QUARTERLY MDRO UPDATE #12

LOS ANGELES COUNTY DEPARTMENT OF PUBLIC HEALTH

5/5/23

HIGHLIGHTED IN THIS ISSUE

Carbapenemase producing organisms including a CP-CRPA case study

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.

MESSAGE FOR CLINICAL LABORATORIES

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

1. Reporting carbapenem-resistant organisms in LAC
2. Surveillance vs diagnostic testing for MDRO
3. Case Study – Carbapenem-resistant *Pseudomonas aeruginosa*
4. Update on *C. auris* in LA County

LAC DPH is adding a new feature, **case studies**, to our quarterly MDRO News Update for Clinical Laboratories. The cases are intended to:

- Highlight results that are likely to have a more significant impact on patient management, infection prevention and/or public health response than the typical pan-susceptible *E. coli*
- Provide suggestions to help laboratories identify protocols that are appropriate for detecting and reporting MDRO to providers and to public health.

A brief commentary as to "Why this Case" will be presented at the beginning of each discussion. Previous editions of LAC MDRO News Updates have covered some topics that will be included in these cases. Links to those will be added, as appropriate.

Acronyms often used related to carbapenem-resistant organisms:

- **CRO**, carbapenem-resistant organism
- **CPO**, carbapenemase-producing organism
- **CRAB**, carbapenem-resistant *Acinetobacter baumannii*
- **CP-CRAB or CPAB**, carbapenemase-producing *Acinetobacter baumannii*
- **CRE**, carbapenem-resistant Enterobacterales
- **CP-CRE or CPE**, carbapenemase-producing Enterobacterales
- **CRPA**, carbapenem-resistant *P. aeruginosa*
- **CP-CRPA,** carbapenemase-producing *P. aeruginosa*

REQUIRED REPORTING AND VOLUNTARY SUBMISSION OF CPO ISOLATES TO LACDPH BY CLINICAL LABORATORIES

As a reminder, the following organisms are laboratory-reportable conditions in LA County.

Required Reporting http://publichealth.lacounty.gov/acd/docs/LabList.pdf

Report the following within 1 working day:

- Confirmed carbapenemase-producing Enterobacterales,
- Confirmed carbapenemase-producing *Pseudomonas aeruginosa*,
- Confirmed carbapenemase-producing *Acinetobacter* spp.

NOTE: A carbapenemase test MUST be performed before reporting a carbapenem-resistant isolate as a carbapenemase producer.

- Suspect pan-resistant gram-negative organisms (resistant to all drugs on your routine test panel)

Voluntary submission of select isolates [see Table 1 for carbapenem-resistant organisms (CRO)]:

- Carbapenem-resistant Enterobacterales,
- Carbapenem-resistant *Pseudomonas aeruginosa*,
- Carbapenem-resistant *Acinetobacter* spp.

Note: CRO are not reportable unless a carbapenemase test is positive.

- *Candida* species (not albicans)

Thank you for considering this volunteer opportunity! Contact hai@ph.lacounty.gov for additional information.

As a reminder, please do not send isolates to a public health laboratory without emailing the Healthcare Outreach Unit (HOU) at hai@ph.lacounty.gov

Table 1. Selection Criteria for Voluntary Submission of CRO

Organism Group	Carbapenem Results	Other Susceptibility Criteria That Must be Met
Enterobacterales	"R" to doripenem, ertapenem, imipenem, and/or meropenem	Exclude: • *Serratia* spp. "S" to ceftriaxone, cefotaxime and/or ceftazidime. This profile likely indicates an bla_{SME} gene, not novel resistance. • *Enterobacter* spp. "I" or "R" to cefotaxime, ceftriaxone, and/or ceftazidime but "S" to cefepime. This profile is consistent with false positive mCIM+ results, likely because of high levels of AmpC beta-lactamase(s).
Pseudomonas aeruginosa	"R" to doripenem, imipenem, and/or meropenem	"Not susceptible ("I" or "R") to ceftazidime, cefepime and/or ceftolozane-tazobactam
Acinetobacter spp.	"R" to doripenem, imipenem, and/or meropenem	None at this time

I, intermediate; S, susceptible; R, resistant

SURVEILLANCE VERSUS DIAGNOSTIC TESTING FOR MDRO

It is important to understand how best to approach surveillance or screening testing to help control the spread of MDRO. Here we briefly review surveillance for MDRO and provide some reminders about surveillance testing.

Definitions:

- **Diagnostic tests** – intended to determine the etiologic agent of infection in symptomatic individuals
- **Surveillance or screening tests** – intended to determine if an asymptomatic individual harbors (is colonized with) an etiologic agent that could lead to infection of the individual or transmission of the agent to another individual
- **Active surveillance** is generally performed to find colonized cases as part of confirmed or suspect outbreak investigations and is much more time- and resource-intensive than passive surveillance. For example, an active surveillance plan might include conducting point prevalence surveys of patients on a unit. Point prevalence surveys involve screening many patients for the suspect microorganism at a single point in time.
- **Passive surveillance** is the regular reporting of diseases and conditions to public health to determine local disease epidemiology. Public health relies on clinical laboratories and healthcare providers (including clinicians and infection preventionists) to detect and report cases in a timely manner, usually as identified from diagnostic tests. Epidemiologists and infection preventionists regularly use laboratory data to identify potential disease clusters that prompt investigations to prevent further spread of disease. When a laboratory enhances identification of organisms in diagnostic cultures, they will likely increase detection of organisms of public health significance, like MDRO.

Table 2. Important Points to Consider when Performing Active Surveillance for MDRO

Criteria	Consideration

Patient selection	• Patient may or may not have signs/symptoms of an active infection
	• Patient at high risk for acquisition of MDRO, such as:
	  • Close contact with an individual who was known to be infected or colonized with MDRO
	  • Persons admitted from long-term acute care hospitals (LTACHs) or subacute units (SAU)
	  • Persons with recent international healthcare exposure

Specimen source	Varies depending on MDRO of interest and body site **most likely** to be colonized. For example: • *Candida auris* – skin (axilla/groin) • *CRO/CPO – rectal/stool • MRSA – nares * Some suggest skin swabs for CRAB
Specimen collection method	Varies depending on specimen source and MDRO of interest. • *Candida auris* – composite swab of both axilla and groin (see CDC website for details) • *CRO/CPO – swab inserted 1-3mm into rectum
Test procedure	Specific tests known to be sensitive and specific for detecting low numbers of the suspect MDRO which includes: • Molecular test for MDRO/gene marker of interest (e.g., NDM or KPC) • Culture – method is selected to optimize recovery of the MDRO of interest in a milieu that often contains much normal flora. Broth enrichment and/or selective agar is generally recommended for MDRO surveillance testing.
Reporting results	• Absence or presence of targeted MDRO/gene marker • Results reported to Infection Preventionists and/or public health as appropriate.

Routine diagnostic culture methods (e.g., routine stool culture) may be inappropriate and could be misleading for use in active surveillance or screening for MDRO.

Both active and passive surveillance for *Candida auris* were discussed in a previous version of this newsletter.

CASE STUDY: CARBAPENEM-RESISTANT PSEUDOMONAS AERUGINOSA

Why this case?

CP-CRPA are increasing in LAC and globally. There are few treatment options for CP-CRPA and identification of patients harboring CP-CRPA requires significant infection prevention and public health intervention. CP-CRPA may be difficult to identify as most CRPA are resistant to carbapenems by mechanisms other than carbapenemase production.

Objectives:

After reviewing this case, you will be able to:

1. Discuss when carbapenemase testing might be considered for CRPA
2. List reliable methods for testing for carbapenemase production in CRPA
3. Describe how to report CP-CRPA results to providers and other stakeholders.

Patient History:

79 yo male

Transferred from SNF to local community hospital for productive cough, shortness of breath and temperature of 101°C.

Blood and sputum cultures obtained on admission.

Blood cultures remained negative for 5 days; sputum culture results below.

Sputum Report Day 0

Gram stain:

Many WBCs

Many GNRs

Moderate normal respiratory flora

Sputum Report Day 1 - Preliminary

Many *Pseudomonas aeruginosa*

Moderate normal respiratory flora

Sputum Report Day 2 - Final

Many *Pseudomonas aeruginosa*

Moderate normal respiratory flora

Antimicrobial Agent	MIC (µg/mL)
Cefepime	**>32 R**
Ceftazidime-avibactam	>32/4 R
Ceftolozane-tazobactam	**>32/4 R**
Ciprofloxacin	>4 R
Meropenem	**>8 R**
Piperacillin-tazobactam	>128/4 R
Tobramycin	16 R
VIM carbapenemase	Positive

Report Comment:

MDRO (VIM-carbapenemase-producing *Pseudomonas aeruginosa*) isolated. Place patient on contact precautions. Infectious Diseases consult suggested.

Once the susceptibility results were obtained, Infection Prevention requested the isolate be tested for carbapenemase because:

- Patient had been transferred from a LTCF where two other patients had VIM-producing *P. aeruginosa*
- *P. aeruginosa* isolates "not susceptible (intermediate or resistant)" to cefepime, ceftazidime and/or ceftolozane-tazobactam are suspicious for carbapenemase production

Notes:

- The specific "signal" ("not susceptible" to cefepime, ceftazidime and/or and ceftolozane-tazobactam) applies to *P. aeruginosa* only, not other carbapenem-resistant organisms. CRPA susceptible to all 3 agents are highly unlikely to produce carbapenemase.
- Patients with CRPA would be placed in contact precautions at the hospital regardless of carbapenemase result

Public health follow up will depend on the carbapenemase result

- Carbapenemase negative – no further investigation
- Carbapenemase positive – DPH will perform an investigation. Additional testing, such as whole genome sequencing, may be requested to determine if the specific isolate may be linked to other *P. aeruginosa* isolates suspected of contributing to an outbreak.

Summary – Key facts about carbapenemase-producing *P. aeruginosa*

- Most CRPA (>95%) are carbapenem resistant by mechanisms other than **carbapenemase** production.[1]
- Intermediate or resistant results for **ceftolozane-tazobactam** and also **cefepime** or **ceftazidime** are a clue that a *P. aeruginosa* isolate may produce a carbapenemase.[2]
- The most common carbapenemase reported in the USA for *P. aeruginosa* is **VIM**.[1]
- VIM- and GES- producing *P. aeruginosa* have recently been associated with contaminated eyedrops with some cases in LAC and other parts of the US.[3,4]
- **GES** is not included in commonly available carbapenemase test kits [3]
- CP-CRPA are resistant to newer beta-lactam combination agents including **imipenem-relebactam** and **ceftazidime-avibactam** in addition to **ceftolozane-tazobactam.**[5]
- Last resort agents such as **cefiderocol** may be considered and testing of this agent may be requested from infectious diseases specialists.[5]

[1] https://arpsp.cdc.gov/profile/arln/crpa

[2] Vallabhaneni, Huang, Grass et al. 2021. J Clin Microbiol. 59:e02874-20.

[3] http://publichealth.lacounty.gov/eprd/lahan/alerts/CDCHANArtificialTears020223.pdf

[4] https://www.cdc.gov/hai/outbreaks/crpa-artificial-tears.html

[5] Tenover FC, Nicolau DP, Gill CM. 2022. Emerg Microbes Infect. 11:811-814.

Important AST Reporting Rule for All Carbapenem-resistant Organisms: Do not report an isolate as **carbapenemase positive** or **carbapenemase producing** unless a phenotypic or genotypic carbapenemase test is performed and is positive.

See Figure 1 for suggested work up of CRPA for carbapenemase.

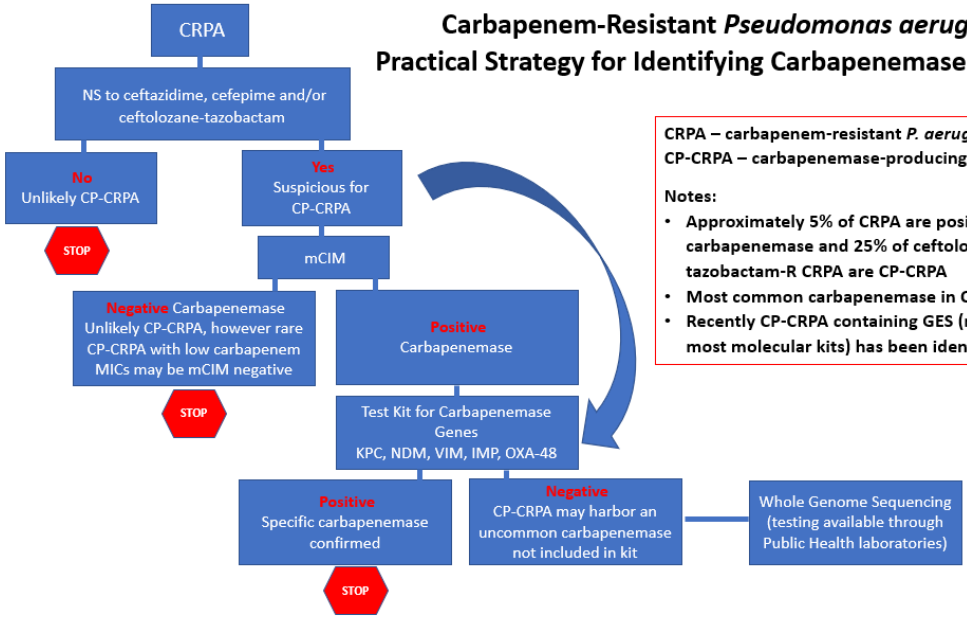
Other Resources:

Previous editions of quarterly **LAC DPH MDRO News Update for Laboratories** that focused on CRPA here and here

Carbapenemase Primer - options for testing for carbapenemase production can be found here

Other antimicrobial agents that physicians may request for testing CRPA here.

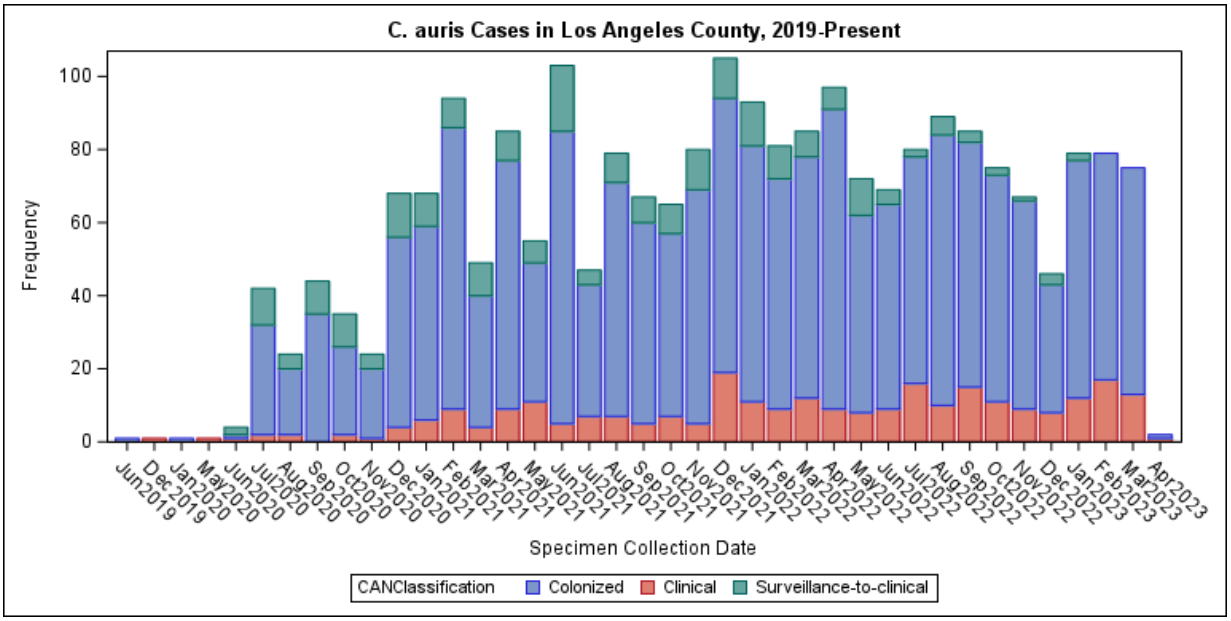
Figure 1.



UPDATE ON C. AURIS IN LOS ANGELES COUNTY (2019-PRESENT)

HCF Type	Clinical^	Surveillance-to-clinical†	Surveillance*	Total
General Acute Care Hospital (GACH)	187	33	256	476
Long Term Acute Care Hospital (LTACH)	78	182	1480	1740
Skilled Nursing Facility (SNF)	4	8	76	88
Other	9	0	3	12
Total	**278**	**223**	**1815**	**2316**

*Note that all cases are counted by case and facility 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).*



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
11 (link)	• VIM-CRPA in LA County • Carbapenemase-producing organisms (CPOs)

We welcome feedback on this Newsletter, previous Newsletters or any other issue related to MDROs - email us at hai@ph.lacounty.org.