Antimicrobial Resistance Lab Network Updates 2021

Logan Patterson, PhD

APHL-CDC Antimicrobial Resistance Fellow

Wisconsin State Laboratory of Hygiene



Outline

- Introduction
- Submission Guidelines
- Summary of 2020 Data
 - Recent and noteworthy outbreaks
- Ongoing and Upcoming Surveillance Activities









N-(3-oxododecanoyl)-L-homoserine lactone interactions in the breast tumor microenvironment: Implications for breast cancer viability and proliferation in vitro

Brittany N Balhouse ^{1 2}, Logan Patterson ^{3 4}, Eva M Schmelz ⁵, Daniel J Slade ³, Scott S Verbridge ^{1 2}





SCHOOL of MEDICINE





SCHOOL of MEDICINE

Glucosylceramide production maintains colon integrity in response to Bacteroides fragilis toxininduced colon epithelial cell signaling

Logan Patterson ¹, Jawara Allen ², Isabella Posey ³, Jeremy Joseph Porter Shaw ¹, Pedro Costa-Pinheiro ¹, Susan J Walker ⁴, Alexis Gademsey ⁴, Xinqun Wu ², Shaoguang Wu ², Nicholas C Zachos ², Todd E Fox ⁴, Cynthia L Sears ², Mark Kester ⁴





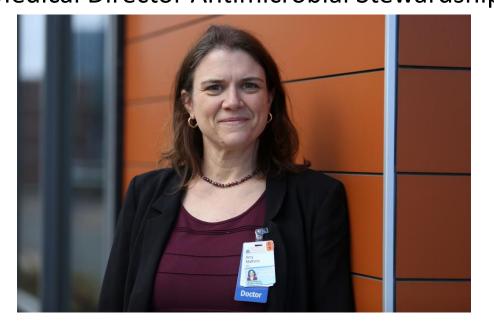
SCHOOL of MEDICINE

Dr. Melinda Poulter, PhD, D(ABMM)

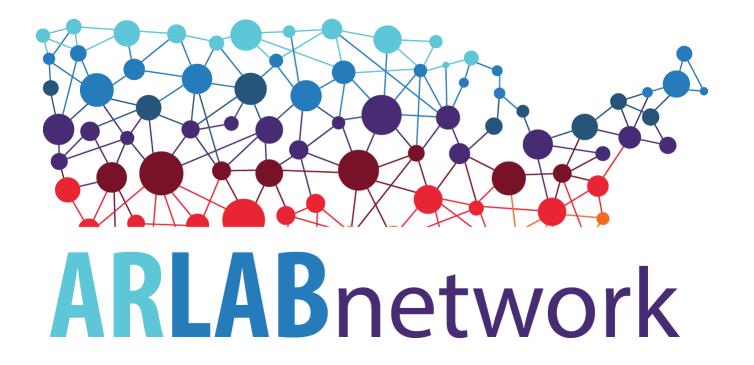
Director, Clinical Microbiology



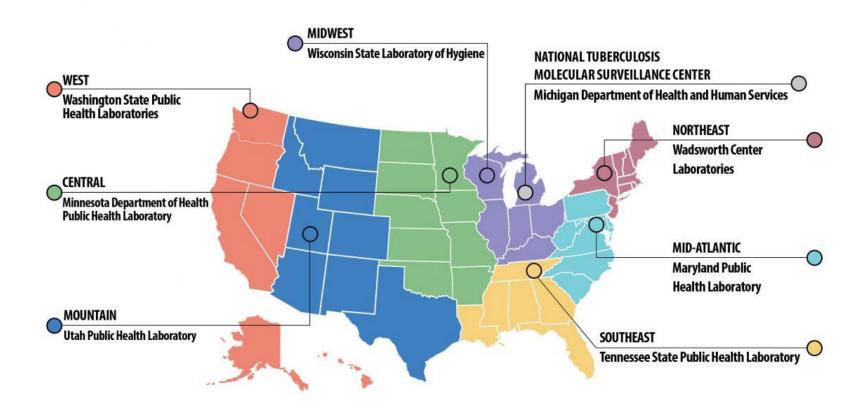
Dr. Amy Mathers, MD Associate Director, Clinical Microbiology Medical Director Antimicrobial Stewardship













- Core testing by all regional labs
 - Molecular testing to detect colonization of carbapenem-resistant Enterobacteriaceae (CRE)



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 - Detection of new and emerging threats



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 - Identification and colonization screening to detect and help prevent spread of Candida auris
 - Perform expanded susceptibility testing to determine if new drugs or drug combinations will be effective to treat rare resistant pathogens
 - Isolates may be used for the CDC and FDA AR Isolate Bank and WGS projects



- Additional testing
 - Antimicrobial susceptibility and serotyping of multidrug-resistant Streptococcus pneumoniae (WI and MN)



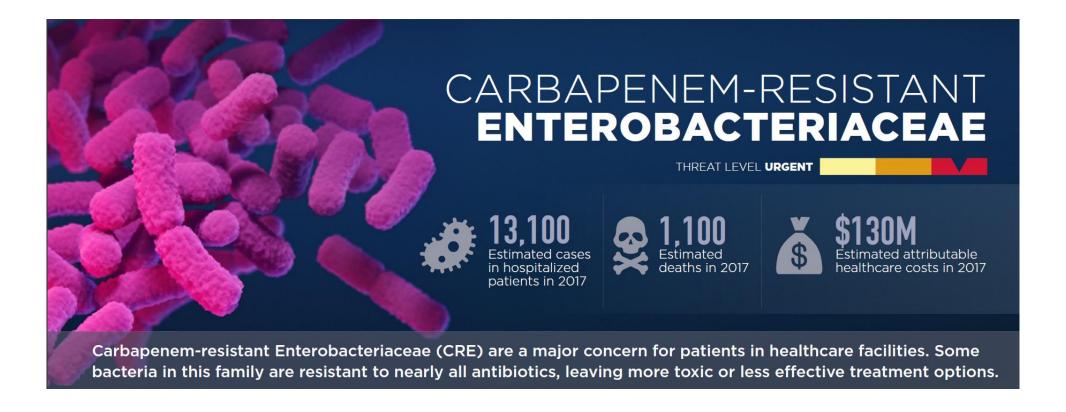
- Additional testing
 - Antimicrobial susceptibility and serotyping of multidrug-resistant Streptococcus pneumoniae (WI and MN)
 - Test CRE and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) isolates for resistance mechanisms and antimicrobial susceptibility (AST)



- Additional testing
 - Antimicrobial susceptibility and serotyping of multidrug-resistant Streptococcus pneumoniae (WI and MN)
 - Test CRE and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) isolates for resistance mechanisms and antimicrobial susceptibility (AST)
 - Modified carbapenem inactivation method (mCIM), PCR, AST, and whole genome sequencing (WGS)



Carbapenem-resistant *Enterobacteriaceae* (CRE)





Carbapenem-resistant *Enterobacteriaceae* (CRE)

- Carbapenem-resistant Enterobacteriaceae (CRE)
 - CRE can carry mobile genetic elements that are easily shared between bacteria
 - Approximately 30% of CRE carry a mobile genetic element that make carbapenem antibiotics ineffective
 - Patients who require devices (e.g., catheters) and patients taking long courses of antibiotics are the most at risk

Organism	Isolates
Enterobacter spp.	176
Klebsiella spp.	165
Escherichia coli	77
Citrobacter freundii	24
Proteus mirabilis	16
Raoultella ornithinolytica	13
Serratia marcescens	11
Providencia rettgeri	8
Morganella morganii	7
Hafnia alvei	3
Pseudomonas aeruginosa	4
Misc.	4
Citrobacter koseri	1
Providencia stuartii	1
Total	510



- Carbapenem-resistant *Enterobacteriaceae* (CRE)
 - Resistant to any carbapenem



- Carbapenem-resistant *Enterobacteriaceae* (CRE)
 - Resistant to any carbapenem
 - Screen positive for a carbapenemase using a phenotypic testing method (mCIM, CarbaNP)



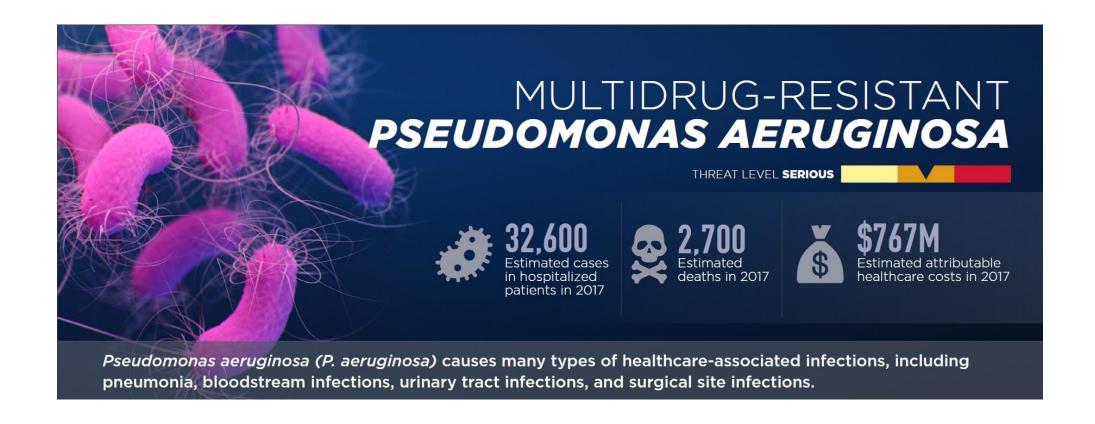
- Carbapenem-resistant *Enterobacteriaceae* (CRE)
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 - Screen positive for a carbapenemase using a phenotypic testing method (mCIM, CarbaNP)
 - Test positive for a carbapenemase gene using molecular methods (KPC, NDM, VIM, IMP, OXA-48)



- Carbapenem-resistant Enterobacteriaceae (CRE)
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 - Screen positive for a carbapenemase using a phenotypic testing method (mCIM, CarbaNP)
 - Test positive for a carbapenemase gene using molecular methods (KPC, NDM, VIM, IMP, OXA-48)
- Exceptions
 - Proteus spp., Providencia spp., and Morganella morganii that are resistant to Imipenem ONLY (susceptible to Meropenem or Doripenem)



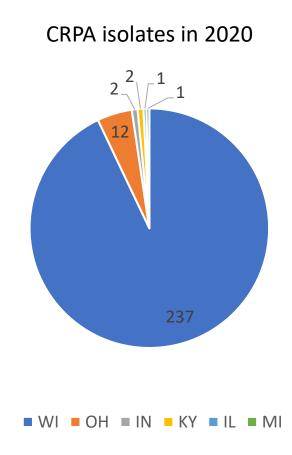
Carbapenem-resistant *Pseudomonas* aeruginosa (CRPA)





Carbapenem-resistant *Pseudomonas* aeruginosa (CRPA)

- Carbapenem-resistant Pseudomonas aeruginosa (CRPA)
 - P. aeruginosa infections usually occur in people in the hospital or with weakened immune systems
 - 2-3% of CRPA carry a mobile genetic element that makes a carbapenemase enzyme





- Carbapenem-resistant Pseudomonas aeruginosa (CRPA)
 - Resistant to a carbapenem (Doripenem, Imipenem, or Meropenem) AND nonsusceptible to Cefepime and/or Ceftazidime



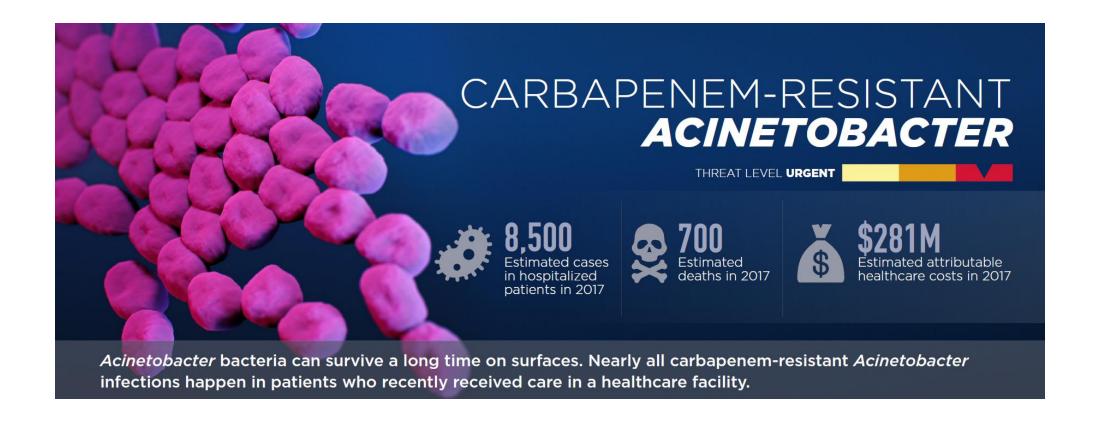
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- Carbapenem-resistant Pseudomonas aeruginosa (CRPA)
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- Exceptions
 - Isolates that are susceptible to Cefepime and/or Ceftazidime but are suspected of producing a carbapenemase may be accepted on a case-by-case basis
 - Do not submit resistant *P. aeruginosa* isolates from cystic fibrosis patients



Carbapenem-resistant *Acinetobacter* baumannii (CRAB)





Carbapenem-resistant *Acinetobacter* baumannii (CRAB)

- Carbapenem-resistant Acinetobacter baumannii (CRAB)
 - Cause pneumonia, wound, bloodstream, and urinary tract infections
 - Infections tend to occur in intensive care units (ICUs)
 - Carry mobile genetic elements that are easily shared between bacteria, further enhancing the spread of carbapenemase producing organisms
 - Some Acinetobacter are resistant to nearly all antibiotics
 - Very few new drugs are in development



Carbapenem-resistant *Acinetobacter* baumannii (CRAB)

- Carbapenem-resistant Acinetobacter baumannii (CRAB)
 - Often carry plasmid-encoded β -lactamases with carbapenemase activity (OXA-23, OXA-24/40, and OXA-58)
 - Denoted as OXA because of their ability to confer resistance to oxacillin
 - Presence of just one carbapenemase-hydrolyzing OXA enzyme may be enough for A. baumannii to become resistant to all carbapenems

Review > Clin Microbiol Rev. 2014 Apr;27(2):241-63. doi: 10.1128/CMR.00117-13.

OXA β-lactamases

Benjamin A Evans ¹, Sebastian G B Amyes

Affiliations + expand

PMID: 24696435 PMCID: PMC3993105 DOI: 10.1128/CMR.00117-13

Free PMC article



- Carbapenem-resistant Acinetobacter baumannii (CRAB)
 - Isolates resistant to a carbapenem from Southeast Wisconsin
 - Jefferson, Kenosha, Milwaukee, Ozaukee, Racine, Walworth, Washington, and Waukesha counties



- Carbapenem-resistant Acinetobacter baumannii (CRAB)
 - Isolates resistant to a carbapenem from Southeast Wisconsin
 - Jefferson, Kenosha, Milwaukee, Ozaukee, Racine, Walworth, Washington, and Waukesha counties
 - Pan-resistant isolates from facilities outside of Southeast Wisconsin, or isolates suspected of being part of an outbreak, please contact WSLH for guidance on submission (wiarln@slh.wisc.edu)



Candida auris





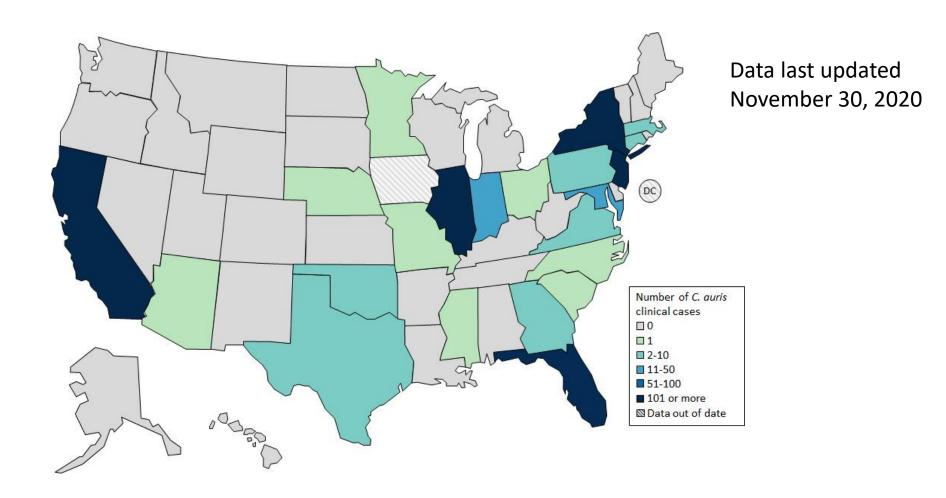
Candida auris

- Candida auris
 - Can cause outbreaks in healthcare facilities
 - Often multidrug-resistant, with some strains resistant to all three available classes of antifungals
 - Can be carried on patient's skin without causing infection, allowing further spread
 - Some common healthcare disinfectants are less effective at eliminating it

Organism	Isolates
C. auris	260
C. parapsilosis	40
C. glabrata	9
C. lusitaniae	8
Candida species, not C. auris	7
S. cerevisiae	6
C. albicans	4
C. dubliniensis	3
C. fermentati	1
C. haemulonii	1
C. orthopsilosis	1
C. kefyr	1
C. neoformans	1
C. tropicalis	1
Total	343



C. auris confirmed cases in the US





- Candida species
 - Candida auris, or suspected C. auris



- Candida species
 - Candida auris, or suspected C. auris
 - Invasive isolates of Candida glabrata



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- Candida species
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 - Candida spp. that are unable to be identified
 - Unusual Candida spp.
 - Species other than *C. albicans, C. dublinensis, C. krusei, C. lusitaniae, C. parapsilosis,* or *C. tropicalis*



- Candida species
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 - Candida spp. that are unable to be identified
 - Unusual Candida spp.
 - Species other than *C. albicans, C. dublinensis, C. krusei, C. lusitaniae, C. parapsilosis,* or *C. tropicalis*
 - Candida spp. resistant to two or more antifungal classes

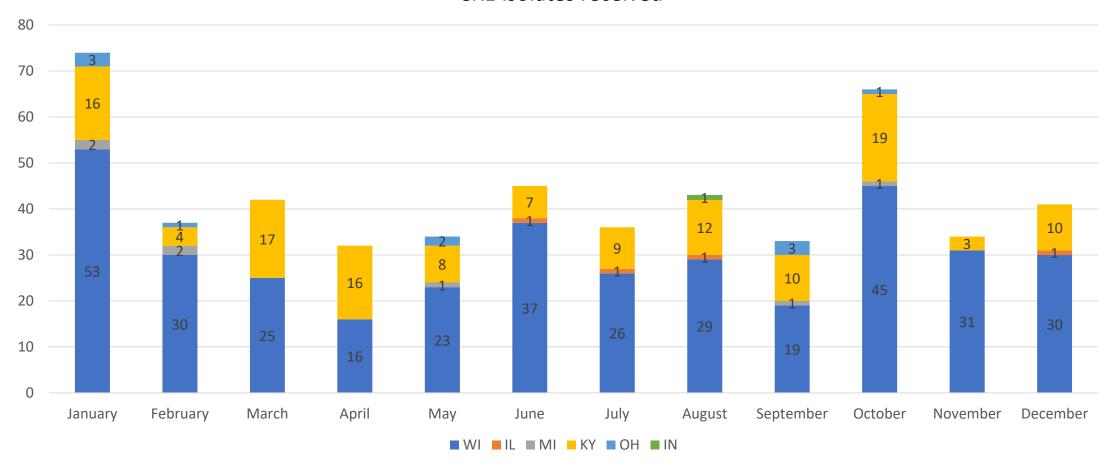


Testing performed on submitted isolates

- CRE/CRPA
 - MALDI, modified carbapenem inactivation method (mCIM), AST, carbapenemase PCR (if mCIM+), and WGS

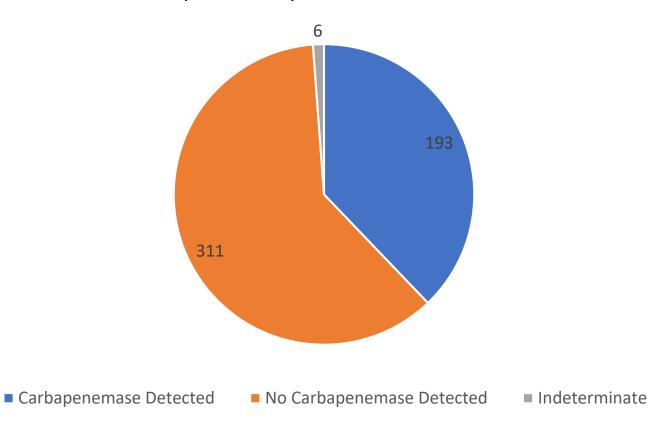


CRE isolates received



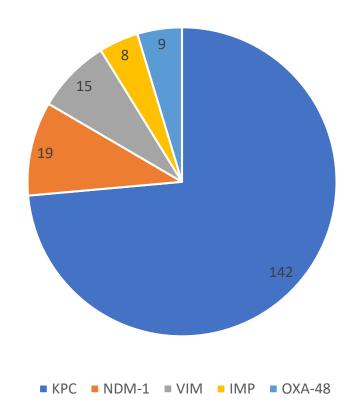


Carbapenemase presence in CRE isolates



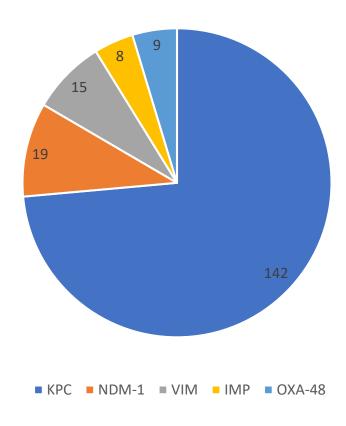


Carbapenemase genes detected

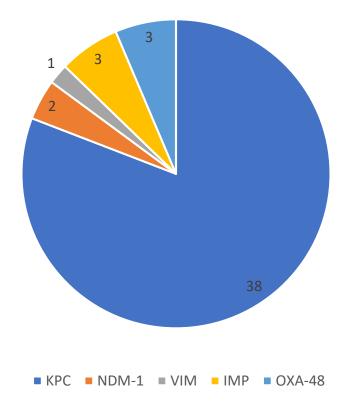




Carbapenemase genes detected



Carbapenemase genes detected-Wisconsin

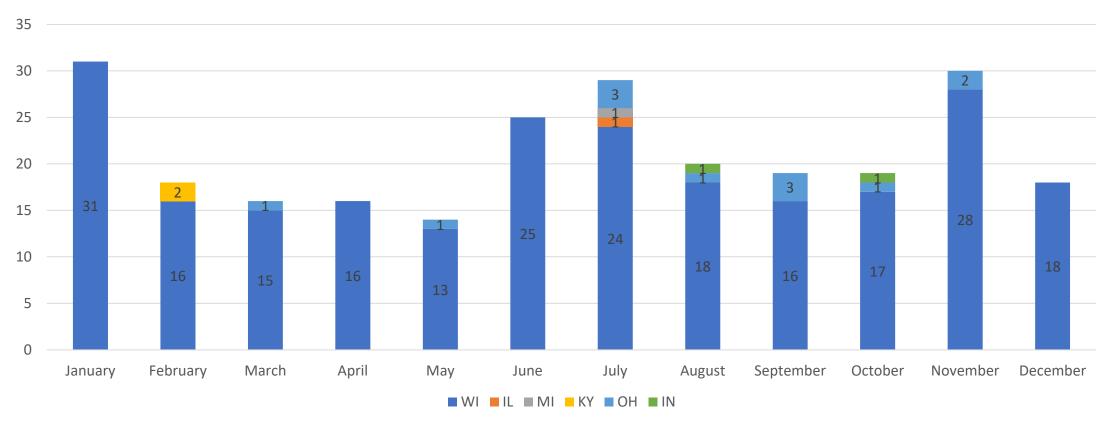




Pan non-susceptible isolates				
Month	State	Organism	Mechanism(s)	
January	ОН	Klebsiella pneumoniae	КРС	
January	MI	Klebsiella pneumoniae	NDM-1	
January	КҮ	Klebsiella pneumoniae	OXA-48	
February	ОН	Klebsiella pneumoniae	KPC	
March	КҮ	Klebsiella pneumoniae	OXA-48	
May	ОН	Klebsiella pneumoniae	КРС	
May	KY	Escherichia coli	NDM-1	
July	KY	Escherichia coli	NDM-1 and OXA-48	
July	IL	Klebsiella pneumoniae	KPC and NDM-1	
October	МІ	Klebsiella pneumoniae	NDM-1 and OXA-48	
December	WI	Klebsiella pneumoniae		

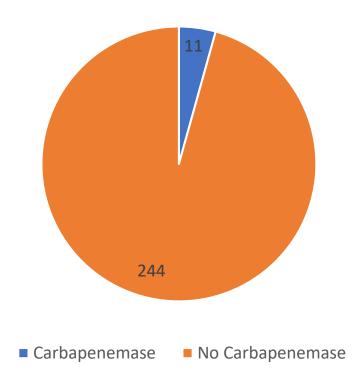


CRPA isolate submissions



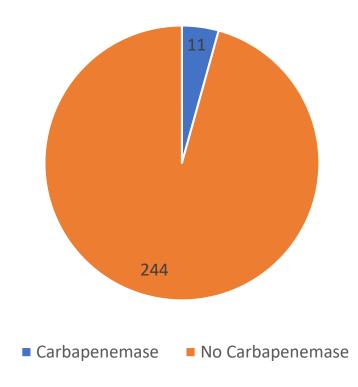


Carbapenemase presence in CRPA isolates





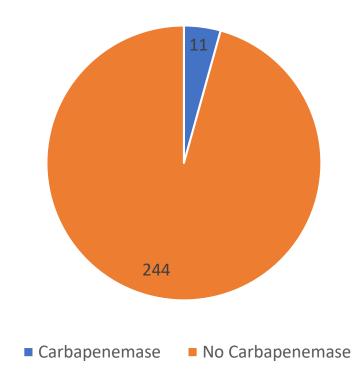
Carbapenemase presence in CRPA isolates



Date	State	Mechanism
March	ОН	VIM
May	ОН	Potential novel
May	WI	Potential novel
July	ОН	Potential novel
July	ОН	Potential novel
July	ОН	Potential novel
July	MI	Potential novel
October	ОН	Potential novel
November	ОН	Potential novel
December	WI	NDM-1
December	WI	NDM-1



Carbapenemase presence in CRPA isolates



Date	State	Mechanism	Pan-NS?
March	ОН	VIM	No
May	ОН	Potential novel	No
May	WI	Potential novel	No
July	ОН	Potential novel	No
July	ОН	Potential novel	No
July	ОН	Potential novel	No
July	MI	Potential novel	No
October	ОН	Potential novel	No
November	ОН	Potential novel	No
December	WI	NDM-1	Yes
December	WI	NDM-1	No



Date	State	Mechanism	Pan-NS?
May	WI	None detected	Yes
June	WI	None detected	Yes
July	WI	None detected	Yes
August	WI	None detected	Yes
August	ОН	None detected	Yes
August	WI	None detected	Yes
December	WI	NDM-1	Yes

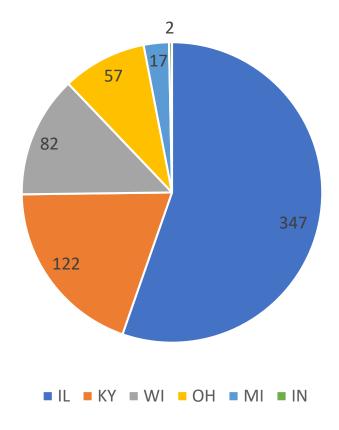


Testing performed on submitted isolates

- CRE/CRPA
 - MALDI, modified carbapenem inactivation method (mCIM), AST, carbapenemase PCR (if mCIM+), and WGS
- CRAB
 - MALDI, AST, carbapenemase PCR, and WGS

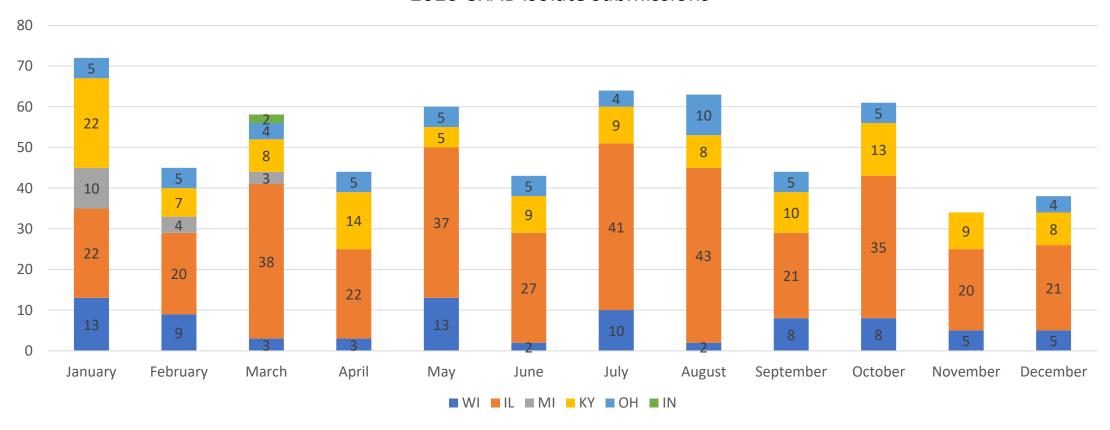






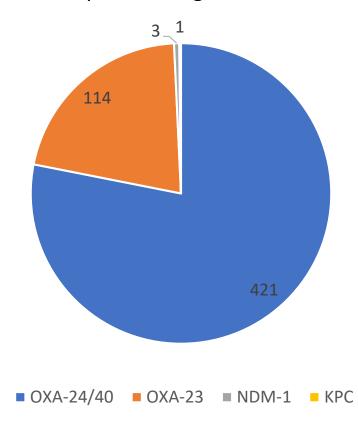


2020 CRAB isolate submissions

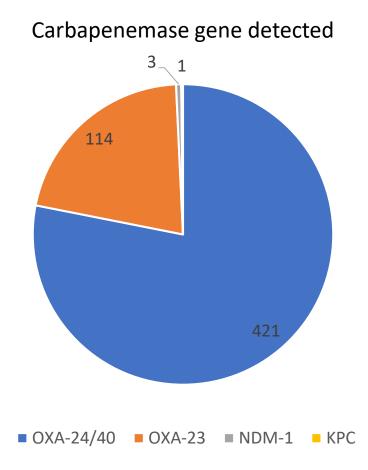


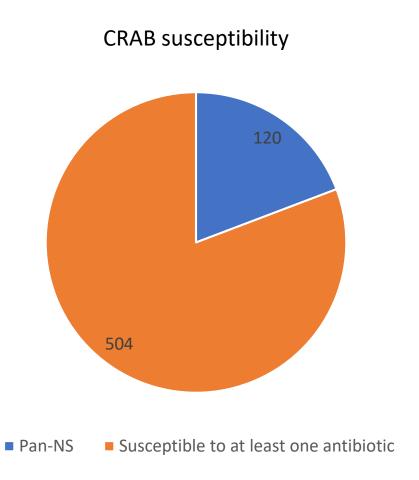


Carbapenemase gene detected











2020 CRAB data-Wisconsin

Month	Isolates	Pan-NS?	OXA-24/40+
January	13	0	8
February	9	0	8
March	3	0	3
April	3	0	3
May	13	6	12
June	2	2	2
July	10	2	10
August	2	0	2
September	8	1	6
October	8	2	5
November	5	1	5
December	5	1	5
Total	81	15	69



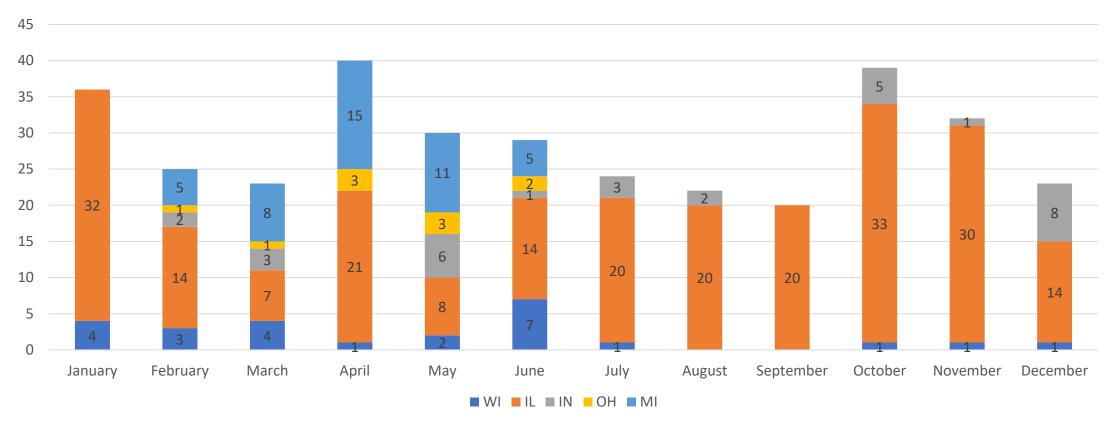
Testing performed on submitted isolates

- CRE/CRPA
 - MALDI, modified carbapenem inactivation method (mCIM), AST, carbapenemase PCR (if mCIM+), and WGS
- CRAB
 - MALDI, AST, carbapenemase PCR, and WGS
- Candida spp.
 - MALDI and AST



2020 Candida data

Candida isolates submitted





The impact(s) of the COVID-19 pandemic

COVID-19 Units Seeing Increasing Rates of Multi-Drug Resistant Organism Outbreaks



December 21, 2020

RE: Possibility of increasing multidrug-resistant organisms (MDROs) amid the COVID-19 pandemic



COVID-19 and the spread of CRE

> J Clin Med. 2020 Aug 25;9(9):2744. doi: 10.3390/jcm9092744.

Antimicrobial Stewardship Program, COVID-19, and Infection Control: Spread of Carbapenem-Resistant Klebsiella Pneumoniae Colonization in ICU COVID-19 Patients. What Did Not Work?

```
Beatrice Tiri <sup>1</sup>, Emanuela Sensi <sup>2</sup>, Viola Marsiliani <sup>2</sup>, Mizar Cantarini <sup>2</sup>, Giulia Priante <sup>3</sup>, Carlo Vernelli <sup>3</sup>, Lucia Assunta Martella <sup>3</sup>, Monya Costantini <sup>4</sup>, Alessandro Mariottini <sup>5</sup>, Paolo Andreani <sup>5</sup>, Paolo Bruzzone <sup>6</sup>, Fabio Suadoni <sup>7</sup>, Marsilio Francucci <sup>8</sup>, Roberto Cirocchi <sup>9</sup>, Stefano Cappanera <sup>1</sup>
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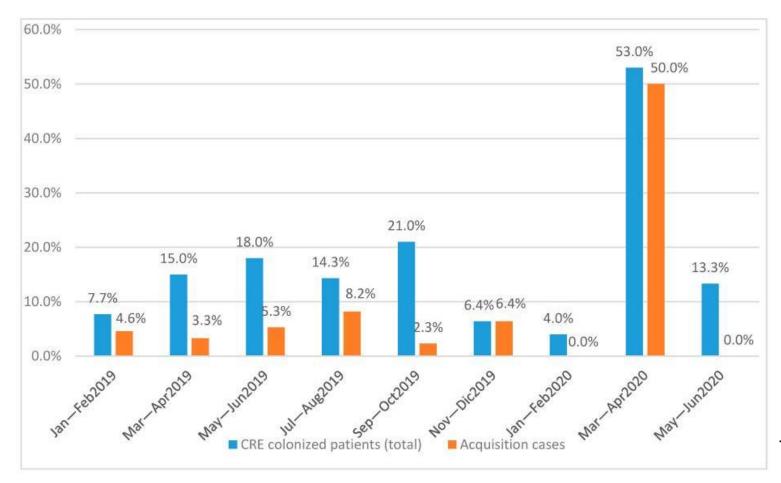
Affiliations + expand

PMID: 32854334 PMCID: PMC7563368 DOI: 10.3390/jcm9092744

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COVID-19 and the spread of CRE



Tiri *et al.*, 2020



COVID-19 and the spread of CRE

> J Antimicrob Chemother. 2021 Jan 19;76(2):380-384. doi: 10.1093/jac/dkaa466.

Carbapenemase-producing Enterobacterales causing secondary infections during the COVID-19 crisis at a New York City hospital

```
Angela Gomez-Simmonds <sup>1</sup>, Medini K Annavajhala <sup>1</sup>, Thomas H McConville <sup>1</sup>, Donald E Dietz <sup>1</sup>, Sherif M Shoucri <sup>1</sup>, Justin C Laracy <sup>1</sup>, Felix D Rozenberg <sup>1</sup>, Brian Nelson <sup>1</sup>, William G Greendyke <sup>1</sup>, E Yoko Furuya <sup>1</sup>, Susan Whittier <sup>2</sup>, Anne-Catrin Uhlemann <sup>1</sup>
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Affiliations + expand

PMID: 33202023 PMCID: PMC7717307 DOI: 10.1093/jac/dkaa466

Free PMC article



Importance of antimicrobial stewardship

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Meta-Analysis > Clin Microbiol Infect. 2020 Dec;26(12):1622-1629.
doi: 10.1016/j.cmi.2020.07.016. Epub 2020 Jul 22.
```

Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis

```
Bradley J Langford <sup>1</sup>, Miranda So <sup>2</sup>, Sumit Raybardhan <sup>3</sup>, Valerie Leung <sup>4</sup>, Duncan Westwood <sup>5</sup>, Derek R MacFadden <sup>6</sup>, Jean-Paul R Soucy <sup>7</sup>, Nick Daneman <sup>8</sup>

Affiliations + expand

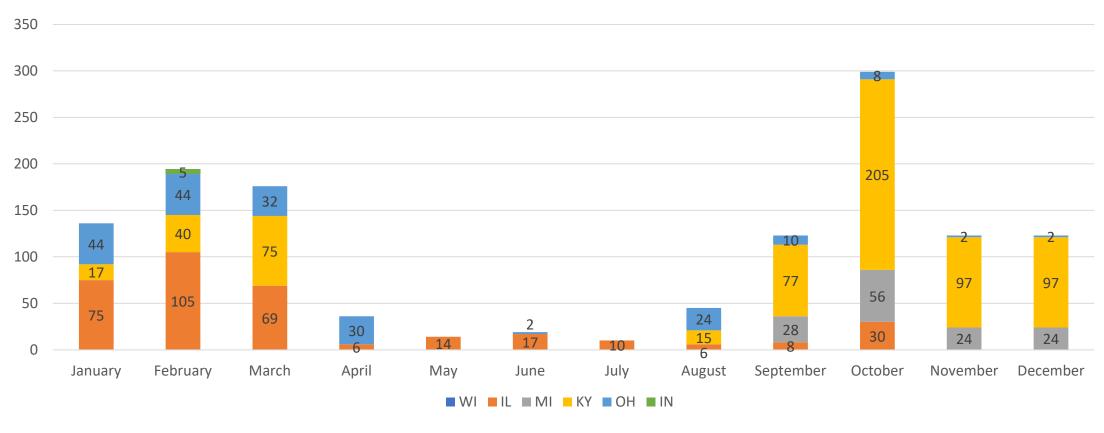
PMID: 32711058 PMCID: PMC7832079 DOI: 10.1016/j.cmi.2020.07.016

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2020 CRE colonization data

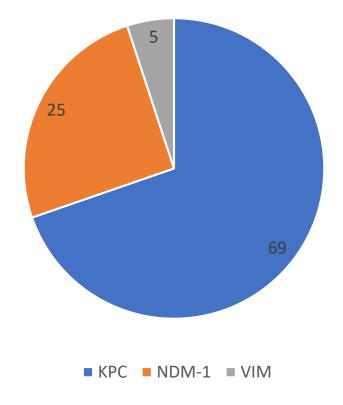
CRE colonization submissions





2020 CRE colonization data

Carbapenemase genes detected during colonization screens





COVID-19 and the impact on CRAB

Infection Prevention in Practice. 2021 Mar; 3(1): 100113.

Published online 2021 Jan 9. doi: 10.1016/j.infpip.2021.100113

An outbreak of carbapenem-resistant *Acinetobacter baumannii* in a COVID-19 dedicated hospital

<u>Tamar Gottesman</u>, a,b <u>Rina Fedorowsky</u>, a <u>Rebecca Yerushalmi</u>, <u>C Jonathan Lellouche</u>, d and <u>Amir Nutman</u>, and and <u>Amir Nutman</u>, and an and an analysis and an

PMCID: PMC7794049



COVID-19 and the impact on CRAB

> MMWR Morb Mortal Wkly Rep. 2020 Dec 4;69(48):1827-1831. doi: 10.15585/mmwr.mm6948e1.

Increase in Hospital-Acquired Carbapenem-Resistant Acinetobacter baumannii Infection and Colonization in an Acute Care Hospital During a Surge in COVID-19 Admissions - New Jersey, February-July 2020

Stephen Perez, Gabriel K Innes, Maroya Spalding Walters, Jason Mehr, Jessica Arias, Rebecca Greeley, Debra Chew

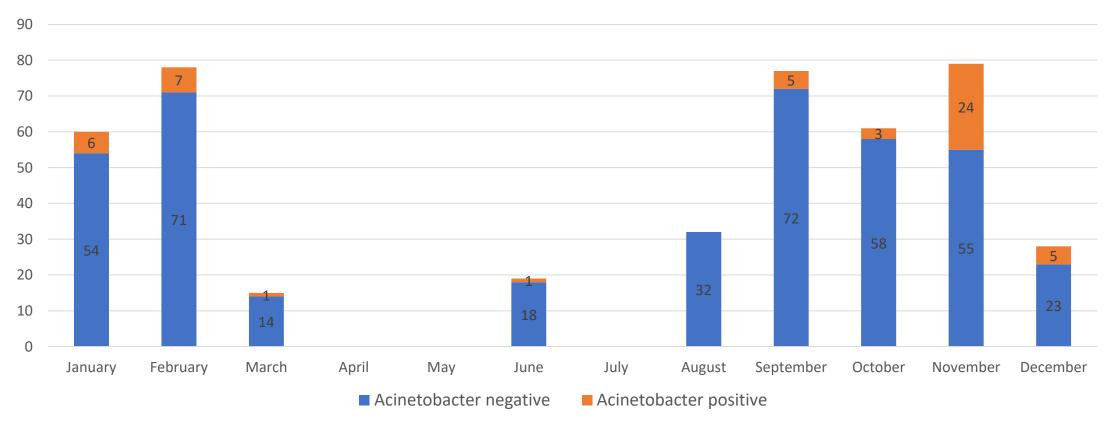
PMID: 33270611 PMCID: PMC7714028 DOI: 10.15585/mmwr.mm6948e1

Free PMC article



2020 CRAB colonization data

2020 CRAB colonization





The rise of *C. auris* during the COVID-19 pandemic

> J Glob Antimicrob Resist. 2020 Sep;22:175-176. doi: 10.1016/j.jgar.2020.06.003. Epub 2020 Jun 12.

The lurking scourge of multidrug resistant Candida auris in times of COVID-19 pandemic

Anuradha Chowdhary ¹, Amit Sharma ²

Affiliations + expand

PMID: 32535077 PMCID: PMC7289732 DOI: 10.1016/j.jgar.2020.06.003

Free PMC article



> Emerg Infect Dis. 2020 Nov;26(11):2694-2696. doi: 10.3201/eid2611.203504. Epub 2020 Aug 27.

Multidrug-Resistant Candida auris Infections in Critically Ill Coronavirus Disease Patients, India, April-July 2020

Anuradha Chowdhary, Bansidhar Tarai, Ashutosh Singh, Amit Sharma

PMID: 32852265 PMCID: PMC7588547 DOI: 10.3201/eid2611.203504

Free PMC article



> Clin Microbiol Infect. 2021 Jan 8;S1198-743X(20)30790-4. doi: 10.1016/j.cmi.2020.12.030. Online ahead of print.

Outbreak of Candida auris infection in a COVID-19 hospital in Mexico

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Hiram Villanueva-Lozano <sup>1</sup>, Rogelio de J Treviño-Rangel <sup>1</sup>, Gloria M González <sup>1</sup>,
María Teresa Ramírez-Elizondo <sup>2</sup>, Reynaldo Lara-Medrano <sup>3</sup>, Mary Cruz Aleman-Bocanegra <sup>3</sup>,
Claudia E Guajardo-Lara <sup>4</sup>, Natalia Gaona-Chávez <sup>3</sup>, Fernando Castilleja-Leal <sup>5</sup>,
Guillermo Torre-Amione <sup>5</sup>, Michel F Martínez-Reséndez <sup>6</sup>
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Affiliations + expand

PMID: 33429028 PMCID: PMC7835657 DOI: 10.1016/j.cmi.2020.12.030

Free PMC article



> MMWR Morb Mortal Wkly Rep. 2021 Jan 15;70(2):56-57. doi: 10.15585/mmwr.mm7002e3.

Candida auris Outbreak in a COVID-19 Specialty Care Unit - Florida, July-August 2020

Christopher Prestel, Erica Anderson, Kaitlin Forsberg, Meghan Lyman, Marie A de Perio, David Kuhar, Kendra Edwards, Maria Rivera, Alicia Shugart, Maroya Walters, Nychie Q Dotson

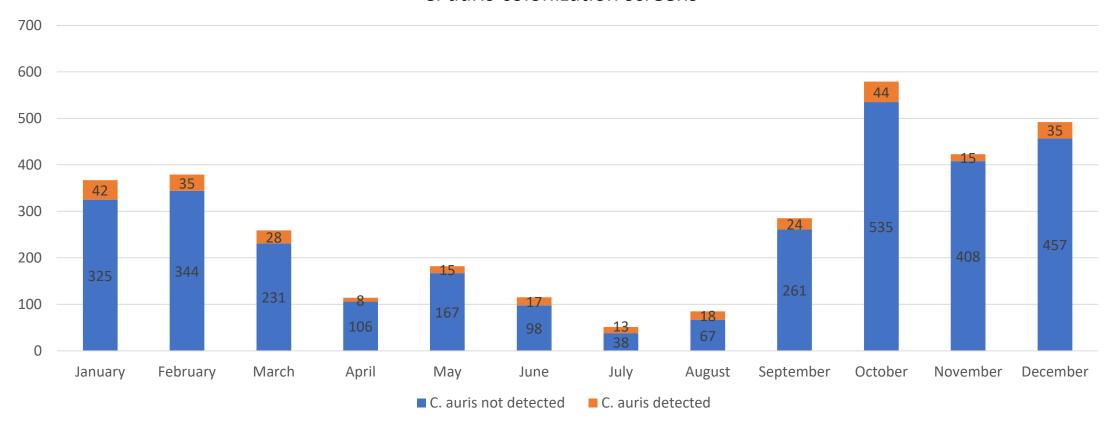
PMID: 33444298 PMCID: PMC7808709 DOI: 10.15585/mmwr.mm7002e3

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2020 Candida colonization data

C. auris colonization screens







CDPH Health Advisory:

Resurgence of *Candida auris* in Healthcare Facilities in the Setting of COVID-19

August 20, 2020

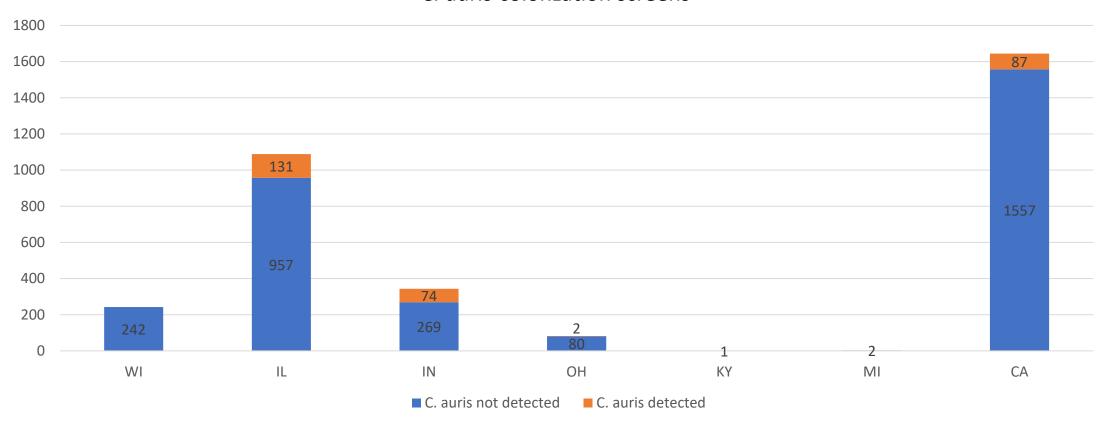
This message is intended for clinicians, infection preventionists, and laboratorians working in healthcare facilities. Please distribute as appropriate.

California Department of Public Health (CDPH) issued a health advisory on 8/19/20. The advisory, key messages, link to resources, and local health department reporting information can be found below.



2020 Candida colonization data

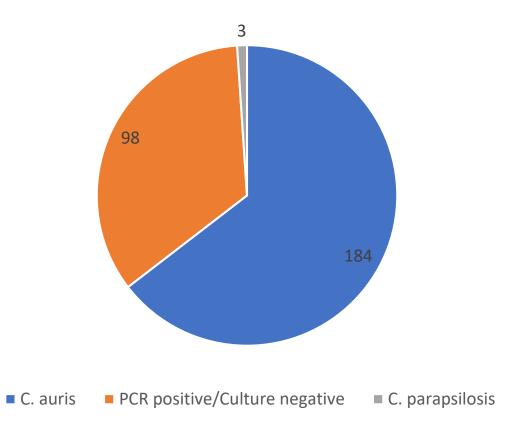
C. auris colonzation screens





2020 Candida colonization data

C. auris cultures from colonization





Ongoing AR activities

- GN7F AST panel validation
- WGS progress
- Other AR activities



GN7F AST panel validation

- GN7F panel will replace GNX2F AST panel
 - Key differences between the two panels

New drugs on the GN7F panel	Drugs not included in the GN7F panel
Ampicillin	Cefotaxime
Ampicillin-Sulbactam	Colistin
Cefazolin	Doxycycline
Ceftazidime-Avibactam	Polymixin B
Ceftolozane-Tazobactam	Ticarcillin/Clavulanic Acid
Ceftriaxone	
Nitrofurantoin	
Tetracycline	



Whole genome sequencing

- Isolates being sequenced
 - Pan-nonsusceptible
 - Novel carbapenemase (mCIM+/PCR-)
 - Non-KPC carbapenemase in Enterobacterales
 - Carbapenemase in *Pseudomonas*
 - Non-OXA carbapenemase in *Acinetobacter*
 - Carbapenemase detected during colonization (excludes KPC)



Other AR activities

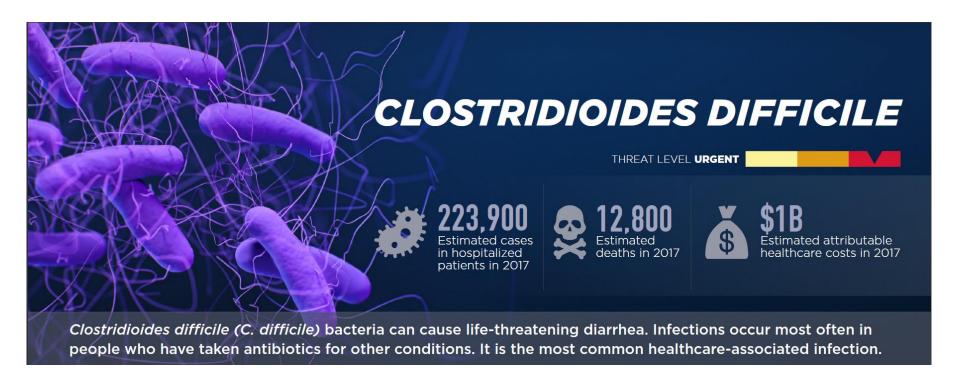
- Drug resistant Neisseria gonorrhoeae
 - Testing handled by Utah Public Health Laboratory, Tennessee State Public Health Laboratory, and Washington State Public Health Laboratories





Other AR activities

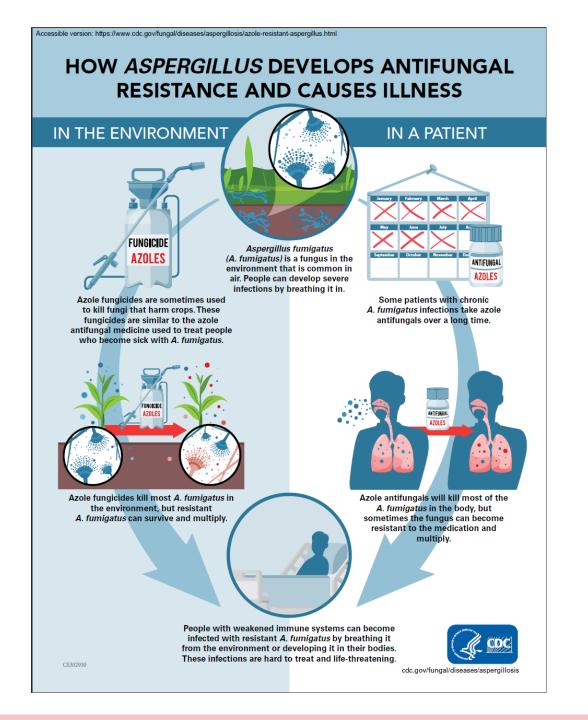
- Clostridioides difficile
 - Testing handled by Minnesota Department of Health Public Health Laboratory





Other AR activities

- Azole-resistant
 Aspergillus fumigatus
 - Now on the CDC AR Watch List
 - Testing by the Maryland Public Health Laboratory and the Tennessee State Public Health Laboratory



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