Efficient Strategies for Communicating MDRO to Our Stakeholders

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Disclosures

- Employee and Stockholder of Labcorp (Diagnostic Reference Lab)
- Opinions expressed are my own

Multidrug-Resist Organisms (MDRO)

- Who are our stakeholders when MDROs are reported
- Strategies for communicating MDROs
- Strategies for testing MDROs

Challenges caused by Multidrug-Resistant Organisms

- Clinically: Infections with MDRO are challenging to treat

- Infection Prevention and Control: MDRO transmission within institutions impacts other patients.

Common MDROs (various definitions)

Gram Positive Cocci

- Methicillin Resistant *Staphylococcus aureus* (MRSA)
- Vancomycin Resistant Enterococcus (VRE)

Gram Negative Bacilli

- Carbapenem-resistant and carbapenemase producing Enterobacterales (CRE, CP-CRE)
- ESBL-producing Enterobacterales
- Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA CP-CRPA)
- Carbapenem-resistant Acinetobacter baumanii (CRAB)
- Multidrug-Resistant GNR

Challenging cases

- 62 yo male with congestive heart failure, extended ICU stay requiring LVAD placement.
- 0.5months post-LVAD placement: ESBL E.coli from sternal wound
- Treated with ertapenem and meropenem
- Recurrence of ESBL *E. coli* at 18mo and 42mo
- Carbapenem resistant Pseudomonas aeruginosa
  - CRPA at 26mo

Susceptibility

	Pseudomonas aeruginosa Not Specified	
Amikacin	<=2 ug/mL	Sensitive
Cefepime	=8 ug/mL	Sensitive
Ceftazidime	=8 ug/mL	Sensitive
Ciprofloxacin	=1 ug/mL	Sensitive
Gentamicin	<=1 ug/mL	Sensitive
Imipenem	R ug/mL	Resistant
Levofloxacin	=2 ug/mL	Sensitive
Meropenem	R ug/mL	Resistant
Piperacillin	=32 ug/mL	Sensitive
Ticarcillin	>=128 ug/mL	Resistant
Tobramycin	<=1 ug/mL	Sensitive

Susceptibility

	Escherichia coli Not Specified	
Amoxicillin + Clavulanate	R ug/mL	Resistant
Ampicillin	R ug/mL	Resistant
Cefazolin	R ug/mL	Resistant
Cefepime	R ug/mL	Resistant
Ceftriaxone	R ug/mL	Resistant
Cefuroxime	R ug/mL	Resistant
Ciprofloxacin	R ug/mL	Resistant
Ertapenem	S ug/mL	Sensitive
Gentamicin	S ug/mL	Sensitive
Imipenem	S ug/mL	Sensitive
Levofloxacin	R ug/mL	Resistant
Meropenem	S ug/mL	Sensitive
Piperacillin + Tazobactam	S ug/mL	Sensitive
Tetracycline	R ug/mL	Resistant
Tobramycin	S ug/mL	Sensitive
Trimethoprim + Sulfamethoxazole	R ug/mL	Resistant

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Impact of MDROs on Clinical Care

- Limits treatment options, forces escalation to broader spectrum antibiotics
  - Difficult to treat and eradicate
  - Treatment generates further resistance
  - Increased length of stay in inpatient setting
  - CDC estimate:
    - Annual2,868,700 infections; 35,900 deaths

Carbapenem resistant Enterobacterales

- Effective treatment requires:
  - Early signal of resistance to escalate drug regimen
  - Accuracy of initial result

Risk of MDRO transmission to other patients

- A healthcare-associated infection (HAI) is an infection that develops during, or soon after, receiving healthcare services or being in a healthcare setting
- Hospitalized patients are vulnerable to HAI

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

COVID-19 Impacts on Antimicrobial Resistance Tracking and Data (CDC)

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Patient with designated MDRO infections are placed under contact precautions

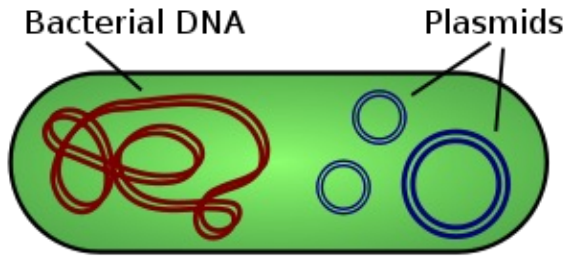
- Transmission based precautions
  - Contact precautions

- Contact precautions alone are not enough to limit transmission
  - Requires compliance with best practice
  - Active surveillance
  - Patient cohorting

Plasmid-based transmission

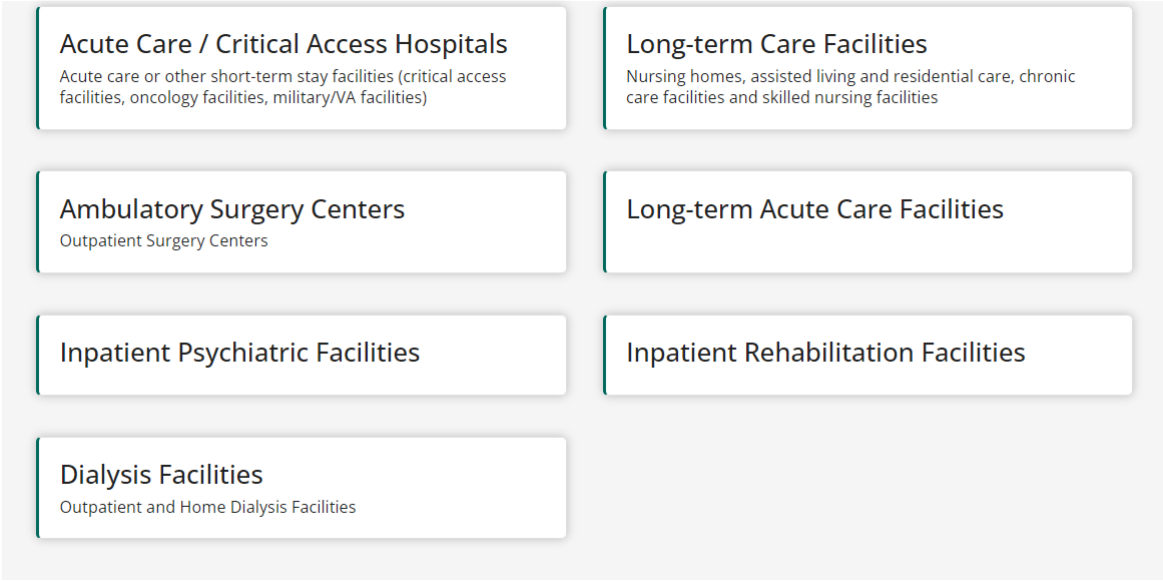
- MDRO mechanism of resistance is often plasmid-mediated
  - resistance plasmids can also carry virulence genes

- MDRO transmission risk
  - Risk of horizontal gene transfer of carbapenemase, extended spectrum beta-lactamase, and mecA producers in healthcare settings



Who are the laboratory's stakeholders for MDRO reporting

- Patient
- Treating Provider
  - Care team, Antimicrobial Stewardship
- Infection Prevention
- Institutional Administration
- Future healthcare facilities
- Public health entities



MDRO: multiple definitions

- Center for Disease Control and Prevention (CDC)
  - Select MDRO must be reported for HAI tracking at intervals

- State and Local Public Health Entities
  - Some MDRO are a subset of lab notifiable conditions upon detection

- Healthcare Facilities
  - Can define MDRO to enhance infection prevention efforts and clinical care requirements

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Center for Disease Control (CDC)

Management of Multidrug-Resistant Organisms in Healthcare Settings (2006)

- Definition: *For epidemiologic purposes, MDROs are defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents.*

Antimicrobial classes (Gram Negative Bacilli)

Penicillins
Penicillin
Piperacillin
Ticarcillin
Ampicillin

Cephems Oral/ Parenteral

Cephems 1st
Cefalotin
Cefazolin

Cephamycin
Cefoxitin

Cephems 2nd
Cefotetan
Cefoxitin
Cefuroxime

Cephems 3rd
Cefotaxime
Cefpodoxime
Ceftriaxone
Ceftazidime

Cephems 4th
Cefepime

Siderophore Cephalosporin
Cefiderocol

Penem
Doripenem
Ertapenem
Imipenem
Meropenem

Monobactam
Aztreonam

B-lactam combination agents
Amoxacillin/Clavulanate
Ampicillin/ Sulbactam
Piperacillin/Tazobactam
Aztreonam/Avibactam
Ceftazidime/Avibactam
Ceftolozane/Tazobactam
Meropenem/Vaborbactam
Imipenem/Relabactam

Aminoglycosides
Gentamicin
Tobramycin
Amikacin

Fluoroquinolone
Moxifloxacin
Norfloxacin
Ciprofloxacin
Levofloxacin

Tetracyclines
Tetracycline
Minocycline
Doxycyline
Tigecycline

Folate pathway antagonist
Trimethoprim
Trimethoprim/ sulfamethoxazole

Fosfomycins
Fosfomycin

Nitrofurans
Nitrofurantoin

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Source: Glossary I CLSI M100 S33

Requirements in CDC MDRO management document (2006)

Implement systems to **communicate information about reportable MDROs to administrative personnel** and as required by state and local health authorities (V.A.1.d.)

Prepare **facility-specific antimicrobial susceptibility reports** as recommended by the Clinical and Laboratory Standards Institute (CLSI) ;

- **monitor these reports for evidence of changing resistance patterns that may indicate the emergence or transmission of MDROs**. (V.A.4.d.)

Establish a **frequency for preparing summary reports** based on volume of clinical isolates, with updates at least annually. (V.A.4.d.ii.)

CDC's National Healthcare Safety Network (NHSN)

- CMS requires that facilities submit data on
  - Healthcare-associated Infections and
  - Antimicrobial Resistance (HAI-AR).
- NHSN electronic solution for meeting reporting requirement.
- Requirements vary by type of facility
- For example: Acute Care Hospitals in CA require monthly submissions for CLABSI, MRSA-BSI, VRE-BSI, SSI, CDI
- NHSN includes the ability to report Multidrug-Resistant Organism and Clostridium difficile Infection (MDRO/CDI) Module

https://www.cdc.gov/nhsn/psc/cdiff/index.html

CDC's National Healthcare Safety Network (NHSN) MDRO definition:

- For institutions uploading HAI-AR into NHSN database: can choose to monitor and report the following:

Staphylococcus aureus
Methicillin-resistant

Enterococcus
Vancomycin resistant

Klebsiella species
Cephalosporin Resistant

Carbapenem Resistant
R to any carbapenem
Or carbapenemase detected
E. coli
Klebsiella oxytoca; pneumoniae
Klebsiella aerogenes
Enterobacter species

Acinetobacter
I/R to 1 agent in 3 classes
Aminoglycosides
Carbapenems
Fluoroquinolones
B-lactam/B-lactamase inhibitor
Cephalosporins
Sulbactams

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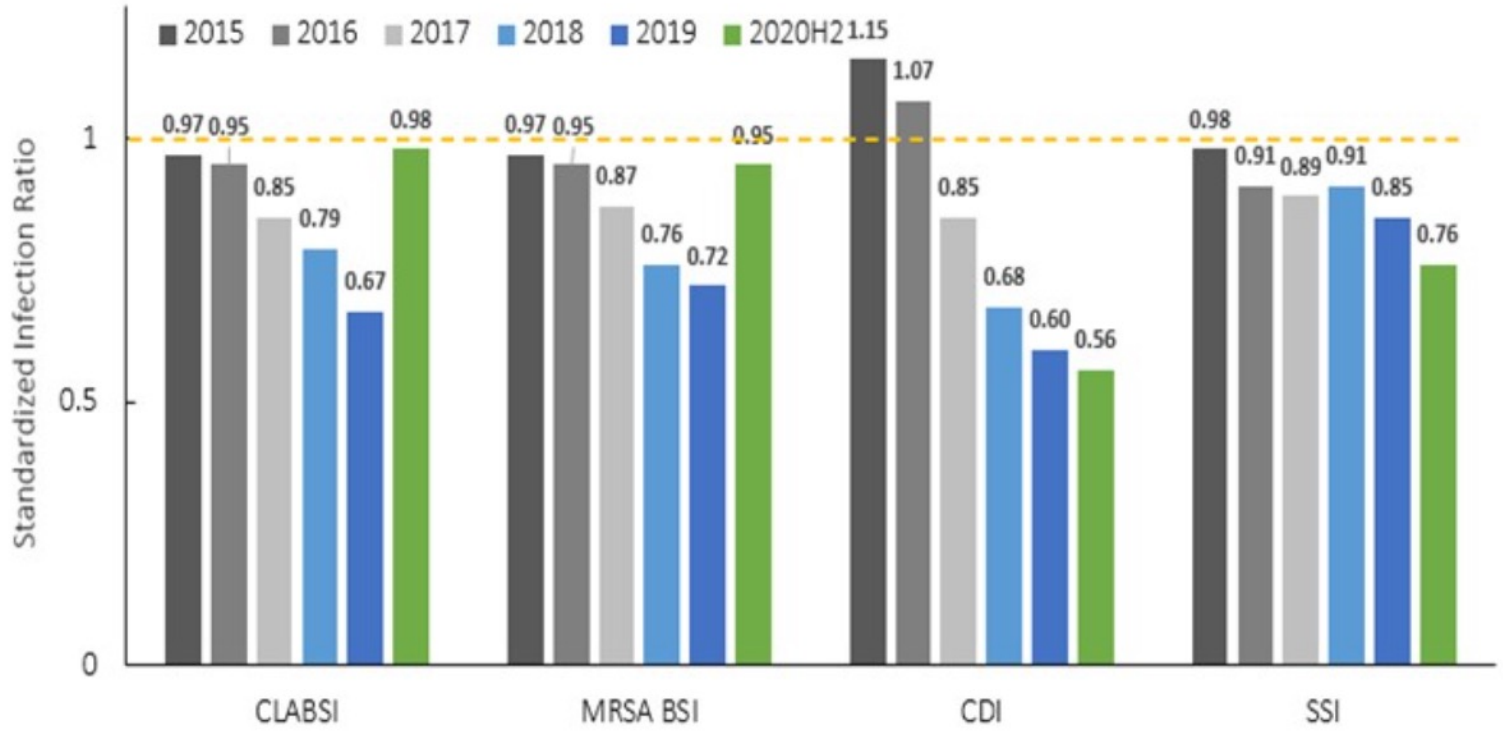
State and Local Public Health Jurisdictions

- California requires reporting HAI, MRSA-BSI and CDI through NHSN at intervals

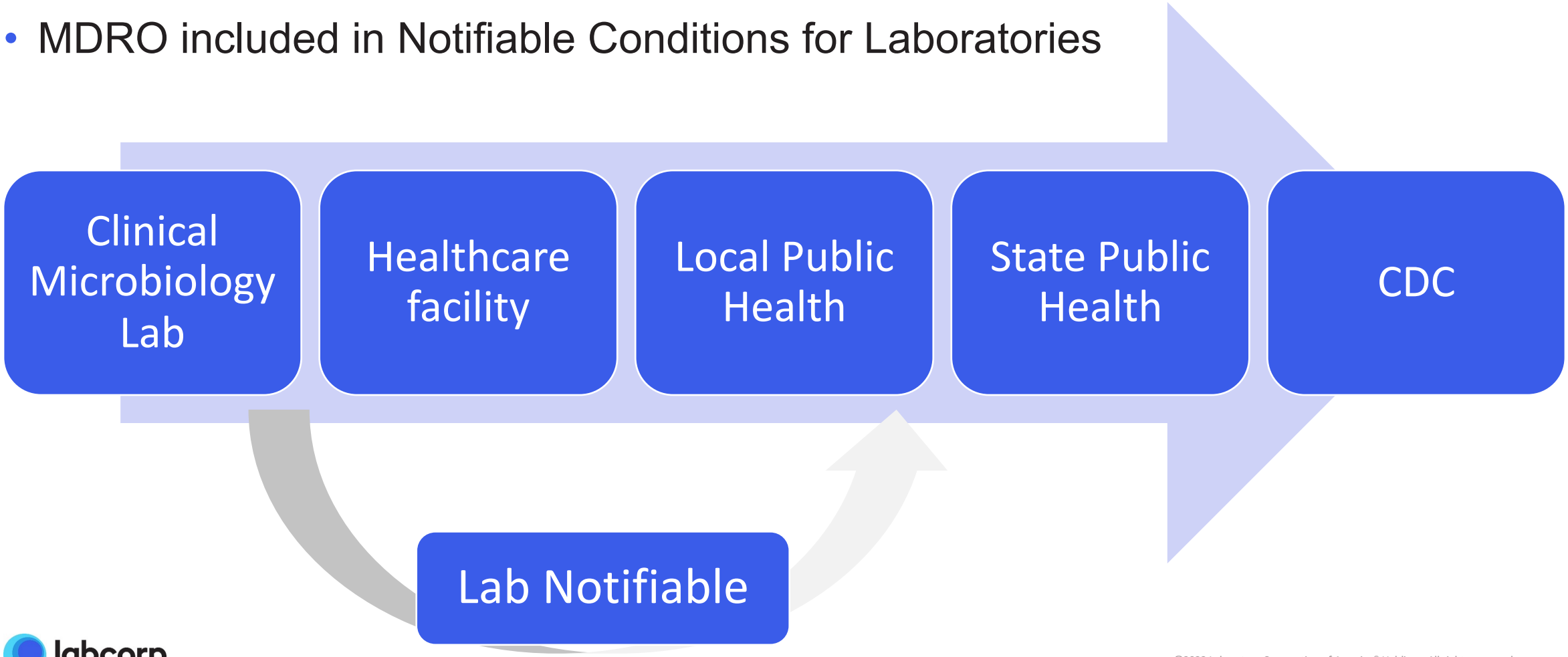
Figure 1. Healthcare-Associated Infection Incidence in California Hospitals, 2015–2020*



https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/HAI_DefinitionsAndInformation.aspx

State and Local Public Health Jurisdictions

- Labs must report the detection of certain pathogens to public health
- MDRO included in Notifiable Conditions for Laboratories



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State and Local Public Health Jurisdictions

- Labs must report the detection of certain pathogens to public health
- Ordering provider (or facility) also reports the infection to public health

Surveillance case definitions	San Diego County	Orange County	Los Angeles County	National	CDPH State
CP-CRE (*E. coli*, *Klebsiella* spp., or *Enterobacter* spp)	✓	?	✓	✓	✓
CP-CRE Enterobacterales			✓		
Carbapenem resistant Enterobacterales		✓	✓		
CP P. aeruginosa	✓		✓		✓
CP Acinetobacter species	✓		✓		✓
Pan-R GNB			✓		
ESBL		✓			
MRSA		✓			
VRSA	✓	✓	✓	✓	?
C. auris	✓	✓	✓	✓	✓

Healthcare facility-specific MDRO definitions

- CDC, state and local requirements
- Institutions continuously update their isolation and tracking rules based on risk assessments
  - Antibiograms are utilized to detect emerging profiles

- Infection prevention precautions in response to defined MDROs
- Clinical care: infectious disease pharmacist develop treatment algorithms around specific MDROs

CDC 2019 Antimicrobial Resistance (AR) Threats Report

Bacteria and Fungi Listed in the 2019 AR Threats Report

Urgent Threats

- Carbapenem-resistant *Acinetobacter*
- *Candida auris*
- *Clostridioides difficile*
- Carbapenem-resistant Enterobacterales
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- ESBL-producing Enterobacterales
- Vancomycin-resistant *Enterococci* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant Tuberculosis

Concerning Threats

- Erythromycin-Resistant Group A *Streptococcus*
- Clindamycin-resistant Group B *Streptococcus*

Watch List

- Azole-resistant *Aspergillus fumigatus*
- Drug-resistant *Mycoplasma genitalium*
- Drug-resistant *Bordetella pertussis*

- Example Job-aide for MDRO reporting
- (not Labcorp's standard)

Category	ORGANISM	Antimicrobials	Phenotype	Beaker codes +Additional Action	BUGSY comments (Autopopulates)
Carba Resistance	All Enterobacterales	Carbapenems ie -Imipenem; Meropenem; Ertapenem; Doripenem; Meropenem/Vaborbactam	R to one	-CRE auto-comment -add JSTAPRE (if sending to state)	Carbapenem-resistant Enterobacterales
	Pseudomonas aeruginosa				CR-Pseudomonas aeruginosa
	Acinetobacter baumanii				CR-Acinetobacter baumanii
ESBL	*Klebsiella pneumoniae; Klebsiella oxytoca; E. coli; P. mirabilis*	Cephalosporins 3rd or 4th Gen i.e. -Ceftazidime; Cefotaxime; Ceftriaxone; Cefepime -Ceftazidime/Avibactam -Cefolozane/Tazobactam	I/R to 1 or more	- ESBL auto-comment	EXTENDED SPECTRUM CEPHALOSPORIN- R (will only populate if ESBL below is not triggered)
	Klebsiella pneumoniae; Klebsiella oxytoca; E. coli; P. mirabilis	ESBL positive on GN79 card: -If ≥1 3-4th Gen Cphlsprn R: release ESBL -If ≥1 3-4th gen Cphlsprn S: confirm w/ ESBL DD	ESBL+ off of Vitek 2 GN79 card	- ESBL auto-comment	Extended Spectrum Beta Lactamase
	Bacteroides sp.	Cephalosporins 3rd or 4th Gen i.e. Ceftazidime; Cefotaxime; Ceftriaxone; Cefepime	I/R to 1 or more	- auto-comment	AmpC Bacteroides
GNR MDRO	*S.maltophilia, Burkholderia cepacia*	any, prior to AST.	any	- JMDRO (manual) - CALL FLOOR	**add using smartphrase .JMDRO, this will not be deployed automatically**
	Pseudomonas species	- Cephalosporins 3rd or 4th Gen - Piperacillin/Tazobactam - Fluoroquinolones - Aminoglycoside - Carbapenem	I/R to ≥ 1 drug in 3 of these classes	- MDR auto-comment	MDR-Pseudomonas
	Acinetobacter species	-Penicillins -Cephalosporins -Fluoroquinolone -Sulfonamide -Aminoglycoside -Carbapenem	I/R to ≥ 1 drug in 3 of these classes		MDR-Acinetobacter
	Gram Negative Rod (not listed above)	-Penicillins -Cephalosporins -Carbapenems -Aminoglycoside -Quinolones	R to ≥ 1 drug in 4 of these classes	- JMDRO (manual) - CALL FLOOR	**add using smartphrase .JMDRO, this will not be deployed automatically**
GPC	Staphylococcus aureus	R to oxacillin/cefoxitin or PBP2+ or mecA+		-auto-comment	-Methicillin-resistant S. aureus -MRSA Nares Only (if from a screen)
	Staphylococcus aureus	Vancomycin (repeat to confirm before releasing)	MIC= 4/ 8 (I)	-auto-comment -CALL FLOOR	Vancomycin Intermediate S. aureus
	Staphylococcus aureus	Vancomycin (repeat to confirm before releasing)	MIC >= 16 (R)		Vancomycin Resistant S. aureus
	E faecalis/ E faecium	R to Vancomycin		-auto-comment	Vancomycin-resistant Enterococcus
Yeast	Candida auris	any, prior to AST.	Any	-auto-comment -CALL FLOOR	

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CDC Antibiotic Resistance & Patient Safety Portal

- Phenotype Analytical Definitions

Susceptibility

	Escherichia coli Not Specified	
Amoxicillin + Clavulanate	R ug/mL	Resistant
Ampicillin	R ug/mL	Resistant
Cefazolin	R ug/mL	Resistant
Cefepime	R ug/mL	Resistant
Ceftriaxone	R ug/mL	Resistant
Cefuroxime	R ug/mL	Resistant
Ciprofloxacin	R ug/mL	Resistant
Ertapenem	S ug/mL	Sensitive
Gentamicin	S ug/mL	Sensitive
Imipenem	S ug/mL	Sensitive
Levofloxacin	R ug/mL	Resistant
Meropenem	S ug/mL	Sensitive
Piperacillin + Tazobactam	S ug/mL	Sensitive
Tetracycline	R ug/mL	Resistant
Tobramycin	S ug/mL	Sensitive
Trimethoprim + Sulfamethoxazole	R ug/mL	Resistant

Escherichia coli

Carbapenem-resistant (CRE)	Any isolate that tested (R) to at least 1 of these: imipenem, meropenem, doripenem, ertapenem
Cephalosporin-resistant	Any isolate that tested (I) or (R) to at least 1 of these: ceftriaxone, ceftazidime, cefepime, cefotaxime
Fluoroquinolone-resistant	Any isolate that tested (I) or (R) to at least 1 of these: ciprofloxacin, levofloxacin, moxifloxacin
Multidrug-resistant (MDR)	Any isolate that tested either (I)* or (R) to at least 1 drug in at least 3 of these categories: 1. Extended-spectrum cephalosporins (ceftriaxone, ceftazidime, cefepime, cefotaxime) 2. Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin) 3. Aminoglycosides (amikacin, gentamicin, tobramycin) 4. *Carbapenems (isolate must have tested (R) to imipenem, meropenem, doripenem, or ertapenem) 5. Piperacillin/tazobactam

- ESBL-producing MDR by Facility definition
- Does not meet CDC MDR-definition

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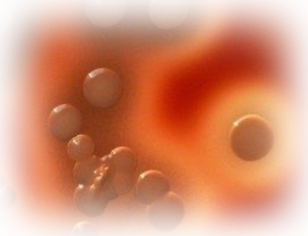
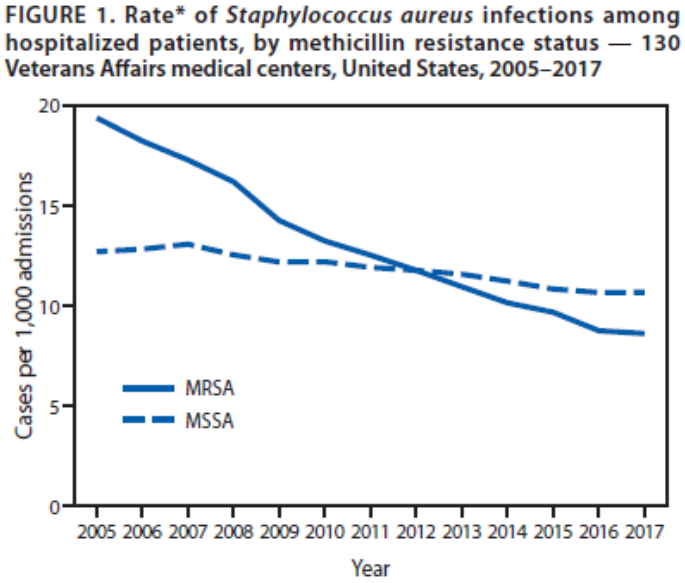
Methicillin resistant *Staphylococcus aureus*

- Method of resistance:
  - Resistant to all 1-4 gen B-lactams
  - mecA (gene product)
  - Produces PBP2a
- Treatment: Vancomycin; Daptomycin, Ceftaroline





Jones et al MMWR Morb Mortal Wkly Rep. 2019

Isolation precautions:	Contact
Reporting:	Facility reports to NHSN in for BSI-MRSA
Lab notifiable to public health	Rarely
Based on resistance to oxacillin this isolate would be resistant to all currently available beta-lactam antimicrobial agents, with the exception of the newer cephalosporins with anti-MRSA activity, such as Ceftaroline	
Call recommended?	No

Staphylococcus aureus

Only report vancomycin I/R After extensive confirmation

- Intermediate (MIC=4-8)
- Resistant (MIC≥16)

- Isolate purity
- Isolate identification
- Susceptibility testing

16 VRSA US cases as of 1/2022

CDC recommends saving all VRE and MRSA isolates from VRSA patient for further investigation

Isolation precautions:	Contact
Lab notifiable to public health	Yes
Call recommended?	Yes, to all stakeholders

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Vancomycin Resistant Enterococcus

- *E. faecalis* and *E. faecium* plasmid mediated Vancomycin R
- *E. casseliflavus/gallinarum* lower MIC chromosomally mediated

Isolation precautions:	Contact
Lab reportable to public health	No
Reporting recommendations	Include VRE in the organism name
Additional nudges	Distinguish between intrinsic R and plasmid R
Call recommended?	No

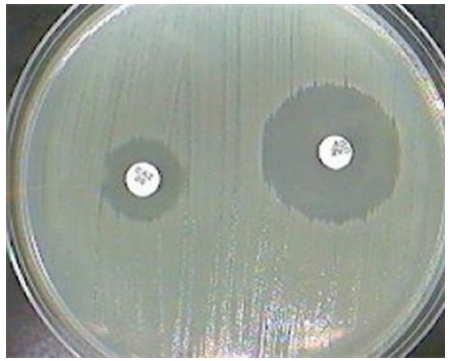
Extended-Spectrum Beta-Lactamase (ESBL) *Klebsiella, E. coli, P. mirabilis*

- ESBL-producing Enterobacterales increased by 53% from 2012 to 2017 (community acquired infections).
- ESBLs: are enzymes that inactivate most penicillins, cephalosporins, and aztreonam.
  - 100s of ESBL ; blaCTX-M most common
- EBSL-producing Enterobacterales generally susceptible to carbapenems.
  - Organisms carrying ESBL genes often harbor additional genes or mutations in genes that mediate resistance to a broad range of antibiotics.

Isolation precautions:	Depends on facility policies
Lab notifiable to public health	Rarely / CephR-Klebsiella reportable in NHSN
Reporting recommendations	Clarify if CTX-M detected, phenotypic ESBL
Call recommended?	No

Extended-Spectrum Beta-Lactamase (ESBL) producing *Klebsiella, E. coli, P. mirabilis*

- Routine EBSL testing: not needed clinically in most labs for AST
- Results could guide management / Infection Prevention
- Phenotypic testing included on some AST panels
- If ESBL+ by phenotypic AND Ceftriaxone S:
  - confirmation by disk diffusion
- Outpatient/Ambulatory:
  - ESBL commonly not reported
  - Non-susceptibility to ceftriaxone: proxy for potential ESBL production
- Transmission-based precautions for ESBL often written into LTCF protocols
  - Requires clear comments regarding presumptive ESBL status
  - NHSN includes Cephalosporin R Klebsiella



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Extended-Spectrum Beta-Lactamase (ESBL) Klebsiella, E. coli

- Syndromic molecular panels often include blaCTXM
- What to do if blaCTXM and Ceftriaxone / phenotypic ESBL are discordant?
  - If blaCTXM is Not Detected but Ceftriaxone = R
  - Report phenotypic results, include Cefepime results
  - Table H3 CLSI M100 Ed33

1 year Biofire BCID2

	Total Detected BCID2 runs	%Agreement Test=CTX-M Ref=Ceftriaxone R	Major Errors CTX-M Detected Ceftriaxone S	Very Major Errors CTX-M Not Detected Ceftriaxone R
E. coli	334	97.6% (326/334)	0% (0/267)	11.9%(8/67)
K. pneumoniae	99	100% (99/99)	0% (0/81)	0% (0/18)
K. oxytoca	13	100% (13/13)	7.7% (1/13)	0% (0/13)

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ESBL vs AmpC

Class	ESBL	AmpC
[B-lactam combination inhibitors] Pip/Taz ; Amp/sulb ; Amox; clav	S	R
[Cephamycin] Cefoxitin	S	R
[3rd gen Cephems] Ceftriaxone; Ceftazidime	R	R
Infection prevention	> concern (plasmid mediated)	< concern (chromosomal de-repression)
Treatment		Can acquire resistance post-Cephalosporin treatment

(25) Some Enterobacterales may develop resistance during therapy with third-generation cephalosporins as a result of derepression of AmpC β-lactamase. This derepression is most commonly seen with *Citrobacter freundii* complex, *Enterobacter cloacae* complex, and *Klebsiella* (formerly *Enterobacter*) *aerogenes*. Isolates that are initially susceptible may become resistant within a few days after initiation of therapy. Testing subsequent isolates may be warranted if clinically indicated. The approach to reporting AST results for these organisms should be determined in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders. See Table 1A, footnotes b and c.[4]

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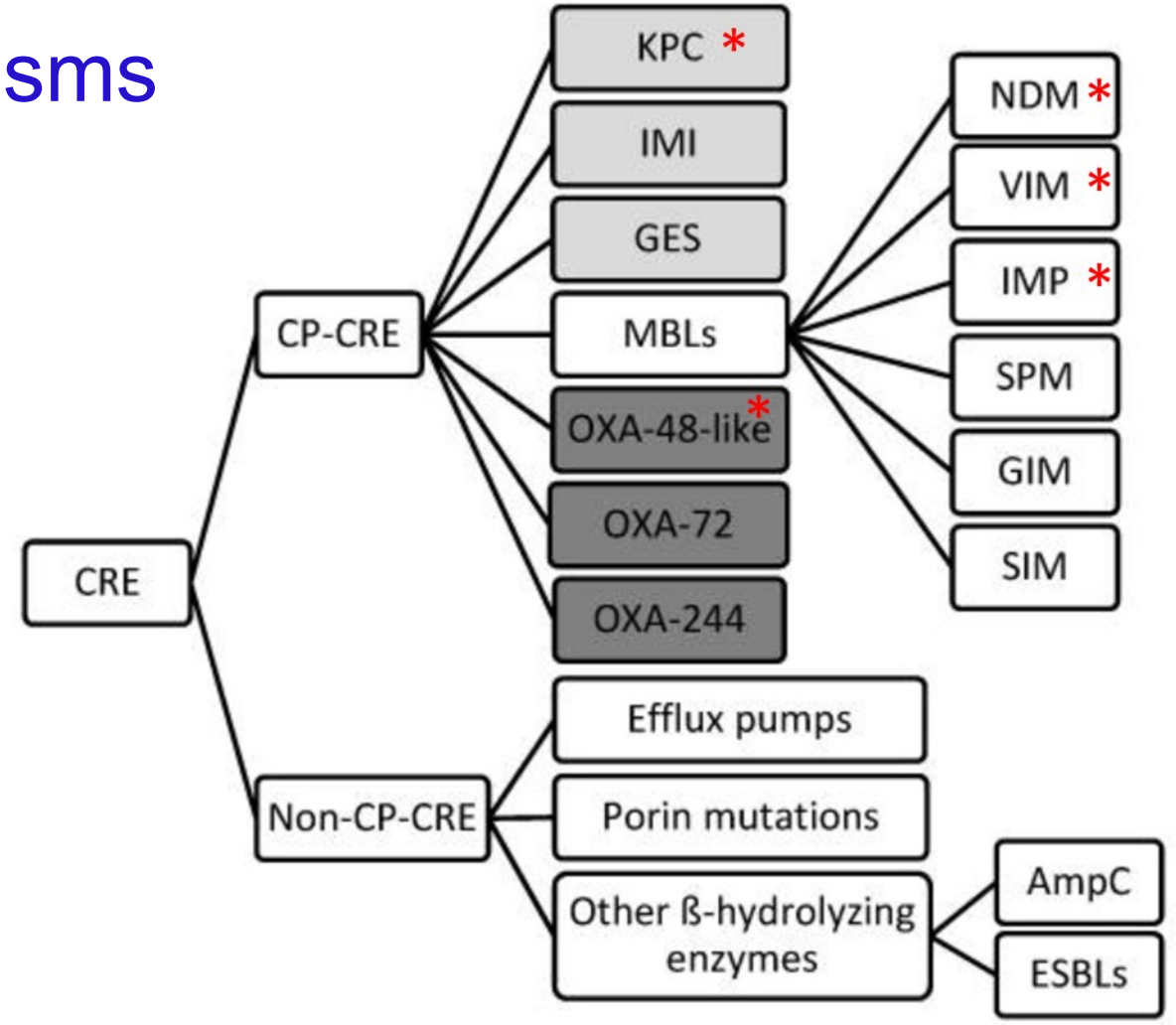
Carbapenem Resistant Organisms

CRE Enterobacterales phenotypically Resistant to Ertapenem, Meropenem, Imipenem, or Doripenem

CP Carbapenemase producers



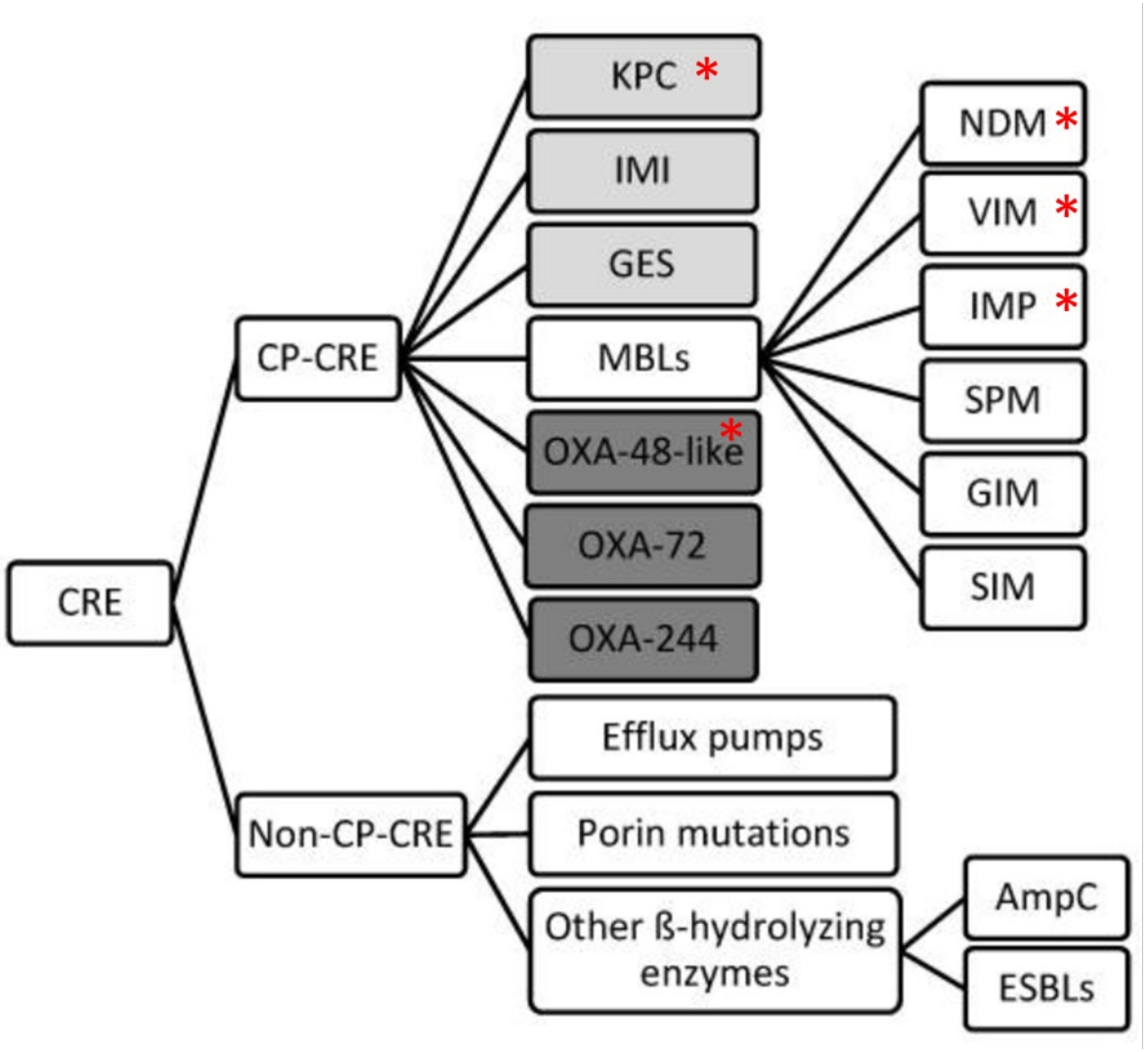
Ensure Accuracy of Results

- Confirm AST=R if only 1 carbapenem R
- Confirm purity

Suay-Garcia et al 2019 Antibiotics PMID 31430964

Test for Carbapenemase Mechanisms of Resistance?

- Important for surveillance
- Important for infection prevention (proves presence of horizontally transmittable plasmid)
- Helpful clinically to direct treatment if Carbapenemase is detected prior to escalated susceptibilities



Suay-Garcia et al 2019 Antibiotics PMID 31430964

Agents for treating CRE

- Narrow spectrum agents?
- Novel agents:
  - AST
  - Empiric treatment

US surveillance:
42,000 CRE 2017-2019
35% CP+
bla$_{KPC}$ (86%)
bla$_{NDM}$ (9%)
bla$_{VIM}$ (<1%)
bla$_{IMP}$ (1%)
bla$_{OXA-48-like}$ (4%)

Sabour et al AAC 2021

Agent	KPC-producer	NDM-producer	OXA-48-like-producer
Aztreonam-avibactam			
Cefiderocol			
Ceftazidime-avibactam[1]			
Ceftolozane-tazobactam[1]			
Eravacycline[1,2]			
Fosfomycin (intravenous)			
Imipenem-relebactam[3]			
Meropenem-vaborbactam[1]			
Plazomicin[1,4]			
Polymyxin B[1,5] or Colistin[1,5]			
Tigecycline[1,2]			

Green, susceptibility anticipated to be >80%;
Yellow, susceptibility anticipated to be 30% -80%;
red, intrinsic resistance or susceptibility anticipated to be <30%.

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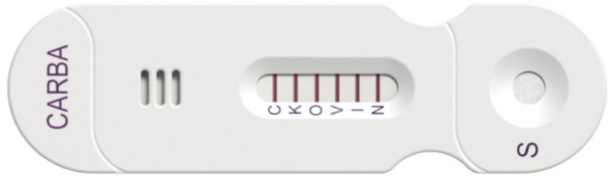
Tamma et al J Pediatric Infect Dis Soc 2019 PMID 30793757

Tests for Carbapenemase

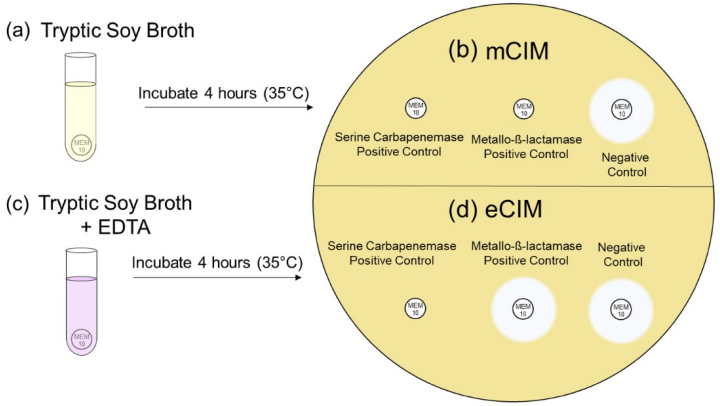
Assays detecting specific enzymes from isolate: [KPC, NDM, VIM, OXA-48,IMP]

- Lateral flow assays:
  - NG-Test® Carba5 (Hardy Diagnostics)
- Molecular panels
  - Xpert® Carba-R



Phenotypic assays

- Rapidec ® Carba-NP (bioMérieux)
- Carbapenem inactivation method: mCIM / eCIM



https://asm.org/Articles/2019/May/Opening-the-Black-Box-Phenotypic-Carbapenemase-Det

Tests for Carbapenemase

Direct molecular detection from specimen:

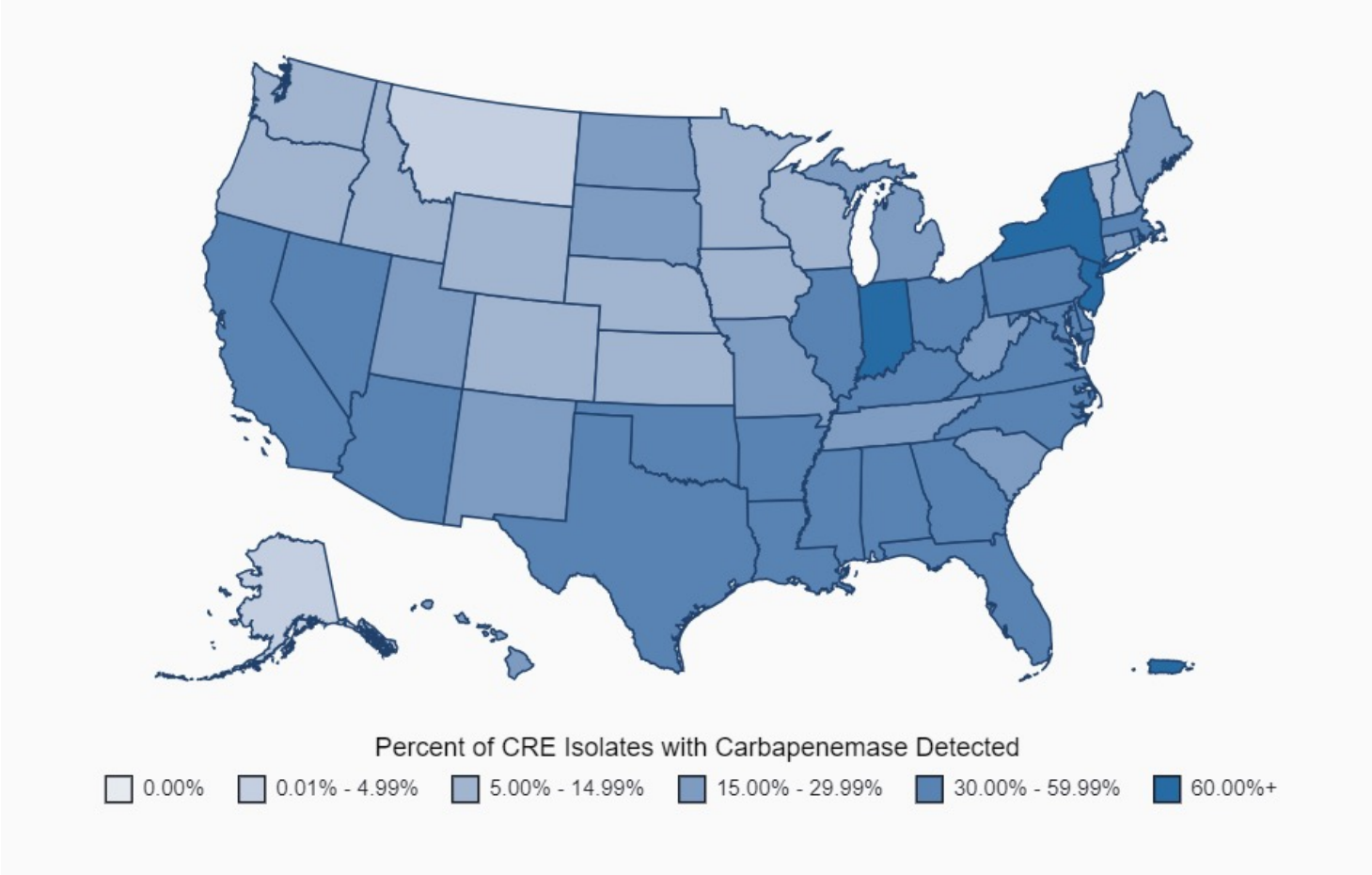
- Syndromic sample to answer panels
  - From Blood Culture
  - From Lower respiratory specimens

- Whole genome sequencing of isolate to detect all potential mechanisms of resistance
  - Subset of clinical microbiology labs within academic research medical center
  - Public health

https://asm.org/Articles/2019/May/Opening-the-Black-Box-Phenotypic-Carbapenemase-Det

Carbapenamase producing CRE prevalence: AR Lab Network

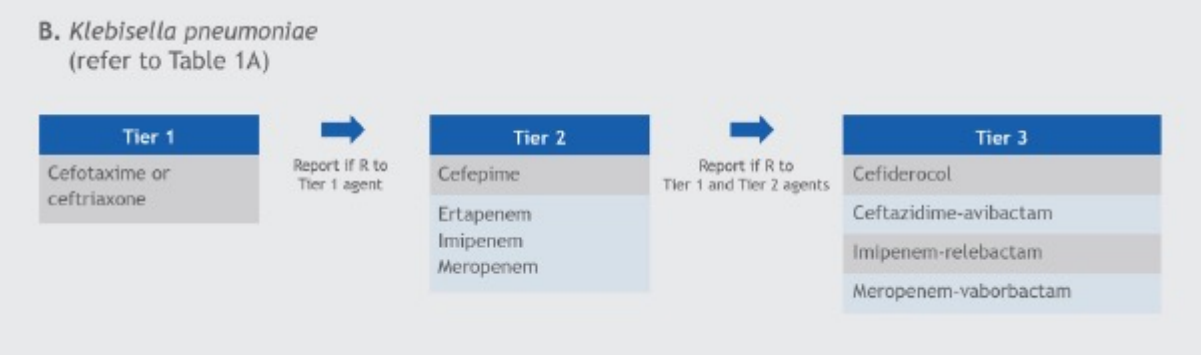
- Requires surveillance to establish prevalence
- Washington State requires isolate submission
  - The AR Lab Network: Isolates tested are a convenience sample and include clinical, surveillance, and outbreak specimens. Within each state, **isolate submissions and testing are determined by state priorities and reporting regulations**.



https://arpsp.cdc.gov/profile/arln/cre

CLSI guidelines for testing: “Antimicrobial Agents That Should be Considered for Testing and Reporting by Microbiology Laboratories”

- Selecting appropriate antimicrobial agents to test
- Implement cascade reporting if appropriate: report broader spectrum drugs only if narrow spectrum are R



	Lab Sets Up	Report (without Cascade)	Report (with Cascade)
Tier 1	Routinely	Routinely	Routinely
Tier 2	Routinely	Routinely	If Narrow = R
Tier 3	Routinely/Upon Request	Upon Request	If Narrow = R
Tier 4	Upon Request	Upon Request	Upon Request

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"Antimicrobial Agents That Should be Considered for Testing and Reporting by Microbiology Laboratories"

Table 1A. Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*)[a]

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ampicillin			
Cefazolin	Cefuroxime		
Cefotaxime or ceftriaxone[b]	Cefepime[c]		
	Ertapenem Imipenem Meropenem	Cefiderocol	
		Ceftazidime-avibactam	
		Imipenem-relebactam	
		Meropenem-vaborbactam	
Amoxicillin-clavulanate Ampicillin-sulbactam			
Piperacillin-tazobactam			
Gentamicin	Tobramycin	Plazomicin	
	Amikacin		
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
	Cefotetan Cefoxitin		
	Tetracycline[d]		
			Aztreonam
			Ceftaroline[b]
			Ceftazidime[b]
			Ceftolozane-tazobactam

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Table 1C. *Pseudomonas aeruginosa*

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution.	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ceftazidime	Imipenem Meropenem	Cefiderocol	
Cefepime		Ceftazidime-avibactam	
Piperacillin-tazobactam		Ceftolozane-tazobactam	
		Imipenem-relebactam	
Tobramycin			
Ciprofloxacin Levofloxacin			
			Aztreonam
Urine Only			
	Amikacin		

Abbreviation: MDRO, multidrug-resistant organism.

NOTE: Information in black boldface type is new or modified since the previous edition.

Isolation precautions:	Depends on facility policies
Lab notifiable to public health	Often. Carbapenemase + reportable nationally
Reporting recommendations	Determine with facility when escalation to novel agents
Call recommended?	No

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Carbapenem Resistant Acinetobacter

Table 1D. *Acinetobacter* spp.

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ampicillin-sulbactam			
Ceftazidime	Imipenem	Cefiderocol	
Cefepime	Meropenem		
Ciprofloxacin Levofloxacin			
Gentamicin Tobramycin	Amikacin		
	Piperacillin-tazobactam		
	Trimethoprim-sulfamethoxazole		
	Minocycline		Doxycycline
			Cefotaxime Ceftriaxone
			Colistin or polymyxin B
Urine only			
Tetracycline[a]			

Abbreviation: MDRO, multidrug-resistant organism.

Isolation precautions:	Depends on facility policies
Lab notifiable to public health	Rarely / MDR-Acineto reportable in NHSN
Reporting recommendations	Determine with institution if Cefiderocol should be tested reflexively if Meropenem or Imipenem R
Call recommended?	No

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MDRO GNR

Klebsiella (limited to *K. oxytoca* and *K. pneumoniae*)	
Carbapenem-resistant (CRE) (*K. aerogenes* added for 2020 data and forward)	Any isolate that tested (R) to at least 1 of these: imipenem, meropenem, doripenem, ertapenem
Cephalosporin-resistant	Any isolate that tested (I) or (R) to at least 1 of these: ceftriaxone, ceftazidime, cefepime, cefotaxime
Multidrug-resistant (MDR)	Any isolate that tested either (I)* or (R) to at least 1 drug in at least 3 of these categories: 1. Extended-spectrum cephalosporins (ceftriaxone, ceftazidime, cefepime, cefotaxime) 2. Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin) 3. Aminoglycosides (amikacin, gentamicin, tobramycin) 4. *Carbapenems (isolate must have tested (R) to imipenem, meropenem, doripenem, or ertapenem) 5. Piperacillin/tazobactam

Isolation precautions:	Depends on facility policies
Lab notifiable to public health	Rarely / MDR Acinetobacter reportable in NHSN
Reporting recommendations	Report as MDRO per institution policies if applicable Follow phenotypic definitions of AR AR_PhenotypeDefinitions
Call recommended?	Only if no flagging in EMR and cohorting/contact precautions are needed

Lab-Based Strategies to enhance effectiveness of MDRO reporting:

- Create procedure to flag patterns for confirmatory testing prior to release
  - Using AST instrument middleware / downstream pre-release flagging

- Create procedure for additional antimicrobial susceptibility sendouts

MIC.21944 **Testing and Reporting Supplemental Antimicrobial Agents** **Phase I**

The laboratory provides supplemental agent testing for organisms resistant to routinely tested antimicrobial agents, when necessary.

NOTE: The policy may include submission of isolates to an outside referral laboratory if testing is not performed onsite.

Evidence of Compliance:

✓ Patient testing reports demonstrating additional antimicrobial testing or referral

- Ensure AST breakpoints are updated

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Lab-Based Strategies to enhance effectiveness of MDRO reporting:

- Electronic aides to recognize MDRO patterns
  - LIS Middleware that automatically recognizes programmed MDRO patterns
  - Use AST instrument software to recognize patterns
  - Strategy for algorithmically tackling intrinsic resistance

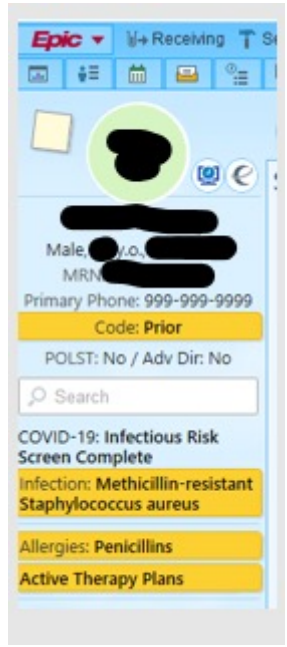
Lab-Based Strategies to enhance effectiveness of MDRO reporting:

- Report MDROs using consistent nomenclature
  - Flags in the chart notifying the floor of isolation precautions Triggers report to public health
  - Initiates electronic reporting to public health
  - Flags Antimicrobial Stewardship and Infection Prevention team
  - Files into data pulls facility submits to state/national databases

- Add approved canned comments regarding
  - Treatment
  - transmission based precaution initiation

Lab-Based Strategies to enhance effectiveness of MDRO reporting:

- EMR-based patient specific flags to alert caregivers
- Infection status impacting clinical care and isolation status displayed in banners



- Avoid systems that rely on lab calling of MDROs
  - Why is the lab calling these non-critical values
    - To alert care-team regarding treatment escalation?
    - To alert care-team regarding isolation precautions?
    - Are the correct stakeholders being called?
    - Is there an electronic method to replace this alert system

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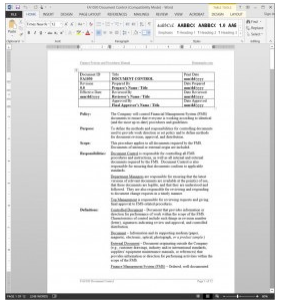
Lab-Based Strategies to enhance effectiveness of MDRO reporting:

- Ensure Public health notifiable conditions are up to date and reporting electronically to local health jurisdictions



- Create document controlled job-aides for staff for LHJ-sendouts

- Develop biobank system for select MDROs

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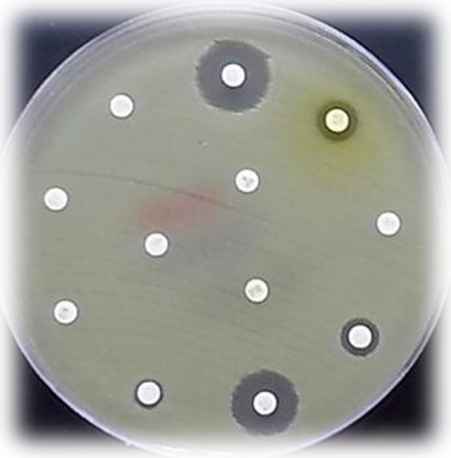
Finally

• MDRO infections endanger patient health and complicate care

•The lab is responsible for accurate and actionable MDRO reporting

•The lab plays a key role in
- •Ensuring appropriate infection prevention interventions
- •Pointing to appropriate treatment pathways
- •Reporting larger antimicrobial resistance trends



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Thank you

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