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Enhancement of a Carbapenemase Producing Organism Colonization Screening Workflow:

Decreasing Time, Increasing Data, and Maximizing Resource Capabilities

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Terms

AR: Antimicrobial Resistance

CPO: Carbapenemase-producing Organisms

CS: Colonization Screening

CRE: Carbapenem-resistant Enterobacterales

CRAB: Carbapenem-resistant *Acinetobacter baumannii*

CRPA: Carbapenem-resistant *Pseudomonas aeruginosa*

MDR: Multi-drug Resistant

Goals

- CPO CS Importance
- Screening Methods
- Wadsworth Center’s Screening Algorithm
- Summary

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Why Screen for CPOs?

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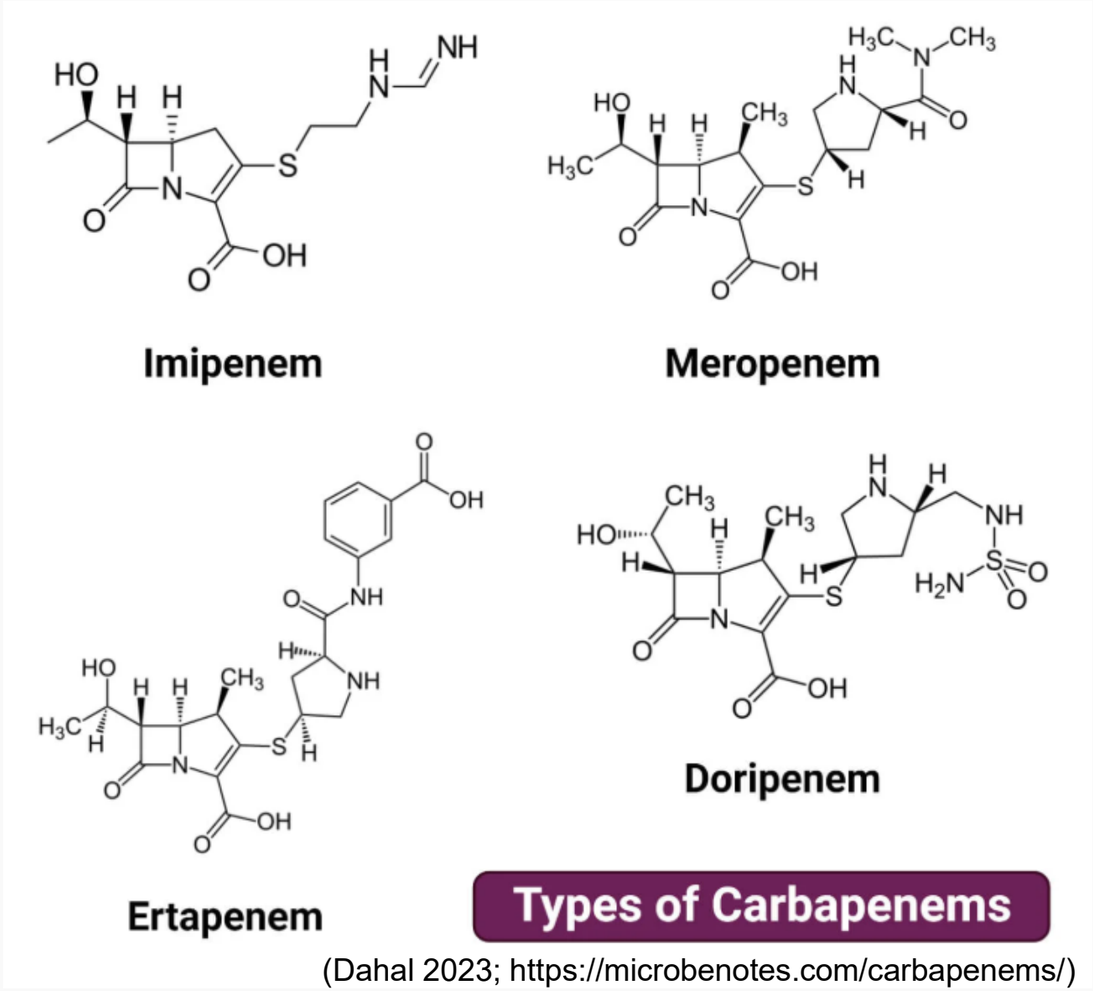
Carbapenems are Last-Resort Antibiotics



(Dahal 2023; https://microbenotes.com/carbapenems/)

MDR gram-negative bacteria

- Enterobacterales
- *Acinetobacter baumannii*
- *Pseudomonas* spp.

Streptococcus spp.

Mycobacterium tuberculosis complex

Haemophilus influenzae

MDR *Staphylococcus aureus*

Septicemia

Bone and joint infection

Meningitis

Healthcare-associated pneumonia

And more…

Carbapenemase-Producing Organisms

CRE

Carbapenem-resistant Enterobacterales

13,100 cases, 1,100 deaths

CRAB

Carbapenem-resistant *Acinetobacter baumannii*

MDR

8,500 cases, 700 deaths

CRPA

Carbapenem-resistant *Pseudomonas aeruginosa*

MDR

32,600 cases, 2,700 deaths

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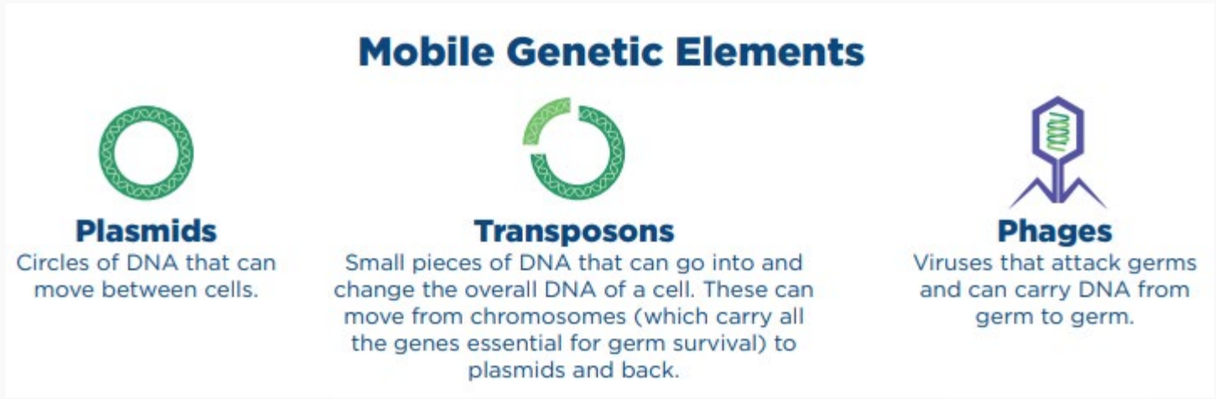
(CDC 2019)

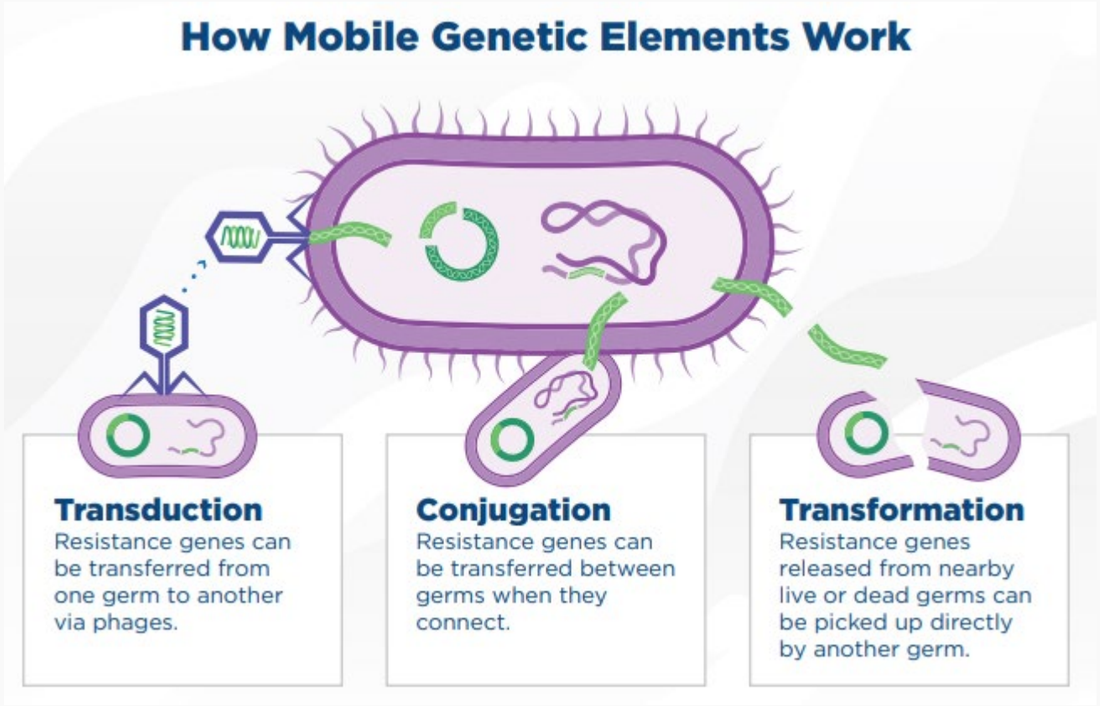
Mobile Genetic Elements Share Resistance

“The Big Five”: *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{IMP}$, *bla*$_{OXA-48}$

CRE

~30% carry mobile genetic elements
Inter- and intra- species gene transfer

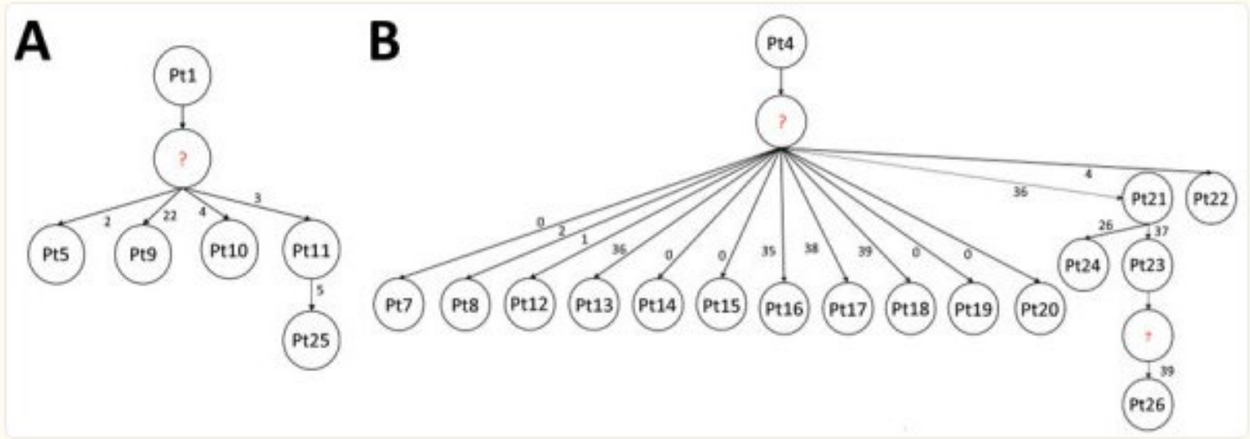




(CDC 2019)

Carbapenem Resistance Spreads Quickly

Figure 4.



Transmission networks among 22 patients with outbreak-associated $bla_{\text{OXA-181}}$ sequence type 307 (A) and $bla_{\text{NDM-1}}$ sequence type 152 (B) clones of *Klebsiella pneumoniae* isolated from a neonatal unit during outbreak, South Africa, October 2019–February 2020. Question marks denote missing isolates; numbers along branches indicate number of single-nucleotide polymorphisms between index isolate and other isolates.

(Magobo et al. 2023)

Rapid Screening Prevents Spread and Saves Lives

FIGUR 1 Screeningsprøverne tolket i henhold til European Committee on Antimicrobial Susceptibility Testing (EUCAST).

	Klebsiella pneumoniae		Morganella morganii	Providencia stuartii	Pseudomonas aeruginosa	Acinetobacter baumannii	Escherichia coli	Citrobacter amalonaticus	Citrobacter freundii
Carbapenemase	NDM-1	OXA-48	OXA-244	NDM-1	NDM-1	OXA-23	OXA-48, NDM-1	NDM-1	OXA-48
Penicilliner									
Piperacillin/tazobactam	R	R	R	R	R	-	R	R	R
Cefalosporiner									
Cefotaxim	R	R	R	R	-	-	R	R	-
Ceftazidim	R	R	S	R	R	-	R	R	-
Ceftazidim/avibactam	R	S	S	R	R	-	R	R	S
Ceftolozan/tazobactam	R	R	R	R	R	-	R	R	S
Carbapenemer									
Imipenem	R	I	I	R	-	R	R	R	S
Meropenem	R	R	S	I	R	R	I	R	S
Monobactamer									
Aztreonam	R	R	R	I	R	-	S	R	S
Fluorquinoloner									
Ciprofloxacin	R	R	R	R	R	R	S	S	S
Aminoglykosider									
Amikacin	S	R	S	R	R	R	R	R	S
Gentamicin	R	R	S	R	R	R	R	R	S
Tobramycin	R	R	R	R	R	R	R	R	S
Andre									
Colistin	S	R	R	R	S	S	S	S	S
Sulfametoxazol/trimetoprim	R	R	R	R	-	R	S	S	S
GenBank-ID[a]	GCA_028994575.1	GCA_029383165.1	GCA_029383145.1	GCA_029008175.1	GCA_028994585.1	GCA_029383195.1	GCA_028994605.1	GCA_028994555	GCA_028994595.1

I = sensitiv ved øget dosering; NDM = New Delhi-metallobetalaktamase; OXA = oxacillinase; R = resistent; S = sensitiv.
a) Sekvenserne er uploaded til National Center for Biotechnology Information.

(Christiansen et al. 2023)

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Reduced Screening Increases CPO Infection Rate

	Threat	Change in Rates or Number of Infections***			
		2020 vs. 2019	2021 vs. 2020	2022 vs. 2021	2022 vs. 2019
URGENT*	Hospital-onset CRE	▲ Increase	▲ Increase	— Stable	▲ Increase
URGENT*	Hospital-onset Carbapenem-resistant *Acinetobacter*	— Stable	— Stable	— Stable	▲ Increase**
URGENT*	Clinical Cases of *C. auris*	▲ Increase	▲ Increase	▲ Increase	▲ Increase
SERIOUS*	Hospital-onset MRSA	▲ Increase	— Stable	▼ Decrease	— Stable
SERIOUS*	Hospital-onset VRE	▲ Increase	▲ Increase	— Stable	▲ Increase
SERIOUS*	Hospital-onset ESBL-producing Enterobacterales	▲ Increase	— Stable	— Stable	▲ Increase
SERIOUS*	Hospital-onset MDR *Pseudomonas aeruginosa*	▲ Increase	▲ Increase	— Stable	▲ Increase

* Threat level for each pathogen, as categorized in CDC's *Antibiotic Resistance Threats in the United States, 2019*.
** There was no statistically significant difference in rate of hospital-onset carbapenem-resistant *Acinetobacter* in 2020, 2021, and 2022 when compared to the previous year. However, there was a statistically significant increase in rate of hospital-onset carbapenem-resistant *Acinetobacter* in 2022 when compared to 2019.
*** Hospital-onset rates were described using multivariable models for all threats except *C. auris*. Please note that in above table, stable indicates there was no statistically significant increase or decrease, decrease indicates a statistically significant decrease where $p<0.05$, and increase indicates a statistically significant increase where $p<0.05$, for all threats except for *C. auris*. Increases or decreases in *C. auris* were indicated by changes in the number of clinical cases reported nationally without hypothesis testing.

C. auris = *Candida auris*
MRSA = MDR *Staphylococcus aureus*
VRE = Vancomycin resistant enterococcus
ESBL = Extended-spectrum beta-lactamase

(CDC 2022)

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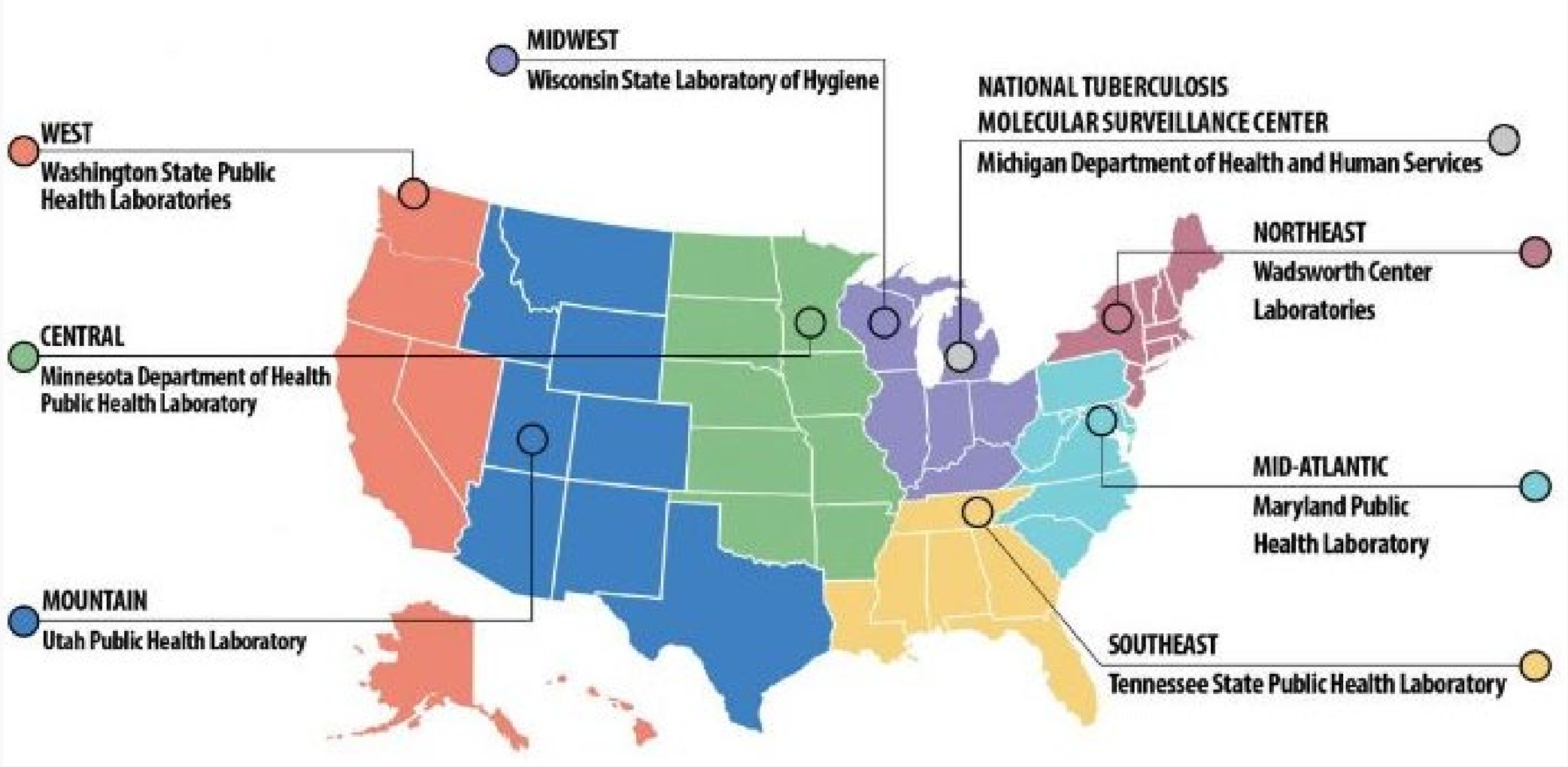
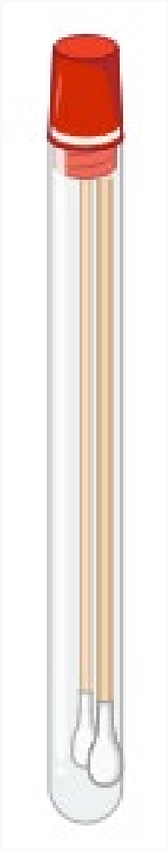
CDC's AR Lab Network Regional Laboratories

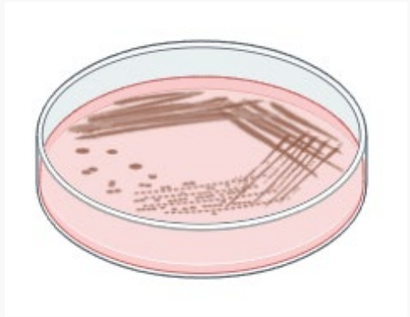


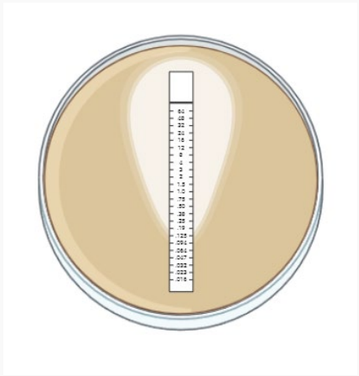
(CDC 2024)

Screening Methods

Culture-First Results in 3 days or More







> 3 Workdays

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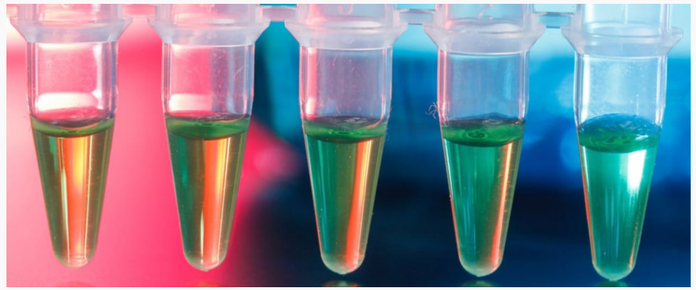
(BioRender.com, BlockScientific.com)

Molecular-First Methods are Complicated



(BlockScientific.com, MicrobeNotes.com, Lab-a-porter.com)

Wadsworth Center's CPO CS Algorithm

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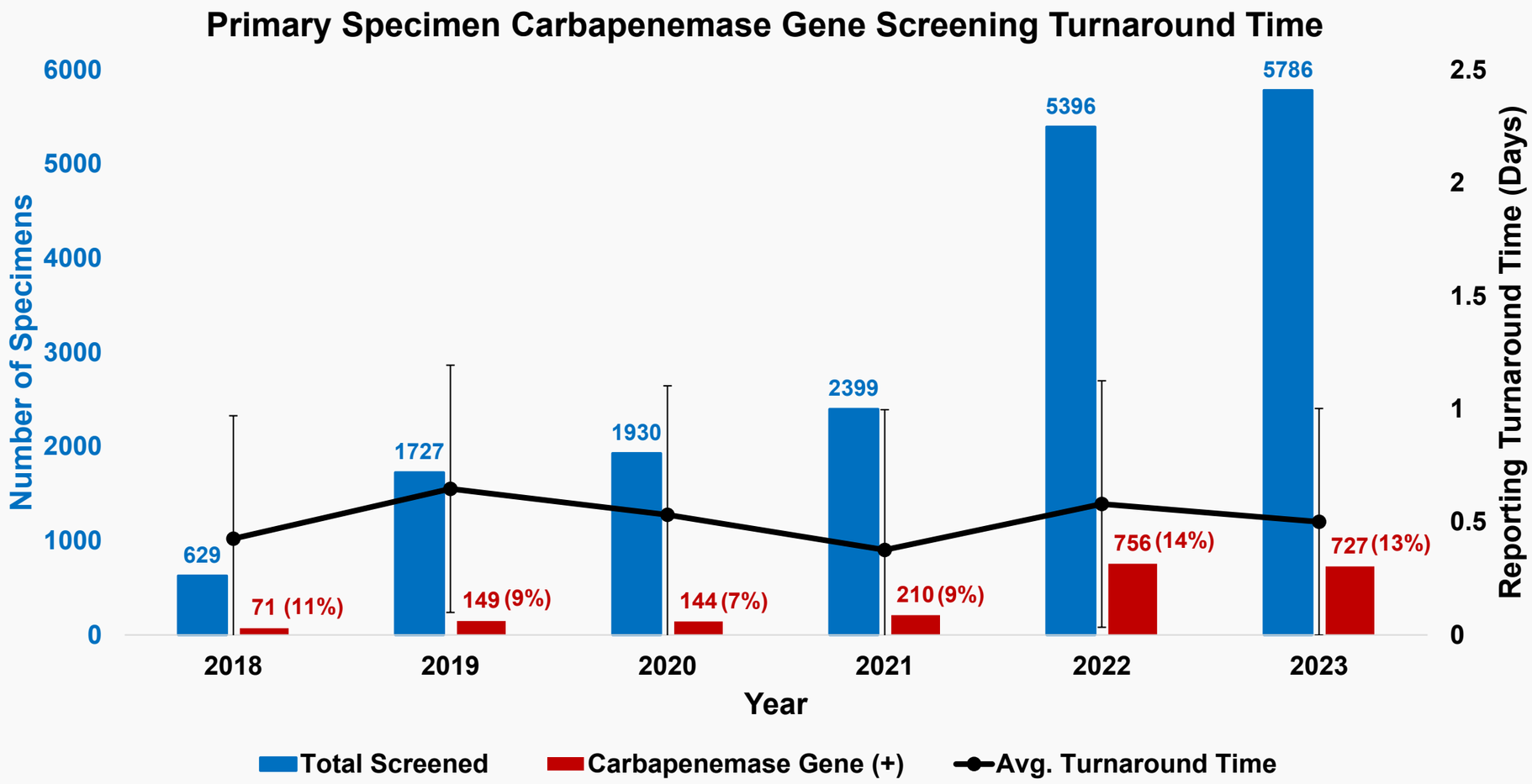
Wadsworth Center Reporting in <24 Hours



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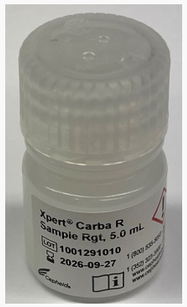
Carbapenemase Gene Screening Process

Dual Rectal Swab

Swab #1

Cepheid Xpert® Carba-R Sample Reagent



GeneXpert® Infinity System
Cepheid Xpert® Carba-R
(KPC, NDM, OXA-48, VIM, IMP)

bioMérieux EMAG®

QuantStudio™ 5 Real-Time PCR System
LDT Real-time PCR
(OXA-23, -24/40 and -58, VIM, IMP)

< 24 hours

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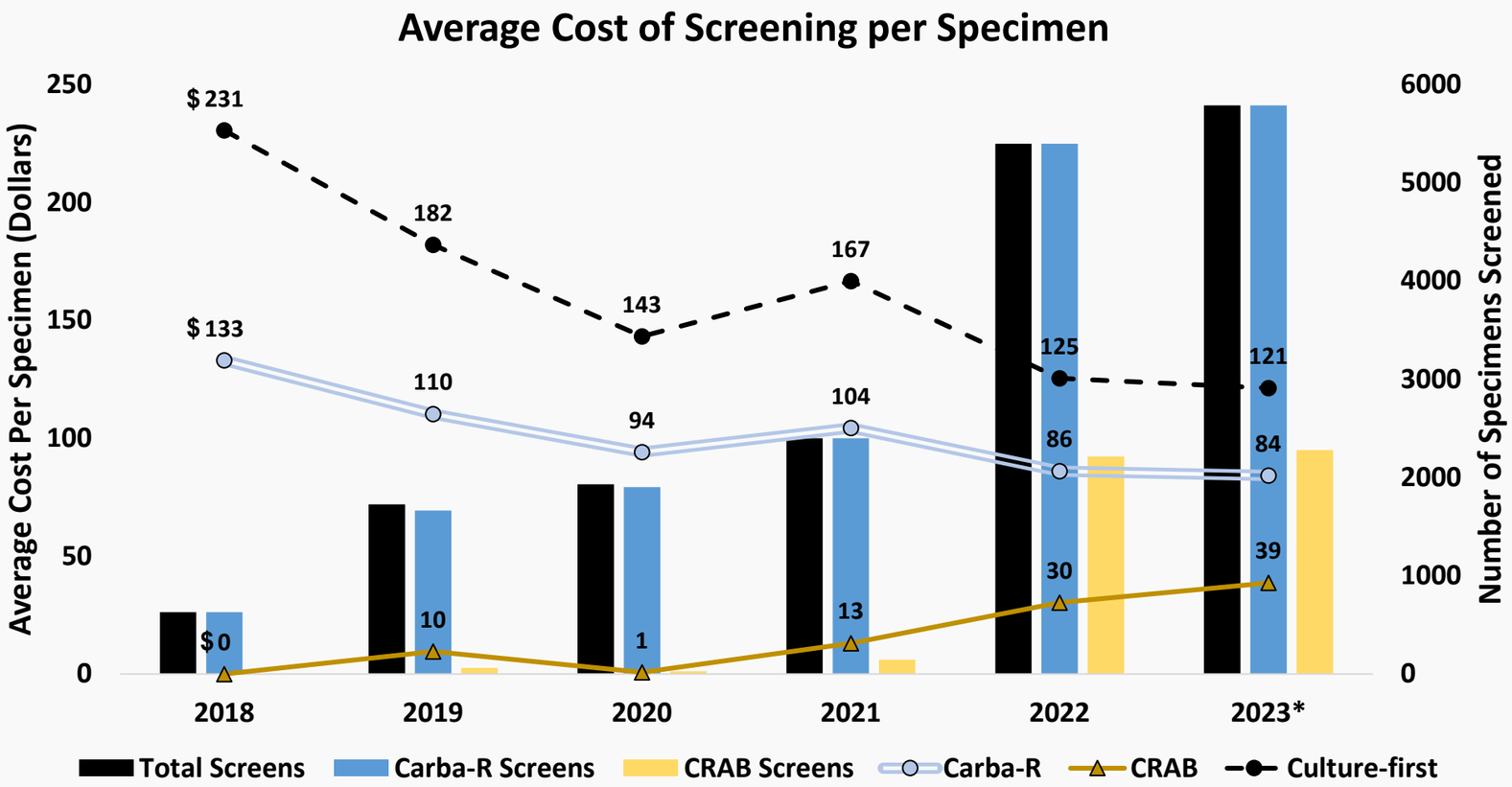
(BioRender.com, Medline.com, BioMerieux.com, BlockScientific.com)

Molecular-First CPO CS is Cost-Effective



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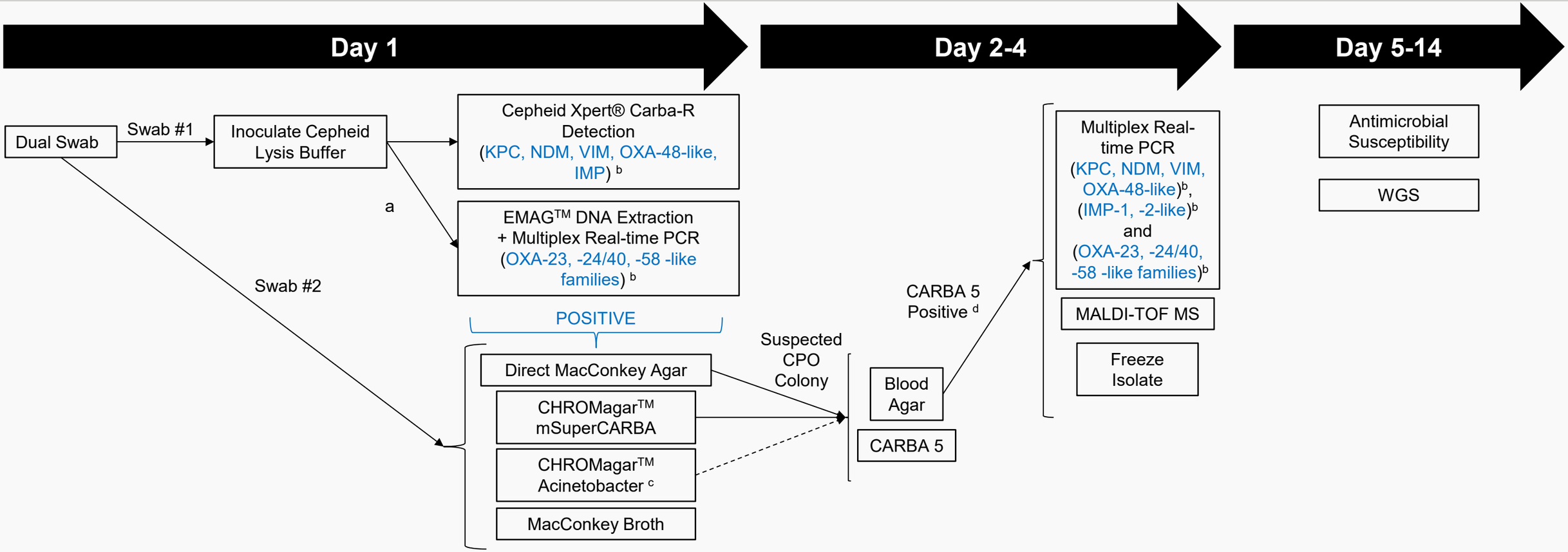
Summary

Wadsworth Center's CPO CS Algorithm



---- Rare occasions

a, If suspected carbapenemase producing *Acinetobacter* spp.

b, Reportable same day

c, OXA positive screens only

d, PCR is performed on all suspected OXA-family CPOs, regardless of CARBA 5 result

CPO= carbapenemase producing organism; WGS= whole genome sequencing; MS= mass spectrometry

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Conclusion

The spread of **carbapenem resistance** by carbapenemase-producing Enterobacterales, *Acinetobacter* spp., and *Pseudomonas* spp. is a major global public health threat.

- **Carbapenemase-producing organism colonization screening** is recommended for pre-admissions, facility transfers, at risk patients, and patients with a history of CPO carriage or exposure.
- **Rapid screening result reporting is essential** for rapid effective healthcare protocol initiation and epidemiological response.
- Employing a **molecular-first workflow** can better achieve public health initiatives to fight the spread of carbapenem resistance by **reducing** reporting **turnaround time, workload, and costs.**

Thank You

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Shannon Morris

Antibiotic Resistance and Bacteriology Laboratories,
Wadsworth Center

APHL Fellowship Program

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Reducing Workload and Overall Expense

Year	Carbapenemase Gene Negative Specimens	Culture Screening Savings	Personnel Savings	Approximate Net Savings
2018	558	$45K	0.5	$70K
2019	1,578	$118K	0.5	$73K
2020	1,786	$103K	1	$129K
2021	2,189	$141K	1	$127K
2022	4,640	$269K	1	$41K
2023	5,059	$284K	1	$32K

CPO MECHANISMS REPORTED BY WADSWORTH CENTER 2018-2023

	2018		2019		2020		2021		2022		2023	
Positive Gene Mechanisms												
KPC	57	76%	102	63%	107	71%	118	48%	440	45%	374	41%
NDM	16	21%	47	29%	32	21%	83	34%	128	13%	154	17%
OXA-48-like	2	3%	3	2%	7	5%	24	10%	53	5%	30	3%
VIM	0	0%	10	6%	5	3%	6	2%	30	3%	35	4%
IMP	0	0%	0	0%	0	0%	5	2%	0	0%	0	0%
OXA-23-like	---		0	0%	0	0%	8	3%	309	32%	316	35%
OXA-24/40-like	---		0	0%	0	0%	0	0%	10	1%	3	0%
OXA-58-like	---		0	0%	0	0%	0	0%	6	1%	0	0%
Total Positive Mechanisms	75		162		151		244		976		912	
Carba-R Screens												
Positive Gene Mechanism(s)												
KPC	57	76%	102	63%	107	71%	118	50%	440	68%	374	63%
NDM	16	21%	47	29%	32	21%	83	35%	128	20%	154	26%
OXA-48-like	2	3%	3	2%	7	5%	24	10%	53	8%	30	5%
VIM	0	0%	10	6%	5	3%	6	3%	30	5%	35	6%
IMP	0	0%	0	0%	0	0%	5	2%	0	0%	0	0%
Total Positive Mechanisms	75		162		151		236		651		593	
CRAB Screens												
Positive Gene Mechanism(s)												
OXA-23-like	---		0		0		8	100%	309	95%	316	99%
OXA-24/40-like	---		0		0		0	0%	10	3%	3	1%
OXA-58-like	---		0		0		0	0%	6	2%	0	0%
Total Positive Mechanisms	---		0		0		8		325		319	

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