QUARTERLY MDRO UPDATE #11

LOS ANGELES COUNTY DEPARTMENT OF PUBLIC HEALTH

12/5/22

HIGHLIGHTED IN THIS ISSUE

MDRO of greatest concern in LAC today

SUMMARY

Vigilance in detection and containment of antimicrobial resistance is essential. LACDPH continues to work closely with healthcare partners to meet current AR challenges. Communication of the most up to date developments is key to successfully meeting these challenges.

KEY RESOURCES

LA County Antibiogram Home Page

LA County N-MDRO Home Page

LA County Reportable Disease List

CDC MDR Data

CDC Urgent AR Threats Report (2019)

CDC HAI Lab Resources Home Page

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 (ACDC) Program.

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

MESSAGE FOR CLINICAL LABORATORIES

The following topics that are currently of note in LAC will be addressed:

1. VIM-producing carbapenem-resistant *Pseudomonas aeruginosa* (VIM-CRPA)
2. *Candida auris* – emerging resistance
    a. Amphotericin B resistance
    b. Echinocandin resistance
3. NDM-producing carbapenem-resistant *Acinetobacter baumannii* (NDM-CRAB)
4. New "resources" for LAC partners
    a. Fall 2022 carbapenemase-producing organism (CPO) webinars and CPO Primer
    b. Antibiogram Dashboard

PREVIOUS NEWSLETTERS

Issue	Featured Content
1 (link)	• Identifying and reporting *C. auris* • Resources for testing for *C. auris*
2 (link)	• Antifungal susceptibility testing of *C. auris* • Validating MALDI-TOF for *C. auris*
3 (link)	• Case Study: A team approach to containing *C. auris* • The Antibiotic Resistance Lab Network
4 (link)	• Passive surveillance systems for *C. auris* • Updated resources for testing for *C. auris*
5 (link)	• Multi-Drug Resistant Organisms (MDRO)
6 (link)	• Carbapenem-resistant *Acinetobacter baumannii* (CRAB) • NDM-CRAB outbreak in Northern California • Testing methods for carbapenemases
7 (link)	• *C. auris* update
8 (link)	• Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)
9 (link)	• Carbapenem-resistant organisms (CRO)
10 (link)	• LAC Multifacility Antibiogram

VIM-PRODUCING PSEUDOMONAS AERUGINOSA (VIM-CRPA)

Carbapenem-resistant *P. aeruginosa* were previously described in LAC MDRO Newsletter # 8.

When reviewing the former publication, please pay particular attention to Table 2 where results from a recent CDC study demonstrated that there should be a high suspicion for carbapenemases in CRPA isolates that are not susceptible to ceftazidime and/or cefepime and a very high suspicion for CRPA that are not susceptible to ceftolozane-tazobactam. These isolates should be targeted for carbapenemase testing and infection control interventions.

From 2017 to date, there have been 38 reports of VIM-CRPA in LAC. Many of these have been in patients following hospitalization or invasive medical procedures in Mexico for routine healthcare visits, medical emergencies, and medical tourism as reported here.

Most recently, 4 cases of VIM-CRPA were identified in LAC which appear to be part of a nation-wide outbreak involving 32 case-patients in 6 jurisdictions (CA, CT, NM, NY, UT, WA) since May 2022. Specifically, isolates in this cluster are sequence type (ST)1203 and harbor both bla_{VIM-80} and bla_{GES-9} carbapenemase genes, making this a unique combination not previously identified in the US. Isolates were from a variety of sources and included diagnostic and surveillance specimens. The cause of this multi-state outbreak is currently under investigation. In LAC, transmission occurred in an outpatient setting which has since been controlled.

Per a recent CAHAN, LACDPH requests that laboratories identifying VIM-CRPA in any specimen collected on or after January 1, 2022 submit available isolates to the LAC Public Health Laboratories (PHL) for further characterization. In addition, laboratories prospectively identifying CRPA not susceptible to cefepime, ceftazidime, and/or ceftolozane-tazobactam should consider performing or accessing carbapenem resistance mechanism testing for these isolates. Testing at LAC PHL is available if clinical laboratories are unable to perform this testing. A susceptibility profile of the outbreak strain is shown in Table 1.

Please do not submit CRPA isolates to LAC PHL without first emailing the Healthcare Outreach Unit at hai@ph.lacounty.gov; our team will confirm if suspect or confirmed VIM-CRPA isolates need to be submitted and provide relevant instructions as needed.

Key facts to help identify carbapenemase-producing (including VIM) *P. aeruginosa* in the laboratory:

1. The antimicrobial susceptibility profile associated with the VIM-*P. aeruginosa* recent outbreak is shown in Table 1. However, many CRPA without VIM can have a similar profile.
2. Approximately 15% of *P. aeruginosa* in LAC are carbapenem resistant. As with most CRPA reported worldwide, they are resistant by a mechanism other than carbapenemase production. See the LAC antibiogram

Carbapenemase production is only found in approximately 5% of CRPA.

3. VIM-*P. aeruginosa* can be detected with most molecular tests for carbapenemases. Please see the new Carbapenemase Primer that includes information about tests available for detection of carbapenemases.
4. As mentioned above, non-susceptible results for cefepime, ceftazidime and especially ceftolozane-tazobactam are signals that a CRPA isolate may produce carbapenemase.

Table 1. Sample VIM-CRPA AST Profile from LAC Clinical Laboratory

Antimicrobial Agent	MIC (µg/mL)	Interpretation
Amikacin	>64	R
Cefepime	>32	R
Cefiderocol	ND	S
Ceftazidime	>32	R
Ceftazidime-avibactam	>32/4	R

Ceftolozane-tazobactam	>32/4	R
Ciprofloxacin	>4	R
Colistin	1	Int
Gentamicin	>16	R
Imipenem	8	R
Meropenem	8	R
Piperacillin-tazobactam	64/4	Int
Tobramycin	>16	R

S, susceptible; Int, intermediate; R, resistant

LAC Laboratory Reporting Requirements for CRPA

Only confirmed carbapenemase-producing *P. aeruginosa* is lab-reportable (phenotypic or genotypic test). If carbapenemase negative or not done, do not report. See reportable conditions by labs in LAC

See LACDPH MDRO Reporting Guidance for more information.

NDM-PRODUCING ACINETOBACTER BAUMANNII (NDM-CRAB)

Carbapenem-resistant *A. baumannii* was previously described in LAC MDRO Newsletter # 6.

In May 2021, CDPH informed healthcare facilities of an NDM-CRAB outbreak that was first noted in May 2020. Facilities reporting NDM-CRAB were primarily from Northern California and 52 patients were confirmed to be colonized and/or infected with NDM-CRAB.

As of November 2022, CDPH confirmed that the last outbreak connected among Northern California facilities had closed. A total of 227 patients were confirmed to be colonized and/or infected with NDM-CRAB as of August 24, 2022.

Key facts to help identify NDM-*A. baumannii* in the laboratory:

1. The AST profile associated with the NDM-*A. baumannii* outbreak is shown in Table 2. However, many CRAB without NDM can have a similar profile.
2. Approximately 60% of *A. baumannii* in LAC are carbapenem resistant. As with most CRAB reported worldwide, approximately 90% of them likely produce a carbapenemase such as OXA-23 or -24, which is not detected with most commercial carbapenemase tests. See the LAC antibiogram
3. NDM-*A. baumannii* can be detected with some molecular tests for carbapenemases. Please see the new Carbapenemase Primer that includes information about tests available for detection of carbapenemases.

Table 2. AST Profile Associated with Recent NDM-CRAB Outbreak

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
Tigecycline	0.5	No BPs [1]
Tobramycin	>8	R
Trimethoprim-sulfamethoxazole	>4	R

S, susceptible; Int, intermediate; R, resistant

[1] no CLSI or FDA breakpoints

LAC Laboratory Reporting Requirements for CRAB

Only confirmed carbapenemase-producing *A. baumannii* is lab-reportable (phenotypic or genotypic test). If carbapenemase negative or not done, do not report. See reportable conditions by labs in LAC

See LACDPH MDRO Reporting Guidance for more information.

EMERGING RESISTANCE IN *CANDIDA AURIS* FROM LAC

The February 2021 issue of this Newsletter included a report indicating that all 38 *C. auris* clinical isolates from LAC tested for susceptibility to date through the Antimicrobial Resistance Laboratory Network (AR Lab Network) had the same profile as shown in Table 3 (Profile #1). Now after review of data from testing nearly 100 isolates in LAC, most continue to display this profile- however, some show increasing resistance (Profiles #2-5). These have been recently isolated from both infected and colonized patients in a small number of healthcare facilities. At this time, it is believed that resistance may have developed in response to antifungal therapy.

Table 3. Antifungal Susceptibility Profiles of *C. auris* from LAC

Antifungal	Drug Class	Profile #1	Profile #2	Profile #3	Profile #4	Profile #5
Amphotericin	Polyene	0.5 S [1]	8 R	0.5 S	8 R	16 R
Fluconazole [2]	Azole	256 R	256 R	256 R	256 R	128 R
Anidulafungin	Echinocandin	0.25 S	2 S	4 R	2 S	0.03 S
Caspofungin		0.06 S	4 R	2 R	1 S	0.03 S
Micafungin		0.12 S	4 R	4 R	2 S	0.03 S

[1] MIC, µg/ml (modal value); interpretation based on CDC's tentative *C. auris* breakpoints here

[2] Fluconazole susceptibility can be considered a surrogate for second generation triazole (voriconazole, posaconazole, isavuconazole, and itraconazole) susceptibility assessment. However, isolates that are resistant to fluconazole may respond to other triazoles occasionally.

Susceptibility profiles of *C. auris* can vary widely. According to CDC, in the United States, about 90% of *C. auris* isolates have been resistant to fluconazole, about 30% have been resistant to amphotericin B, and less than 5% have been resistant to echinocandins[1]. *C. auris* can develop resistance during therapy and laboratories are encouraged to perform antifungal susceptibility testing (AFST) on repeat isolates from individual patients.

[1] Jacobs SE et al. 2022. *Candida auris* Pan-Drug-Resistant to Four Classes of Antifungal Agents. Antimicrob Agents Chemother. 10.1128/aac.00053-22

Case: To illustrate a recent case in LAC, *C. auris* was isolated from an 86-year-old female with numerous underlying conditions including chronic respiratory failure and congestive heart failure. Patient was hospitalized in a long-term care facility for 6 months prior to testing positive for *C. auris* in a urine specimen on 6/1/2022. Antifungal susceptibility testing was not done at the time. Patient was initially treated with anidulafungin, then switched to micafungin on and off for several months. On 10/3/2022 another urine isolate grew *C. auris*, now displaying resistance profile #2. Because this isolate was resistant to at least one drug in each of the main drug classes shown in Table 3, it is considered pan-resistant[2]. Patients harboring *C. auris* isolates that are resistant to several drug classes should not be cohorted with patients harboring more susceptible isolates.

Requirements for Laboratory Reporting of *C. auris* and Submitting *C. auris* Isolates in LAC

Complete details for reporting *C. auris* can be found here and a summary of required reporting is presented in Table 4.

Table 4. Required Reporting of *C. auris* for All Healthcare Facilities

Organism	Criteria	Who Reports
C. auris positive	*C. auris* identified from any body site (final results only). Include AFST, if done.	Laboratory & Provider
C. auris positive from sterile sites	*C. auris* isolates identified from sterile sites should be submitted to LAC PHL within 10 days of specimen collection date per CDPH Title 17 requirement	Laboratory
Outbreak of *C. auris*, suspected or confirmed	Per CDPH AFL-19-18, the occurrence of cases above the expected or baseline level. This includes the identification of new positives upon screening of epi-linked contacts.	Provider

In accordance with the updated Title 17 C. auris reporting requirements, please send all *C. auris* isolates isolated from sterile sites to LAC PHL. Please email us at hai@ph.lacounty.gov to let us know that an isolate will be sent so that we can notify PHL.

Status of *C. auris* in LAC

Candida auris continues to pose a threat to persons residing in LA County healthcare facilities. LACDPH recommends that clinical labs increase detection of *C. auris* within LAC to control its spread via two key actions:

- *C. auris* admission screening
- Identifying *Candida* spp. to the species level for non-sterile sites

If conducting these actions is not possible for all patients/residents, LACDPH advises laboratories work with clinical/IP staff to find high-risk patients on which to focus this testing. High risk patients for *C. auris* include:

- Persons being admitted from any long-term acute care hospital (LTACH) (per 3/18/21 CAHAN) or any subacute unit of a skilled nursing facility (aka ventilator-capable SNFS (vSNFs))
- High-risk contacts of new *C. auris* cases (i.e., roommates) -use CDPH Screening Decision Tree
- Persons on a mechanical ventilator or with presence of tracheostomy
- Persons who are colonized with MDROs, especially rare carbapenemase-producing organisms
- Persons who have had a recent overnight stay in a healthcare facility outside of the US

[2] Jacobs SE et al. 2022. *Candida auris* Pan-Drug-Resistant to Four Classes of Antifungal Agents. Antimicrob Agents Chemother. 10.1128/aac.00053-22

If your laboratory cannot conduct *C. auris* testing on-site, refer to the LACDPH List of Laboratories with *C. auris* Testing Capacity to find a reference lab that provides this service. Note that the LAC Public Health Laboratories (PHL) can only conduct rule-out *C. auris* testing at this time for confirmed or presumptive *C. auris* isolates. **Please do not send any *C. auris* isolates nor swabs to LAC PHL without contacting the HOU first.** You may either call us at 213-240-7941 or email us at hai@ph.lacounty.gov.

***C. auris* by the numbers (Updated 11/01/22)**

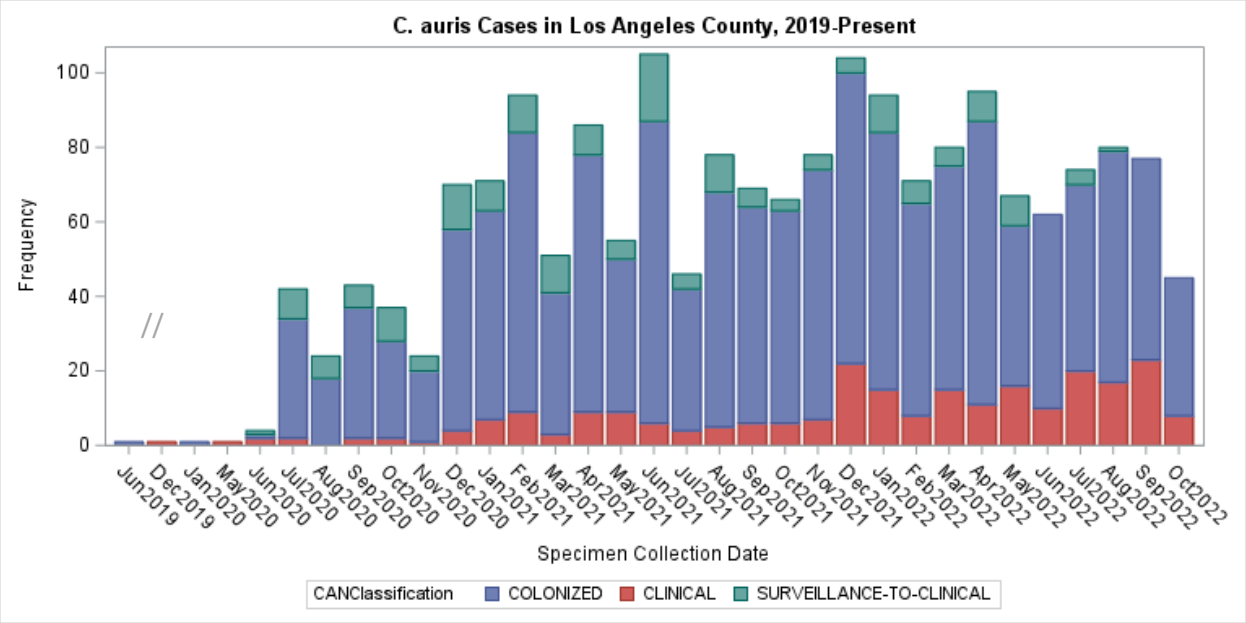
To date, 146 bloodstream infections have been reported in LA County (7.8% of total LAC *C. auris* cases).

Table 5. *C. auris* Cases in Los Angeles County by Facility and Case Type, 2019-2022 (n=1865)

HCF Type	Clinical^	Surveillance-to-clinical†	Surveillance*	Total
General Acute Care Hospital (GACH)	157	21	137	315
Long Term Acute Care Hospital (LTACH)	78	148	1243	1469
Skilled Nursing Facility (SNF)	2	7	66	75
Other	0	0	6	6
Total	**237**	**176**	**1452**	**1865**

Note that all cases are counted by facility type and case type at time of first positive specimen collection.
** Swab collected for the purpose of screening for C. auris colonization.*
^ Specimen collected for clinical purposes.
† Cases who were first identified via screening swab and later had one or more positive clinical specimen(s).

Figure 1. *C. auris* Cases in Los Angeles County by Month, June 2019-October 2022 (n=1865)



See footnotes from *Table 5* above.

NEW RESOURCES FOR LAC PARTNERS

CPO Webinar Series

Together with the California Department of Public Health (CDPH), LAC is hosting a series of (free) webinars that focus on CPO. Two have been completed and are available on demand and accessible here.

- Carbapenemase-producing Organisms: Guidance for Reporting and Containment. (September 29, 2022)
- Testing for Carbapenemase Production Among Carbapenem-Resistant Organisms: When and How? (October 27, 2022)
- The Role of Carbapenemase Testing in Clinical Practice, December 6, 2022

A companion document for the October webinar entitled "**Carbapenemase Testing for Carbapenem-Resistant Organisms (CRO); A Primer for Clinical and Public Health Laboratories"** has been developed to assist clinical laboratories enhance their understanding of carbapenemase testing and testing and reporting options available. Highlights from this include tables that list:

- CLSI and FDA-cleared tests available for carbapenemase testing
- Features of various carbapenemase tests
- Current CLSI and FDA-recognized carbapenem breakpoints
- Potential activities of newer agents for bacteria producing common carbapenemases
- Strategies for testing isolated colonies for carbapenemase production and/or carbapenemase genes and results reporting including optional report comments
- CRO Examples

Antibiogram Dashboard

LAC appreciates the efforts of healthcare facilities throughout LAC for continuing to submit their facility's antibiogram data on annual basis. The most recent LAC multifacility antibiogram that was developed from these data was highlighted in MDRO Newsletter #10.

LAC recently added an Antibiogram Dashboard feature that enables users to search the 2018, 2019 or 2020 multifacility antibiogram databases by year, organism, antimicrobial agent, facility type, and region. For example, the dashboard was used to extract data for *P. aeruginosa* as shown below. Approximately 3000 isolates were tested with each agent and %S for cefepime and ceftazidime was similar at 82% and 79%, respectively. For both, these %S rates were lower than those in 2019.

Search criteria: 2020; *P. aeruginosa*; cephalosporins; all facility types; Antelope and San Fernando Valleys

Change in %S from 2019

Antimicrobial Agent	Organism	Region	Isolates Tested[3]	Hospitals Reported	Susceptibility (%)[2] (IQR)	Change in Susceptibility (%)[5]
Cefepime	Pseudomonas aeruginosa	Antelope and San Fernando Valleys	2,685	14	82% (73%, 85%)	▼ -5%
Ceftazidime	Pseudomonas aeruginosa	Antelope and San Fernando Valleys	3,036	15	79% (72%, 83%)	▼ -2%