complex, Enterobacter (non-cloacae complex), Escherichia coli, Morganella morganii, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus species, Serratia species, and Salmonella species

*Non-fermenting Gram-negative bacilli: Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia

*Bacteroides fragilis
*Fusobacterium species: F. necrophorum, F. nucleatum
*Haemophilus influenzae
*Neisseria meningitidis

Klebsiella (Enterobacter) aerogenes
in Aerobic Bottle

J - JOHNS HOPKINS MEDICAL LABS 600 N. Wolfe Street Balt

Positive for *bla*$_{KPC}$

MICROBIOLOGY

Source: Blood, peripheral *Collected: 06/05/19 08:00 Received: 06/05/19 17:23 Order#: G20500066*

Site

BACTERIOLOGY

Bac Blood Cult *** PRELIM** **06/05/19 17:25** **J**

Gram stain positive for Gram Negative Bacilli
Critical action value called to and read back by
Dr. Carroll 06/05/2019 17:24

Citrobacter species detected by Nucleic Acid Testing.
Carbapenemase producer
KPC detected by Nucleic Acid Testing.

Gram-negative panel includes the following targets:
*Enterobacterales: Citrobacter species, Cronobacter sakazakii, Enterobacter cloacae complex, Enterobacter (non-cloacae complex), Escherichia coli, Morganella morganii, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus species, Serratia species, and Salmonella species

*Non-fermenting Gram-negative bacilli: Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia

*Bacteroides fragilis
*Fusobacterium species: F. necrophorum, F. nucleatum
*Haemophilus influenzae
*Neisseria meningitidis

Citrobacter species
in Aerobic Bottle
Carbapenemase producer.
KPC detected by nucleic acid amplification test.
Patient requires contact precautions if hospitalized. Infectious diseases consultation is strongly recommended.

Now Wait!?! The mCIM Isn't a 100% Specific?

Screened 6,868 r

esistant Organisms

- 812 (11.8%) s
- 853 CRO were

hod

Organism	
Enteroba (N: 35)	
Pseudomo (N: 10)	

[a]: 14 were

Workneh *et al*, manuscript in preparation.

Combining AMR Testing With The Antibiogram

Organism	No. Strains	%S									
		AMK	ATM	AMP	FEP	CRO	CIP	ERT	GEN	MEM	PTZ
K. pneumoniae (All blood isolates)*	197	93	72	R	77	72	78	97	81	99	85
K. pneumoniae Negative for bla_{CTX-M} and carbapenemase genes	151	98	95	R	99	94	94	99	94	99	95
K. pneumoniae Positive for bla_{CTX-M}	35	96	0	R	33	0	36	96	46	100	50
K. pneumoniae Positive for bla_{KPC}	11¥	78	0	R	25	0	17	0	17	0	0
K. pneumoniae Positive for bla_{NDM}	10*¥	0	70	R	0	0	10	0	0	0	0

* Data collected over 3 years. ¥ Calculated from fewer than the standard recommendation of 30 isolates.
Abbreviations: %S, percent susceptible; AMK, amikacin; ATM, aztreonam; CFZ, cefazolin; CIP, ciprofloxacin; CRO, ceftriaxone; ERT, ertapenem; FEP, cefepime; GEN, gentamicin; IPM, imipenem; MEM, meropenem; No., number; PTZ, piperacillin-tazobactam; TET, tetracycline; R, resistant; SXT, trimethoprim-sulfamethoxazole.

M39-A5, CLSI, Coming Soon!

CLSI

In Summary: They Are Complementary Methods

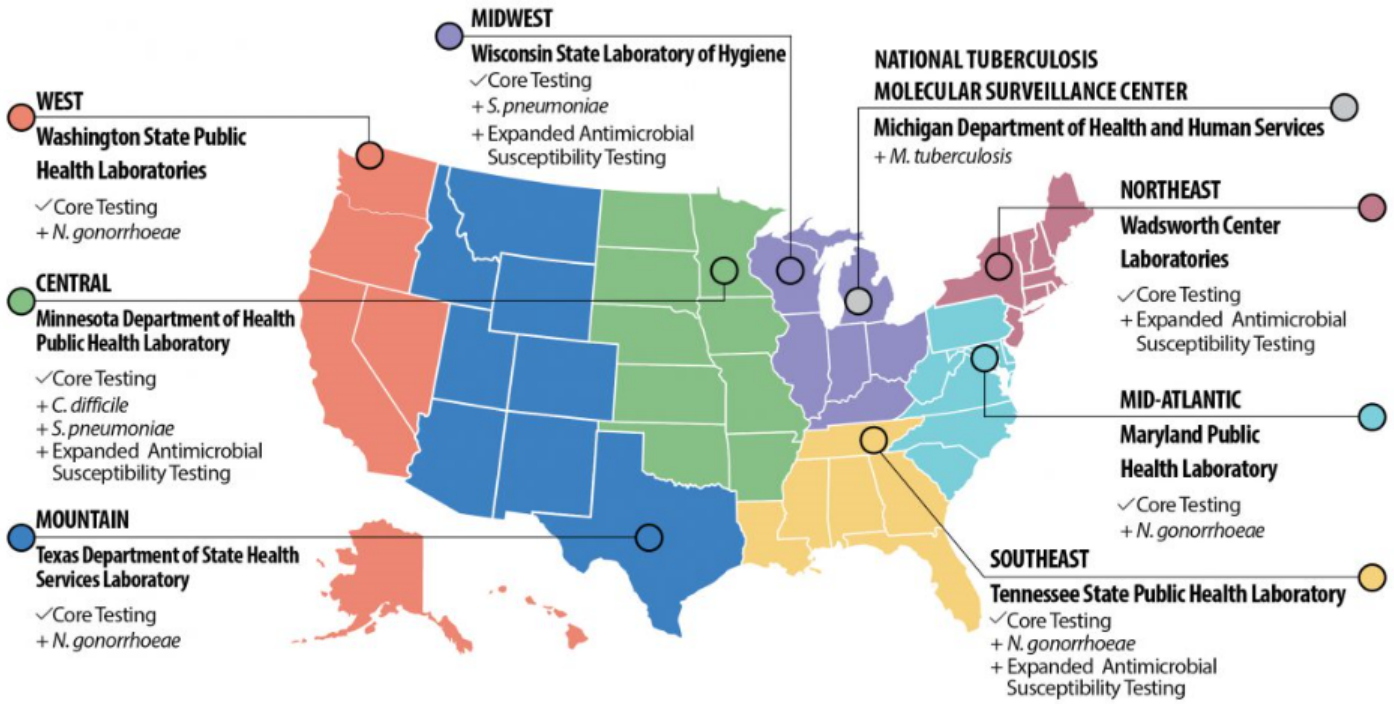
Phenotypic ***"What concentration of the drug inhibits growth of the bug?"***	**Genotypic** ***"Is there a gene(s) that predicts the drug won't kill the bug?"***
Standardized methods	Growing field
Slow – growth dependent	Fast - Direct from specimen & cultured growth
Provides a MIC	Only detects the specific targets or known targets in the case of WGS
Breakpoints available to interpret results	If present, assume resistant
Independent of resistant mechanism	Less than ideal sensitivity & specificity for predicting susceptibility **and** resistance
Methods accurately detect S, I, R	**Physicians are likely to escalate if a AR gene is detected**
Physicians are more experienced, confident & reliant on AST profile	**Physicians do not understand what ALL the AR genes "mean"**
	Physicians are hesitant to de-escalate without the AST profile

Do I Dare Say It?!?

- Phenotypic AST is an imperfect standard
  - Standard error ± 1 doubling dilution
  - Can vary significantly more depending on the organism/antimicrobial agent

- Variability in results – not accounted for clinically
  - Biology of the organism
  - Subtle testing differences (human or automated)
  - Highly standardized methods which does not reflect the variation in the environment and expression of phenotype that can occur during human infection
  - Expression can vary due to heteroresistant subpopulations, mixed infections, biofilm formation, further selection and persistence based on selective pressure → all leading to *in vivo* resistance but not detected *in vitro*

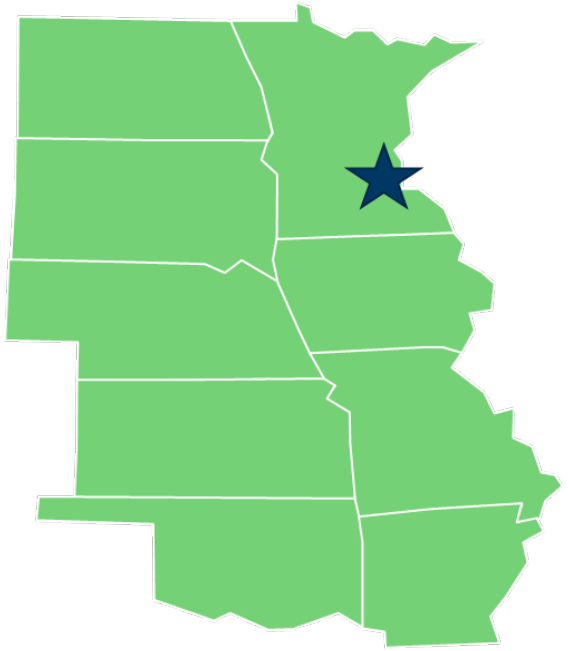
Case 3: Antibiotic Resistance (AR) Lab Network



Case 3: Antibiotic Resistance (AR) Lab Network

50 State Core Testing - AST, phenotypic and molecular ID for Carbapenemases

- Carbapenem resistant Enterobacteriaceae (CRE)
  - MICs ≥ 4µg/mL for doripenem, imipenem, or meropenem or > 1µg/mL for ertapenem
- Carbapenem resistant *P. aeruginosa* (CRPA)
  - MICs ≥ 8µg/mL for doripenem, imipenem, or meropenem



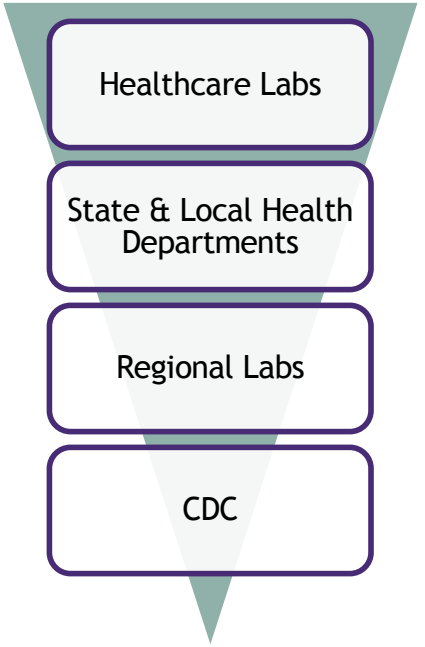
Regional Lab Testing

- CRE and CRPA - possible novel AR mechanisms
- Carbapenem resistant *Acinetobacter baumannii* (CRAB)
- Colonization screening for CPOs
- *Candida auris* confirmation and colonization screening
- Expanded AST (4 pilot labs)

Case 3: Antibiotic Resistance (AR) Lab Network

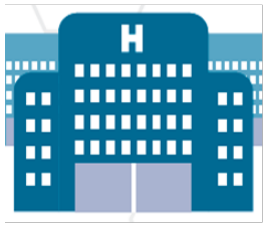
The AR Lab Network ensures consistent and improved communication, coordination, and tracking at all levels

- When resistance threats are detected within healthcare facilities or state/local labs, regional labs can provide support to characterize, support response, and track these discoveries.
- Flexibility in surveillance testing to focus on the next emerging threat.
- CDC's AR Lab Network team and Programs provide logistics support, subject matter expertise, and tailored solutions.

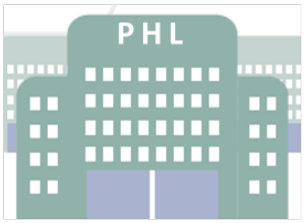


Case 3: Antibiotic Resistance (AR) Lab Network

Testing in 50 states and 6 large jurisdictions



Suspected CRE/CRPA isolates are forwarded to State PHLs



Testing at the State/Jurisdictional PHL may include:

- Species confirmation
- Antimicrobial susceptibility testing confirmation
- Phenotypic screening for carbapenemase production
- Molecular detection of mechanism

Isolates with suspected novel resistance*

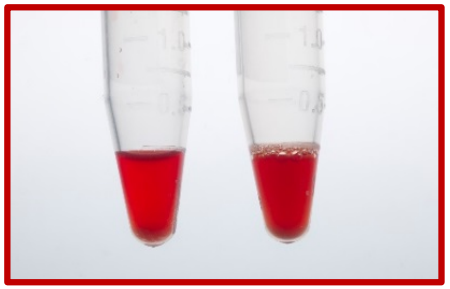
*Positive for carbapenemase production by phenotypic methods and negative by PCR; **Alert sent to state HAI coordinator and CDC within 1 day**

Case 3: AR Lab Network Testing

Enterobacter cloacae isolate submitted to AR Lab Network Lab

- Carbapenemase testing (mCIM):
  - **POSITIVE**
  - 16mm with colonies throughout
- Carbapenemase testing (Carba NP):
  - Negative

mCIM +

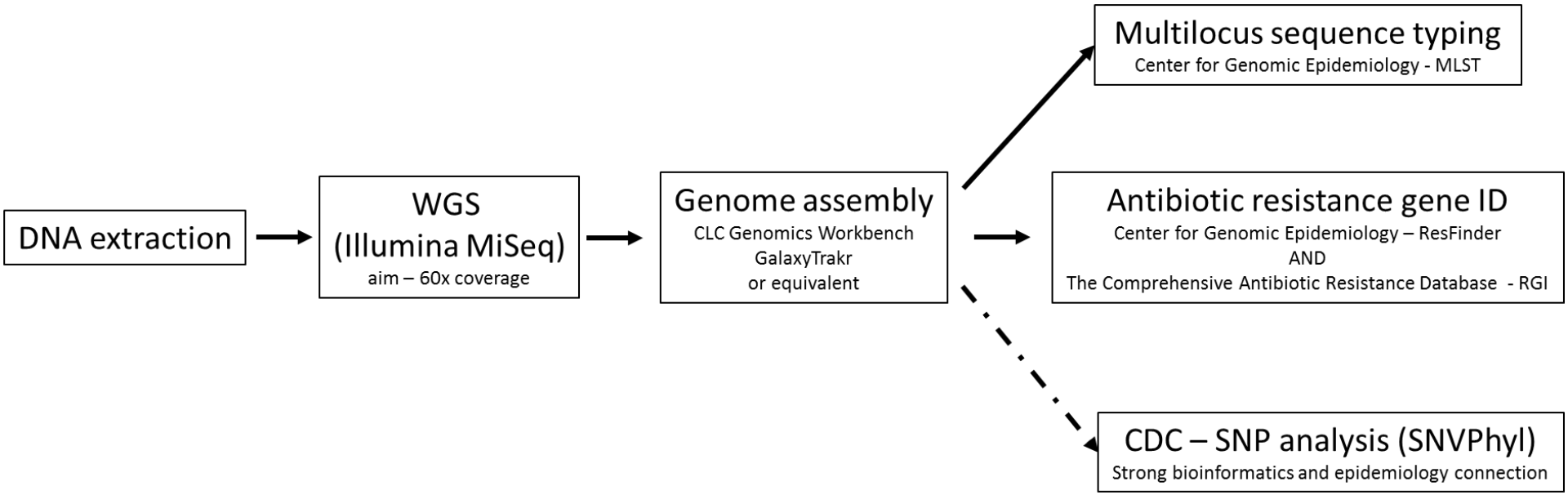


CarbaNP negative

- Real-Time PCR (LDT):
  - KPC: Negative
  - NDM: Negative
  - OXA-48-like: Negative
  - VIM: Negative
  - IMP: Negative

- Whole Genome Sequencing: Performed – **potential novel carbapenemase** suspected

Case 3: AR Lab Network Regional Lab Testing



Case 3: AR Lab Network Regional Lab Testing

WGS - Plasmids, Resistance Genes, MLST

- WGS – Center for Genomic Epidemiology Batch Analysis:
- **(2) plasmid types, (4) resistance gene types, MLST: Sequence type-32**

Bacterial Analysis Summary Report

Pipeline Version: *1.1*
Submission Date: *2018-08-24*
Sample Name: **C2017005792**

Contigs Analysis

Assembly File	No. of contigs	No. of bases
C2017005792_S2_L001_R1_001_2assembly.fa.gz	111	4877210

Taxonomy

Predicted Lineage:
cellular organisms; Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Enterobacter; Enterobacter cloacae complex; Enterobacter cloacae; Enterobacter cloacae subsp. cloacae; Enterobacter cloacae subsp. cloacae ENHKU01

Predicted Species: *Enterobacter cloacae*
Closest Template *Enterobacter cloacae subsp. cloacae ENHKU01*
Template Coverage 0.91

MLST Scheme[ST] ecloacae [ST-32]

Plasmid[pMLST] ColRNAI

Resistance Genes
Fosfomycin
Sulphonamide
Beta-lactam
Aminoglycoside

Virulence Genes

Center for Genomic Epidemiology

Home Services Instructions

MLST-1.8 Server - Typing Results

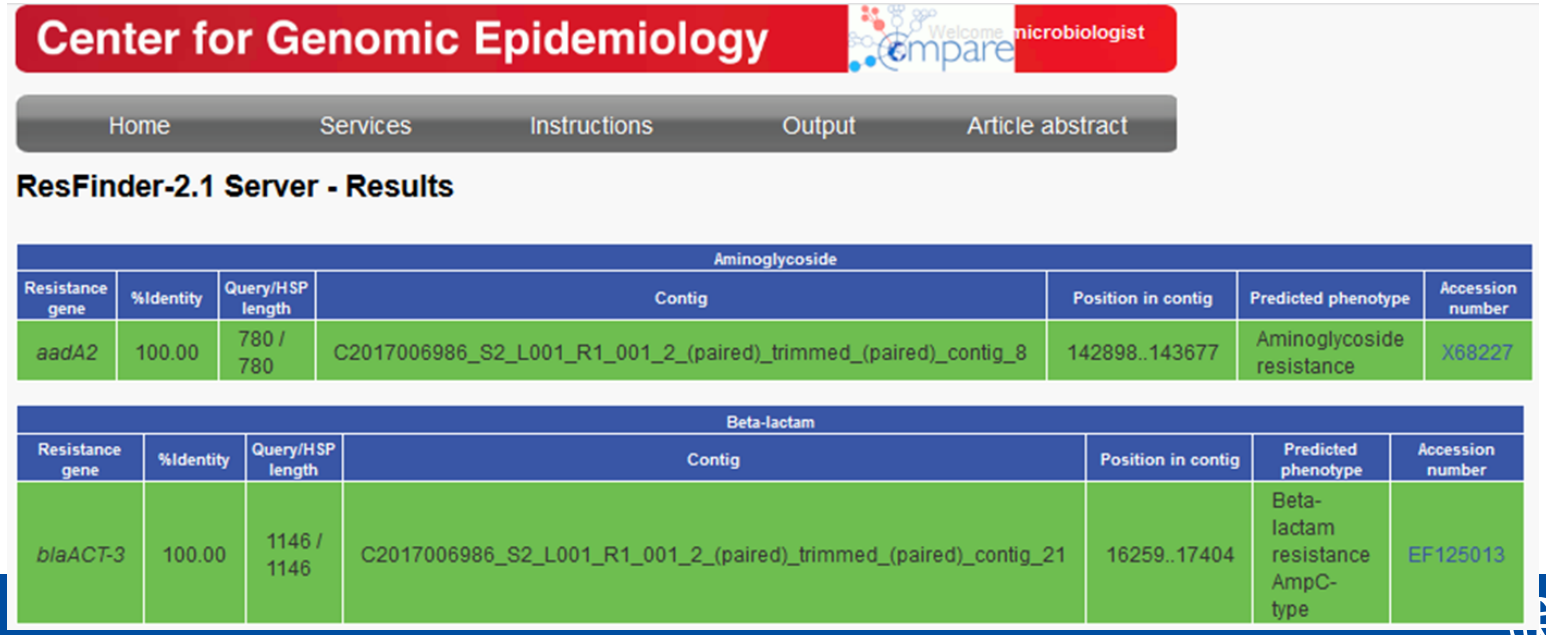
Sequence Type: ***ST-32***

Locus	% Identity	HSP Length	Allele Length	Gaps	Allele
dnaa	100.00	442	442	0	*dnaa_3*
fusa	100.00	646	646	0	*fusa_24*
gyrb	100.00	434	434	0	*gyrb_3*
leus	100.00	578	578	0	*leus_35*
pyrg	100.00	259	259	0	*pyrg_3*
rplb	100.00	607	607	0	*rplb_16*
rpob	100.00	545	545	0	*rpob_17*

Case 3: AR Lab Network Regional Lab Testing

WGS - Plasmids, Resistance Genes, MLST

- WGS – Center for Genomic Epidemiology ResFinder:
- **Intrinsic AmpC beta-lactamase**



Center for Genomic Epidemiology

Welcome, microbiologist

Home | Services | Instructions | Output | Article abstract

ResFinder-2.1 Server - Results

Aminoglycoside						
Resistance gene	%Identity	Query/HSP length	Contig	Position in contig	Predicted phenotype	Accession number
aadA2	100.00	780 / 780	C2017006986_S2_L001_R1_001_2_(paired)_trimmed_(paired)_contig_8	142898..143677	Aminoglycoside resistance	X68227

Beta-lactam						
Resistance gene	%Identity	Query/HSP length	Contig	Position in contig	Predicted phenotype	Accession number
blaACT-3	100.00	1146 / 1146	C2017006986_S2_L001_R1_001_2_(paired)_trimmed_(paired)_contig_21	16259..17404	Beta-lactam resistance AmpC-type	EF125013

Snapshot: resistance genes for other drug classes found during analysis

CLSI

Case 3: AR Lab Network Regional Lab Testing

WGS - Plasmids, Resistance Genes, MLST

- WGS – CARD database – Resistance Gene Identifier (RGI):
  - **Intrinsic AmpC beta-lactamase (ACT-3) + Porin loss**
  - **This database is more comprehensive than ResFinder**

B-lactamase

Porin

PBP

ARO Term	SNP	Detection Criteria	AMR Gene Family	[illegible] Class	Resistance Mechanism
ACT-3		protein homolog model	ACT beta-lactamase	cephalosporin, carbapenem, penam, cephamycin	antibiotic inactivation
marA		protein homolog model	resistance-nodulation-cell division (RND) antibiotic efflux pump, General Bacterial Porin with reduced permeability to beta-lactams	monobactam, penem, phenicol antibiotic, cephalosporin, rifamycin antibiotic, triclosan, penam, cephamycin, fluoroquinolone antibiotic, glycylcycline, carbapenem, tetracycline antibiotic	antibiotic efflux, reduced permeability to antibiotic
ramA		protein homolog model	resistance-nodulation-cell division (RND) antibiotic efflux pump, General Bacterial Porin with reduced permeability to beta-lactams	monobactam, penem, phenicol antibiotic, cephalosporin, rifamycin antibiotic, triclosan, penam, cephamycin, fluoroquinolone antibiotic, glycylcycline, carbapenem, tetracycline antibiotic	antibiotic efflux, reduced permeability to antibiotic
Haemophilus influenzae PBP3 conferring resistance to beta-lactam antibiotics	S357N, D350N	protein variant model	Penicillin-binding protein mutations conferring resistance to beta-lactam antibiotics	carbapenem, monobactam, cephamycin, penam, cephalosporin	antibiotic target alteration

Case 3: AR Lab Network Regional Lab Testing

Summary

- Note differences in resistance profile between a KPC+ *E. cloacae* and this isolate - cefepime and carbapenems resistance

Antibiotic	Beta-lactam Class	Non-CP (This isolate): Value, Interpretation	CP (KPC+ isolate): Value, Interpretation
Ceftazidime	3rd Gen Cephalosporin	32, R	>=64, R
Ceftriaxone	3rd Gen Cephalosporin	>=64, R	>=64, R
Cefepime	4th Gen Cephalosporin	4, SDD	>=64, R
Ertapenem	Carbapenem	8, R	>=8, R
Meropenem	Carbapenem	4, R	>=16, S

CLSI

Case 3: AR Lab Network Regional Lab Testing

Summary

- mCIM test is prone to **RARE** false positive results with *E. cloacae*
  - Discovered by looking at the whole picture:
  - MIC, Phenotypic, and Molecular Results – Important to question unusual results!
  - MDH now uses Carba NP test as backup method for mCIM+ *E. cloacae*

Case 3

Molecular AR

From Positive Blood Cx	
bla_{CTX-M}	Not Detected
bla_{IMP}	Not Detected
bla_{KPC}	Not Detected
bla_{NDM}	Not Detected
bla_{OXA}	Not Detected
bla_{VIM}	Not Detected

From Colony Growth	
mCIM	Positive

Clinical Lab Results

MIC Testing

Antimicrobial	MIC µg/mL
Aztreonam	≥ 64 R
Cefepime	4 SDD
Ceftriaxone	≥ 64 R
Ertapenem	8 R
Gentamicin	≤ 1 S
Levofloxacin	4 I
Meropenem	4 R
Piperacillin-tazo	≥ 128 R

Antimicrobial	MIC µg/mL
Ceftazidime-avi	4 /4 S

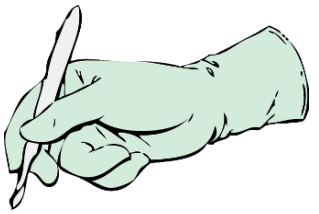
CLSI

Clinicians need to get comfortable assessing the mechanism of carbapenem resistance

- Need to know types and antimicrobial substrates of common carbapenemases
- Need to understand possibilities of non-carbapenemase resistance
- Need to understand the spectrum of the Beta-lactamase inhibitors

You are saying that
I need to know genotype AND phenotype?

These cases often arise in the setting of poor source control

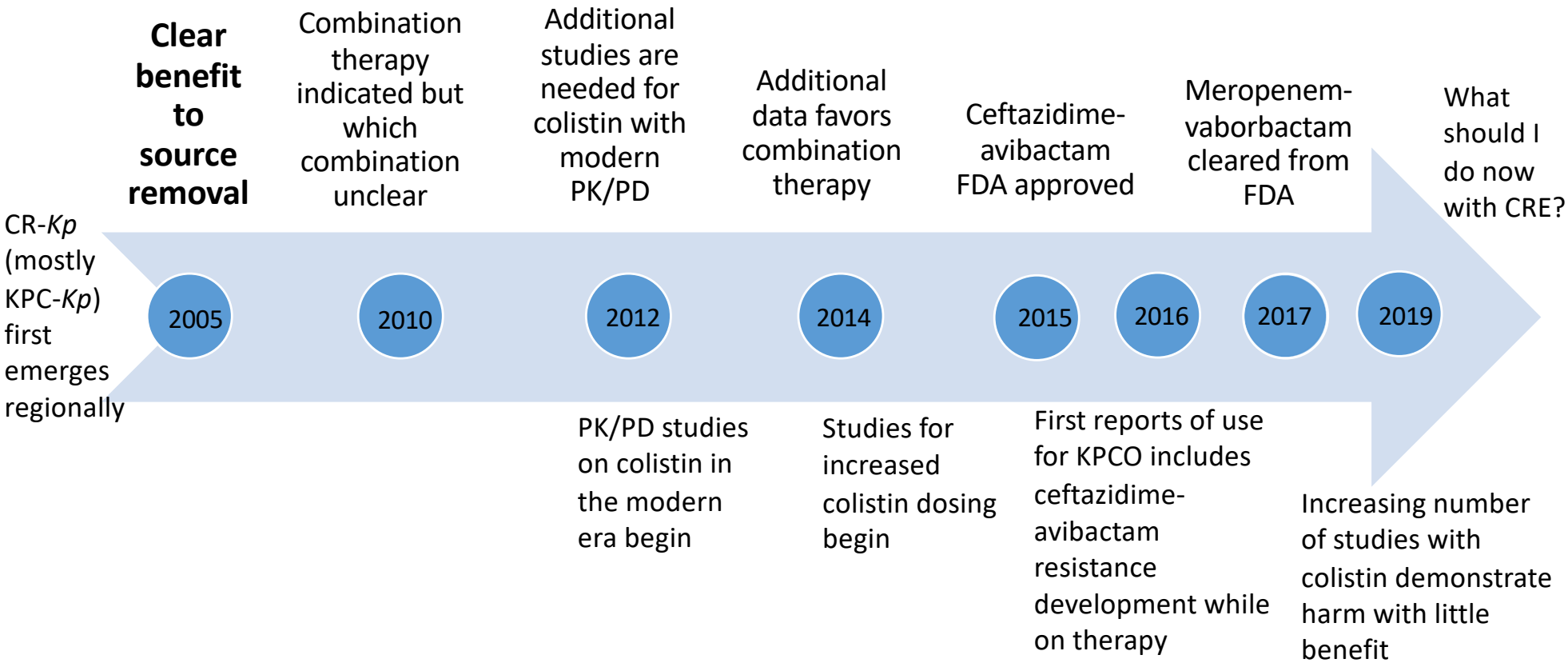


- Stop teasing the *Enterobacter* sp. with antimicrobials!!!
- Usually requires dialog with multidisciplinary team explaining decreasing medical options
- The bacteria likely has a significant porin mutation and thus is likely struggling to thrive
- Outcomes appear to be worse for CP-CRE versus non-CP-CRE

Villegas M et al. PloS one 2016;11:e0154092, Tamma PD et al. CID (2017)64(3):257-264
Tamma Pd et al AAC (2019)pii: AAC.00757-19.

CLSI

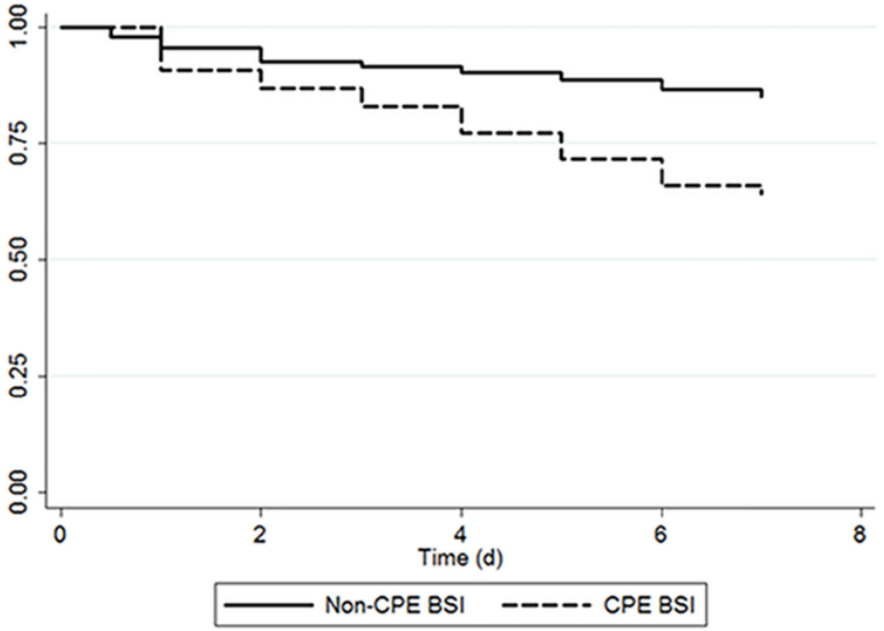
The evolution of treatment of Carbapenem resistant Enterobacterales



Outcomes are worse for CPE compared to non-CPE-CRE

- 2013-2014 11 hospitals from 7 Latin American countries
- CPE-CRE=53/Non-CPE-CRE=202
- Multivariate for in independent hospital mortality
  - CPE BSI [aOR] 4; [CI] 1.7–9.5 p < 0.001
  - Critical illness [aOR] 6.5; [CI] 3.1–13.7; p < 0.001

Kaplan-Meier survival at 7 days of patients CPE bloodstream infection (BSI) (dashed line) vs. non-CPE BSI (solid line).



Villegas M et al. PloS one 2016;11:e0154092

Log rank p<0.001

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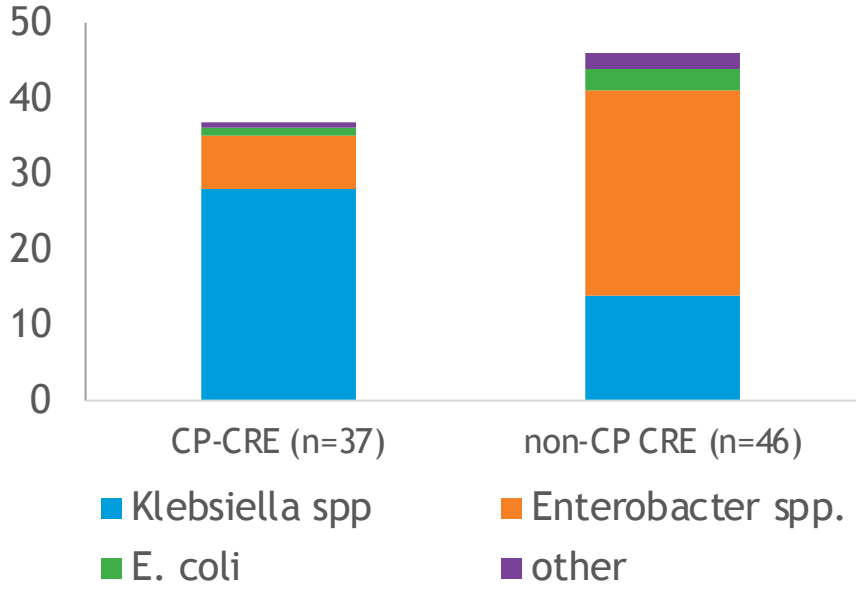
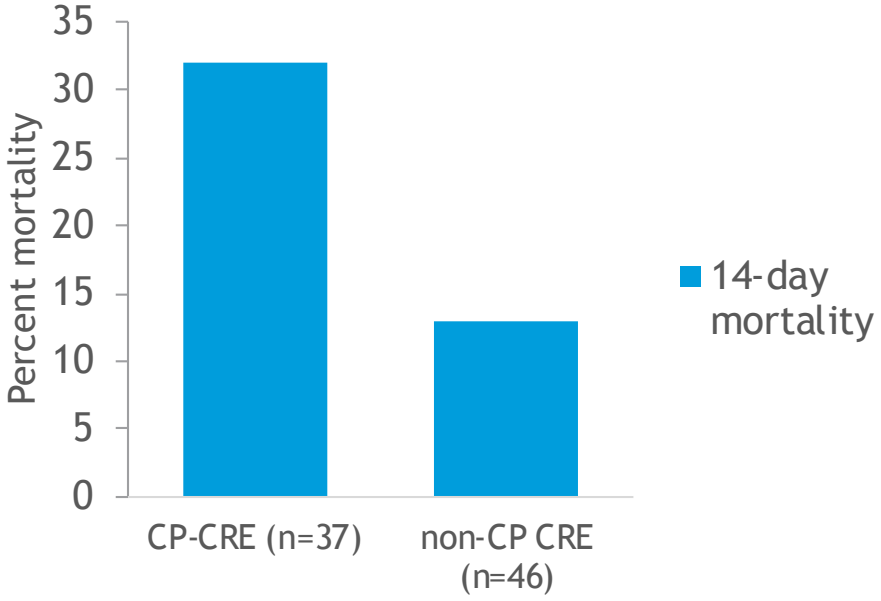
Another more recent study

- Single center retrospective study 2011-16
- Compared 14-day mortality
- Also 30-day and 30-day recurrent bacteremia
- CRE was defined as an *Enterobacteriaceae* isolate with resistance to any carbapenem



Again CPE-CRE do worse than non-CPE CRE

- CPE-CRE
  - higher meropenem MICs
  - Fewer directed antimicrobials given
  - More combination therapy
- Multivariate analysis
  - CP-CRE compared with non-CP-CRE bacteremic patients (aOR 4.92; 95% CI 1.01-24.81).



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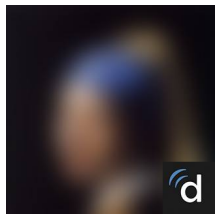
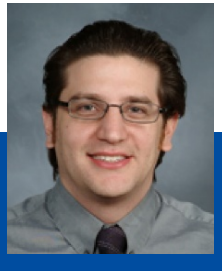
What would expert colleagues do?





Pranita Tamma	Cefepime 2gm q8 (if I believe the cefepime result)
Jim Lewis	Cefepime 2gm q8
Howard Gold	Cefepime (any other data?)
Mike Satlin	Cefepime 2gm q8 (any other data?)

Use cefepime if you believe the cefepime result

Cefepime does not always perform well when class A ß-lactamases present on automated systems

Plasmid-mediated β-lactamase genes identified	Piperacillin-tazobactam ≤16 mcg/mL	Ceftriaxone ≤1 mcg/mL	Cefepime ≤8 mcg/mL	Aztreonam ≤4 mcg/mL	Ertapenem ≤0.5 mcg/mL	Meropenem ≤1 mcg/mL	Imipenem ≤1 mcg/mL	Gentamicin ≤4 mcg/mL	Tobramycin ≤4 mcg/mL	Amikacin ≤16 mcg/mL	Ciprofloxacin ≤1 mcg/mL	Tigecycline ≤2 mcg/mL	Colistin ≤2 mcg/mL
Carbapenemase-producing carbapenem resistant *Enterobacteriaceae*													
bla$_{KPC}$ (n=32)	0	0	23	6	0	41	30	38	19	84	23	58	75
bla$_{NDM}$ (n=2)	0	0	0	50	0	0	0	100	0	100	0	50	100
bla$_{OXA-48-type}$ (n=1)	0	0	0	100	0	0	0	0	0	0	0	100	100
Non-carbapenemase-producing carbapenem resistant *Enterobacteriaceae*													
None identified[1] (n=21)	9	5	79	14	0	90	71	95	86	95	71	100	100
Narrow or extended-spectrum β-lactamase (n=17)	0	6	35	19	0	41	55	71	59	100	35	89	100
AmpC β-lactamase (n=8)	33	0	88	25	0	100	50	100	100	100	88	100	100
ESBL + AmpC (n=2)	0	0	50	0	0	50	0	50	50	100	0	100	100

[1]The majority of these are presumed to be derepressed chromosomally-mediated *ampC* β-lactamases

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CLSI

Trusting the cefepime MIC in *Enterobacter* sp.

Known issues with automated susceptibility testing and cefepime when class A ESBL present

Gives some reassurance that cefepime of ≤4µg/mL is AmpC alone especially with the meropenem

With such high meropenem MICs it is unlikely that an additional enzyme is present that would have good cefepime affinity

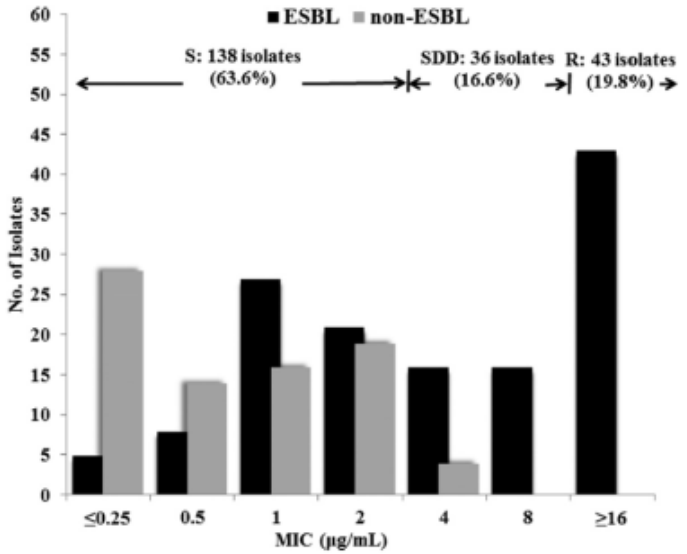

FIG 1 Distribution of cefepime MICs of 217 *Enterobacter cloacae* blood isolates, with or without extended-spectrum beta-lactamase (ESBL) production. S, susceptible; SDD, susceptible dose dependent; R, resistant.

Lee, N-Y et al AAC (2015) 59:7558 -7563.

Would

- Talk to the surgeons
- Perform necessary source control
- Give cefepime (and metronidazole)

Conclusion

- Genotypic results have complicated the work in the clinical lab but likely for the better
- Many genotypic resistance results can have public health consequences who increasingly have resources to help
- Clinically knowing when to trust the MIC versus a genotypic result can be challenging
- More genotypic outcomes data will likely be very useful in interpreting the MIC/genotype conundrums

Q & A