

# MONTHLY MDRO UPDATE #6

LOS ANGELES COUNTY DEPARTMENT OF PUBLIC HEALTH  
6/30/21

## HIGHLIGHTED IN THIS ISSUE

- Carbapenem-resistant *Acinetobacter baumannii* (pg.2)
- *Candida auris* update (pg. 7)

## SUMMARY

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is one of the most challenging organisms to manage from both clinical and public health perspectives. It is important to use appropriate tests to identify CRAB and communicate results to appropriate stakeholders when CRAB is found.

## KEY RESOURCES

[LA County NMDRO Home Page](#)

[LA County Reportable Disease List](#)

[CDC HAI Lab Resources Home Page](#)

[2019 CDC Urgent Threats Report](#)

Note: When calling 213-240-7941 to report MDROs (which is currently routed to a COVID-19 Call Center), please state that you are calling to report an MDRO to the Acute Communicable Disease Control Program.

## MESSAGE FOR CLINICAL LABORATORIES

In the last issue of our Newsletter, we indicated we would be branching out beyond discussing only *Candida auris*, to other multi-drug resistant organisms (MDROs) of concern. We will continue to provide an update on *C. auris* in Los Angeles County (LAC).

In this issue, we are providing some specific information about carbapenem-resistant *Acinetobacter baumannii* (CRAB). We want to again emphasize that the California Department of Public Health (CDPH) recently [reported](#) the isolation of carbapenemase-producing *A. baumannii* due to the presence of New Delhi metallo- $\beta$ -lactamase, NDM, a very unusual finding resulting in extensive drug resistance. We will provide lab-related information and share what we know about CRAB in LAC.

We welcome feedback on this Newsletter, previous Newsletters or any other issue related to MDROs (mail [hai@ph.lacounty.org](mailto:hai@ph.lacounty.org)).

Previous Newsletters can be found by clicking the links below:

Issue	Featured Content*
<a href="#">1 (link)</a>	<ul style="list-style-type: none"> <li>• Identifying and Reporting <i>C. auris</i></li> <li>• Resources for testing for <i>C. auris</i></li> </ul>
<a href="#">2 (link)</a>	<ul style="list-style-type: none"> <li>• Antifungal susceptibility testing of <i>C. auris</i></li> <li>• Validating MALDI-TOF for <i>C. auris</i></li> </ul>
<a href="#">3 (link)</a>	<ul style="list-style-type: none"> <li>• Case Study: A team approach to containing <i>C. auris</i></li> <li>• The Antibiotic Resistance Lab Network</li> </ul>
<a href="#">4 (link)</a>	<ul style="list-style-type: none"> <li>• Passive surveillance systems for <i>C. auris</i></li> <li>• Updated resources for testing for <i>C. auris</i></li> </ul>
<a href="#">5 (link)</a>	<ul style="list-style-type: none"> <li>• Multi-Drug Resistant Organisms</li> </ul>
<a href="#">6 (link)</a>	<ul style="list-style-type: none"> <li>• Carbapenem-resistant <i>A. baumannii</i> (CRAB)</li> <li>• NDM-CRAB outbreak in Northern California</li> </ul>

QUESTIONS? CONTACT THE LACDPH HEALTHCARE OUTREACH UNIT AT  
[HAI@PH.LACOUNTY.GOV](mailto:HAI@PH.LACOUNTY.GOV) OR 213-240-7941

## CARBAPENEM-R ACINETOBACTER BAUMANNII – AN URGENT THREAT

*Acinetobacter baumannii* are commonly found in the environment, including healthcare facilities (HCFs), and are highly transmissible. Infection or colonization with CRAB are most likely to affect individuals with weakened immune systems, chronic illnesses or other health issues as described [here](#). CRAB are typically resistant to multiple classes of antimicrobial agents, are difficult to treat, and pose a significant clinical and public health threat.

### DEFINITION OF CRAB

Resistant to imipenem, meropenem or doripenem using standard antimicrobial susceptibility testing (AST) methods and the following breakpoints:

Agent	Disk Content (µg)	Disk Diffusion (mm)			MIC (µg/ml)		
		Susc	Int	Res	Susc	Int	Res
Doripenem	10	≥18	15-17	≤14	≤2	4	≥8
Imipenem	10	≥22	19-21	≤18	≤2	4	≥8
Meropenem	10	≥18	15-17	≤14	≤2	4	≥8

Source: CLSI M100 31<sup>st</sup> edition.

### CARBAPENEM RESISTANCE MECHANISMS

- Carbapenemases (e.g., OXA, KPC, NDM)
- Non-carbapenemase due to changes in permeability and activation of efflux pumps

### CARBAPENEMASES AND *A. BAUMANNII* <sup>1,2,3</sup>

- The most common carbapenemases in *A. baumannii* are carbapenem-hydrolyzing class D beta-lactamases, specifically the OXA enzymes. However, other carbapenemases including KPC, NDM, VIM and IMP have also been reported in this species.
- OXA carbapenemases are very diverse. They are separated into groups and there can be many variants within each group. For example, the OXA-23 group, which is the most common group conferring carbapenem resistance in CRAB, contains 19 variants (e.g., OXA-23, OXA-27, OXA-49, etc). Groups may also be referred to as “like”, e.g., “OXA-23 like”.
- OXA-48 and its variants have been circulating in the *Enterobacterales* and have become a significant cause of carbapenem resistance, particularly in Europe and Southeast Asia. OXA-48 like can be found in CRAB but much less frequently.

**Note:** It is important to know which genes and gene variants are detected when using a commercial test for carbapenemases.

<sup>1</sup> Evans, BA and S.G.B. Amyes. 2014. Clin Microbiol Rev. 27:241. doi: [10.1128/CMR.00117-13](https://doi.org/10.1128/CMR.00117-13)

<sup>2</sup> Poirel, L, A Potron, P Nordmann. 2012. J Antimicrob Chemother. 67:1597. DOI: [10.1093/jac/dks121](https://doi.org/10.1093/jac/dks121)

<sup>3</sup> Ramirez, MS, RA Bonomi, ME Tolmasky. 2020. Biomolecules. 10:720. doi:10.3390/biom10050720

## TESTS FOR CARBAPENEMASES IN GRAM-NEGATIVE BACTERIA

Method	<i>Enterobacterales</i>	<i>Pseudomonas aeruginosa</i>	<i>Acinetobacter baumannii</i>
<b>Phenotypic (for isolates)</b>			
Modified Carbapenem Inactivation Method (mCIM) with or without EDTA Carbapenem Inactivation Method (eCIM)	yes <sup>1</sup>	yes (mCIM only)	no
CarbaNP <sup>2</sup>	yes	yes	no
BioMerieux Rapidec® Carba NP	yes	yes	yes
BD Phoenix™ CPO Detect	yes	yes	yes
<b>Genotypic</b>			
Cepheid Xpert® Carba-R for rectal swabs or isolates	KPC, NDM, VIM, IMP, OXA-48-like <sup>3</sup>	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like
Hardy NG-Test® CARBA 5 <sup>4</sup> for isolates	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like	Not approved
Biofire® FilmArray® BCID Panel for positive blood cultures	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like
GenMark® ePlex BCID for positive blood cultures	KPC, NDM, VIM, IMP, OXA (groups 23 & 48)	KPC, NDM, VIM, IMP, OXA (groups 23 & 48)	KPC, NDM, VIM, IMP, OXA (groups 23 & 48)
Luminex® VERIGENE gene detection for positive blood cultures <sup>5</sup>	KPC, NDM, VIM, IMP, OXA (groups 23, 40, 48 and 58)	KPC, NDM, VIM, IMP, OXA (groups 23, 40, 48 and 58)	KPC, NDM, VIM, IMP, OXA (groups 23, 40, 48 and 58)
Check-Points Check-Direct CPE for BD MAX™ for rectal swabs	KPC, NDM, VIM, OXA-48	-	-
Real Time PCR or Traditional PCR	unlimited	unlimited	unlimited

<sup>1</sup> Test appropriate for organism group

<sup>2</sup> Performs poorly for OXA-48

<sup>3</sup> Gene / gene variant targets

<sup>4</sup> Phenotypic immunological assay that detects specific antigens associated with the 5 main carbapenemases

<sup>5</sup> *Acinetobacter* target is *Acinetobacter* spp.

### Notes:

This list is not exhaustive nor an endorsement of specific products.

Modified Hodge Test (MHT) is no longer considered a reliable method for carbapenemase detection.

## WHERE DOES CRAB FIT ON THE PRIORITY LIST WITH OTHER MDRO?

**Urgent Threats**

These germs are public health threats that require urgent and aggressive action:

- CARBAPENEM-RESISTANT *ACINETOBACTER*
- CANDIDA AURIS*
- CLOSTRIDIROIDES DIFFICILE*
- CARBAPENEM-RESISTANT *ENTEROBACTERIACEAE*
- DRUG-RESISTANT *NEISSERIA GONORRHOEAE*

Identification and reporting of patients infected or colonized with CRAB should be approached with equal importance as identifying other “Urgent Threats” as described by CDC.

[Image Source \(link\)](#)

**QUESTIONS? CONTACT THE LACDPH HEALTHCARE OUTREACH UNIT AT [HAI@PH.LACOUNTY.GOV](mailto:HAI@PH.LACOUNTY.GOV) OR 213-240-7941**

## RECENT OUTBREAK OF NDM-CRAB IN NORTHERN CALIFORNIA

On May 20<sup>th</sup>, the California Department of Public Health (CDPH) released a CAHAN (California Health Alert Network) alerting HCFs to a multi-facility regional outbreak of CRAB that produces New Delhi metallo-beta-lactamase (NDM). See details [here](#). This is the first known appearance of NDM CRAB in the state.

### NDM CRAB OUTBREAK IN BRIEF

- **Dates:** May 2020- April 2021
- **Location:** At least 10 HCFs in Northern California
- **Extent:** 52 patients identified; 24 clinical isolates (variety of specimen types); 28 positive on colonization screening
- **Isolates** (see additional information below):
  - Most also harbored OXA-23 (79% of isolates)
  - Most not susceptible (I or R) to all antimicrobials (85% of isolates)
  - WGS demonstrated isolates are highly related

The fact that the outbreak strain has spread among multiple HCFs indicates its high transmissibility, which requires that healthcare facilities and laboratories coordinate activities to contain its spread.

### OUTBREAK STRAIN PHENOTYPE

There is no specific signal from the phenotype observed by CDPH that would suggest a carbapenem-resistant *A. baumannii* might produce NDM. The CRAB isolates with NDM from the outbreak tested to date by the Washington State Regional AR Lab Network laboratory generally displayed the susceptibility profile below.

Antimicrobial Agent	MIC (µg/ml)	Interpretation
Amikacin	>32	R
Cefepime	>16	R
Ceftazidime	>16	R
Cefotaxime	>32	R
Ciprofloxacin	>2	R
Colistin	≤0.25	Int
Doxycycline	>16	R
Gentamicin	>8	R
Imipenem	>8	R
Meropenem	>8	R
Minocycline	8	Int
Piperacillin-tazobactam	>128/4	R
Polymyxin	0.5	Int
Tigecycline	0.5	No BPs <sup>1</sup>
Tobramycin	>8	R
Trimethoprim-sulfamethoxazole	>4	R

S, susceptible; Int, intermediate; R, resistant | <sup>1</sup>no CLSI or FDA breakpoints

Other agents that might be requested for testing against CRAB as listed in the Sanford Guide to Antimicrobial Therapy, 2021 include:

Cefiderocol  
Eravacycline\*  
Omadacycline\*  
Plazomicin\*

\*no CLSI or FDA breakpoints for *Acinetobacter*

### Notes:

- Antimicrobial agents recommended for testing and reporting against *A. baumannii* can be found in CLSI M100 31<sup>st</sup> addition in Table 1A [here](#).
- Ampicillin-sulbactam is listed as a Group A agent in CLSI Table 1A. It was not tested against the NDM-producing strain but it would be highly unlikely for this agent to have activity against CRAB.
- Newer β-lactam combination agents including ceftazidime-avibactam, ceftolozane-tazobactam, imipenem-relebactam and meropenem-vaborbactam would not have activity against metallo-β-lactamase (e.g. NDM) producing isolates.

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## OUTBREAK STRAIN CARBAPENEMASE TESTING

No phenotypic testing was done and NDM and OXA-23 genes were detected using Cepheid Xpert® Carba-R and/or an in-house developed PCR assay at the Washington State Regional AR Lab Network laboratory.

## CRAB IN LA COUNTY

### LAC ANTIBIOGRAM

For the [cumulative 2017 antibiogram data](#) submitted from 75 hospitals, approximately 60% of nearly [1400 isolates of A. baumannii](#) were NOT susceptible to meropenem and/or imipenem. However, the rate varied widely among submitters.

### Carbapenem-R A. baumannii Testing in LAC (2018-2021)

No. A. baumannii Reports	OXA carbapenemase detected from:	
	Isolates <sup>1,2</sup>	Screening Swab <sup>2</sup>
69	54/64 (84%)	5/18 (28%)

<sup>1</sup> submitted as part of sentinel surveillance

<sup>2</sup> submitted as part of an outbreak investigation

### NATIONAL DATA ON CRAB

- CDC's [2019 Antibiotic Resistance Threats Report](#) indicates that CRAB caused an estimated 8,500 infections and 700 deaths in 2017 per [CDC's CRAB Fact Sheet](#).
- Between 2017 and 2019, just under 1% (40/4,427) of isolates tested by [ARLN](#) were positive for one or more high-profile carbapenemase genes (KPC, NMD, VIM, IMP, OXA-48).<sup>1</sup>
  - 70% (28/40) were positive for NDM. <sup>1</sup>
  - In 2019, ARLN began testing for other OXA groups, including OXA-23 and OXA-58.

<sup>1</sup> <https://arpsp.cdc.gov/profile/arln/cra>

## What can we do about containing CRAB in LA County?

**We are seeking clinical laboratories to serve as sentinel sites for CRAB.  
Can you please help? See "How can your laboratory become a sentinel site for submission of CRAB?"**

### WHAT IS LAC HEALTHCARE OUTREACH UNIT DOING?

The Healthcare Outreach Unit (HOU) has employed several strategies to detect and prevent the spread of CRAB in LAC, particularly any carbapenemase-positive (CP) CRAB, including the following:

- Generate County-level prevalence of CRAB vs other MDROs using the LAC antibiogram, to target interventions
- Made CP-A. baumannii a reportable condition as of 2019, to enhance surveillance and response activities
- Investigate reports of CP-CRAB, including screening of high-risk contacts when novel CP-CRAB are detected
- Support healthcare providers and laboratorians on how to detect and contain CRAB and CP-CRAB
- Educate providers on antimicrobial stewardship activities, to slow the onslaught of MDROs

### WHAT ARE LAC PUBLIC HEALTH LABORATORY AND THE AR LAB NETWORK DOING?

1. Collecting and analyzing<sup>1</sup> CRAB isolates and screening swabs related to outbreak investigations
2. Collecting and analyzing<sup>1</sup> CRAB isolates obtained from sentinel laboratories.
3. Informing stakeholders about the CRAB situation in LAC

<sup>1</sup> Analysis includes testing for carbapenemases and incorporates whole genome sequencing, when indicated.

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## WHAT SHOULD CLINICAL LABORATORIES DO?

1. Consider performing AST on all *A. baumannii* isolates, especially from high-risk patients (see #2 below), even when isolated from a culture that suggests colonization. For example, performing AST on a few colonies of *A. baumannii* from a mixed sputum or wound culture. This can aid in putting patients on proper isolation.
2. Perform carbapenemase testing using an appropriate phenotypic or genotypic method on CRAB isolates from high-risk patients that are NOT susceptible (I or R) to all drugs on your panel. High-risk patients are defined as:
  - Recent admission from any long-term acute care hospital (LTACH) or ventilator-equipped SNF (vSNF)
  - Recent international healthcare exposure
  - High-risk contact of a CP-CRAB case
    - i. High-risk contacts include: Roommates (including patients in adjacent rooms that share a bathroom), discharges from facilities with ongoing transmission, patients who share medical equipment or primary healthcare personnel (eg nursing assistants)

**Note:** If you do not perform carbapenemase testing for CRAB, the LAC Public Health Laboratory may be able to provide carbapenemase testing for select isolates. Please email [hai@ph.lacounty.gov](mailto:hai@ph.lacounty.gov) to confirm isolate meets criteria before sending to the lab.

3. Communicate results of CRAB isolates, especially CP-CRAB, to Infection Preventionists as quickly as possible.
4. Maintain ability to test agents beyond those on your routine test panel (in house or refer out), when requested.
5. Report certain CRAB results to LAC Public Health (see instructions in box below).

## HOW CAN YOUR LABORATORY BECOME A SENTINEL SITE FOR SUBMISSION OF CRAB?

1. Your lab submits:
  - An agreed upon number of CRAB isolates accompanied with a completed form as shown [here](#). Submissions can be scheduled when convenient.
2. AR Lab Network ([ARLN](#)) provides (**free** of charge):
  - Slants and packaging/shipping materials
3. Benefits to your facility for your participation:
  - Confirmation of your bacterial identification and antimicrobial susceptibility testing results
  - Results for carbapenemase gene, if carbapenemase AR mechanism present
  - Possible early warning of unique carbapenemase genes in your facility and in LAC

Please contact us at [hai@ph.lacounty.gov](mailto:hai@ph.lacounty.gov) if interested. We would be most appreciative of your assistance!

### Please remember:

- Clinical laboratories that serve LAC HCFs must report the following to LAC DPH within 1 working day as instructed [here](#):
  - Confirmed carbapenemase-producing *Acinetobacter* spp.
  - Suspect pan-resistant CRAB (R to all drugs on your routine test panel)
- As with other MDRO, notify your infection preventionists of CRAB in a timely manner so they can initiate appropriate infection control precautions as described here ([link](#))

LACDPH recently released a [REDCap MDRO Reporting Portal](#) where providers and laboratories may submit reports. Please note that submission of a report through the REDCap portal is sufficient to satisfy reporting requirements, however, electronic lab reporting (ELR) remains the preferred method. It is **not** a required additional form of reporting, but an alternative to faxing results when ELR is not yet set up.

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# CANDIDA AURIS UPDATE

## C AURIS BY THE NUMBERS

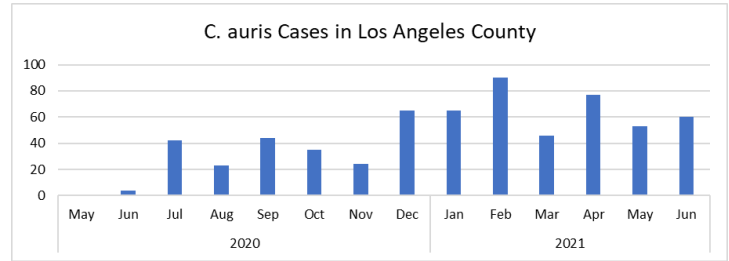
HCF Type	Screening*	S-t-C <sup>^</sup>	Clinical <sup>†</sup>	Total
LTACH	442	59	24	525
SNF	40	6	0	46
GACH	33	8	16	57
Other	1	0	0	1
Total	516	73	40	629

Note that all cases are counted by facility type at time of first positive specimen collection.

Swab collected for the purpose of screening for *C. auris* colonization.

† Screening-to-clinical: cases who were first identified via screening swab and later had one or more positive clinical specimen(s).

^ Specimen collected for clinical purposes.



## CANDIDA AURIS LAB LIST UPDATE

Reference Lab	Screening Method*	Test (Order Code)	Contact
ARUP	Fungal Culture	<ul style="list-style-type: none"> <li>Fungal culture, yeast (0060149)</li> <li>Yeast ID - MALDI Bruker; sequencing if no ID (0060163)</li> </ul>	<a href="http://www.aruplab.com">www.aruplab.com</a> 1-800-522-2787
Genetic Technological Innovations	PCR	<ul style="list-style-type: none"> <li><i>Candida auris</i> surveillance (RT-PCR) (87481)</li> </ul>	<a href="http://www.gtilaboratories.com">www.gtilaboratories.com</a>
LabCorp	Fungal Culture	<ul style="list-style-type: none"> <li>Fungal culture, yeast (182776)</li> <li>Yeast ID – MALDI Vitek MS; sequencing if no ID (182212)</li> </ul>	<a href="http://www.labcorp.com">www.labcorp.com</a>
Mayo	PCR	<ul style="list-style-type: none"> <li><i>Candida auris</i> surveillance (PCR) (CAURS 607883)</li> <li>Yeast ID – MALDI Bruker; sequencing if no ID (FUNID 8223)</li> </ul>	<a href="http://www.mayocliniclabs.com">www.mayocliniclabs.com</a> 800-533-1710
Premier Lab Solutions	PCR	<ul style="list-style-type: none"> <li><i>Candida auris</i> surveillance (PCR) (6146)</li> </ul>	<a href="http://www.premierlabsolutions.com">www.premierlabsolutions.com</a> 602-441-2808
Quest	Fungal Culture	<ul style="list-style-type: none"> <li>Fungal culture, yeast (20541)</li> <li>Yeast ID - MALDI Vitek MS or Bruker; sequencing if no ID (39507)</li> </ul>	<a href="http://www.questdiagnostics.com">www.questdiagnostics.com</a> 866-697-8378
Soft Cell Labs, Inc.	NAAT, qPCR	<ul style="list-style-type: none"> <li><i>Candida auris</i> RT-PCR 15002</li> </ul>	POC: Lisa Justesen ( <a href="mailto:lisa@softcellbio.com">lisa@softcellbio.com</a> ) 435-628-2215 ; <a href="http://www.softcelllabs.com">www.softcelllabs.com</a>

\*for fungal culture, indicate "Rule out *Candida auris*" | Please note that this list is not an endorsement from LACDPH, and the information provided here is self-reported. We encourage HCFs to utilize these resources when on-site testing is not possible.

## WEBINAR ANNOUNCEMENT

### ***Candida auris* – Testing Methods and Resources for Clinical Laboratories**

**July 14, 2021 11:00 AM PST**

This webinar will discuss the importance of timely detection of *C. auris* and provide examples of successful testing implementation in clinical settings. Speakers will also provide information on resources laboratories can utilize when testing for *C. auris*. Registration is free.

Please see details & registration information here: [https://aphl.zoom.us/webinar/register/WN\\_7dE1Z15ITbqmLv1QBkrg8w](https://aphl.zoom.us/webinar/register/WN_7dE1Z15ITbqmLv1QBkrg8w)

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