Novel Multi-Drug Resistant Organisms (N-MDROs): How to Detect, Report, and Contain

Sandeep K. Bhaurla, MPH, CIC
Epidemiologist
Healthcare Outreach Unit (HOU)
Acute Communicable Disease Control Program (ACDC)
Los Angeles County Department of Public Health
Objectives

• Review novel multi-drug resistant organisms (N-MDROs)
• Describe the epidemiology of and response efforts to N-MDROs
• Discuss the role of infection preventionists in detecting, reporting, and containing novel MDROs
What “Novel” MDRO Means

• “Rare” or non-endemic types of MDROs
• For LA County, organisms in this group include:
  – Rare carbapenemase producing organisms (CPO)
  – mcr-producing organisms
  – Pan-resistant organisms
  – Vancomycin-resistant *Staphylococcus aureus* (VRSA)
  – *Candida auris*
RARE CARBAPENEMASES in LAC
CRE isolates that have a non-KPC carbapenemases identified; or CR-\textit{Pseudomonas} spp. or CR-\textit{Acinetobacter} spp. isolates that have any carbapenemase detected
Types of Carbapenemases

- *Klebsiella pneumoniae* carbapenemase (KPC)
- New Delhi Metallo-β-lactamase (NDM)
- Oxacillinase/ Class D β-lactamase (OXA)
- Verona Integron-encoded Metallo-β-lactamase (VIM)
- Imipenem Metallo-β-lactamase (IMP)

- All are plasmid-mediated
Wait... What is a plasmid?
Worldwide Distribution of Carbapenemases

Rare Carbapenemases: Epidemiology in US

https://www.cdc.gov/hai/organisms/cre/trackingcre.html
Rare Carbapenemases: Epidemiology in LA County

• Overall, 71% of CR isolates submitted to LAC DPH Public Health Laboratory between 2015-2019 were carbapenemase-positive – 6% were non-KPC-producing organisms, which include:
  • 26 OXA (first detected 2015)
  • 25 NDM (first detected 2015)
  • 13 VIM (first detected 2016)
  • 5 IMP (first detected 2017)
Rare Carbapenemases: Clinical Impact

• Different types of carbapenemases have different antimicrobial activity
  – Metal-containing carbapenemases (NDM, IMP, VIM) may be more difficult to treat
• Carbapenemase-producing organisms (CPOs) can be more difficult to treat because the plasmid may carry additional resistance genes
## Rare Carbapenemases: Laboratory Detection

<table>
<thead>
<tr>
<th>Genotypic</th>
<th>Phenotypic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PCR-based molecular tests can detect and identify specific carbapenemase genes</td>
<td>• eCIM (EDTA-modified carbapenem inactivation method) can detect metal-containing carbapenemases (i.e., NDM, VIM, IMP)</td>
</tr>
<tr>
<td></td>
<td>– Must be done in addition to mCIM test</td>
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<tr>
<td></td>
<td>• Resistant to new antibiotic agents (only for CRE and <em>Pseudomonas</em> spp.):</td>
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<tr>
<td></td>
<td>– Ceftazidime-avibactam, ceftolozane-tazobactam, plazomicin, and meropenem-vaborbactam</td>
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</tbody>
</table>
**MCR-TYPE RESISTANCE**

Production of the *mcr* gene as demonstrated by PCR.
**mcr-Type Resistance: Clinical Impact**

- Plasmid-mediated
- Colistin is considered to be a “last line” antibiotic for difficult-to-treat infections
  - However, newer, less toxic agents are being approved
**mcr-Type Resistance: Epidemiology**

- First identified in China in 2015
- First US case in May 2016
- First LA County case in December 2016 – total of 3
- Total 29 human cases reported across US
  - 85% had history of international travel

Photo credit: CDC. [https://www.cdc.gov/drugresistance/biggest-threats/tracking/mcr.html](https://www.cdc.gov/drugresistance/biggest-threats/tracking/mcr.html)
### mcr-Type Resistance: Laboratory Detection

<table>
<thead>
<tr>
<th>Genotypic</th>
<th>Phenotypic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PCR-based molecular tests can detect and identify <em>mcr</em> genes</td>
<td>• None...</td>
</tr>
</tbody>
</table>


SUSPECT PAN-RESISTANT ORGANISMS

Enterobacteriaceae, *Pseudomonas* spp., or *Acinetobacter* spp. resistant (R) to all drugs tested
Suspect Pan-Resistant Organisms: Epidemiology

• Organisms that are resistant to ALL antimicrobials are very uncommon in US

• None identified in LA County
  – However, 20% of CRE sent to the LAC Public Health Laboratory are resistant to all drugs tested
Suspect Pan-Resistant Organisms: Clinical Impact

• If truly pan-resistant, will be EXTREMELY difficult to treat
• New drugs being approved by FDA = hope!
Suspect Pan-Resistant Organisms: Lab Detection

- Look for organisms that are resistant (R) to all drugs tested on your gram negative panel
  - Ensure isolate was not susceptible (S/I) to secondary drugs tested
VANCOMYCIN-INTERMEDIATE or -RESISTANT STAPHYLOCOCCUS AUREUS (VISA/VRSA)

*Staphylococcus aureus* isolates with MIC $\geq 4 \mu g/ml$
VRSA: Epidemiology

• 14 VRSA infections in US
  – All carried \textit{vanA} vancomycin resistance gene (plasmid-mediated)
• None identified in LA County nor California
VRSA: Clinical Impact

• Vancomycin is drug of choice for MRSA infections, and is used empirically in populations where MRSA rate is high
• Infections are treatable; all isolates reported to CDC have been susceptible to other drugs
VRSA: Laboratory Detection

• Look for \textit{S. aureus} isolates with a vancomycin MIC
  – 4-8 $\mu$g/ml for VISA
  – $\geq$ 16 $\mu$g/ml for VRSA

• All automated susceptibility testing (AST) systems can reliably detect VISA/VRSA
CANDIDA AURIS
Confirmed *C. auris*, possible *C. auris*, or isolates of *C. haemulonii* and *Candida spp.* that cannot be identified after routine testing.
Candida auris: Epidemiology

- First identified in 2009 in Japan
- Has caused several outbreaks in healthcare settings, including multiple healthcare facilities in Orange County in 2019
  - Over 150 colonized cases identified
- 1 identified in LA County

Candida auris: Clinical Impact

• Causes severe infections
  – More than 1 in 3 patients with invasive C. auris infection die
  – 50% of central-line bloodstream infections (CLABSI) due to C. auris in New York healthcare facilities

• Difficult to treat
  – Some C. auris infections have been resistant to all three available antifungal medications
Candida auris: Laboratory Detection

• Can be difficult to identify with standard methods
  – Approximately 40% of LAC labs can accurately detect

• Review CDC site for more details: https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html

• Determine whether your lab can detect *C. auris* or not
LAC NOVEL MDRO RESPONSE
Detect, Report, and Contain
Reporting Novel MDROs in LA County

### Novel MDROs in LA County

The Los Angeles County Department of Public Health (LACDPH) has become aware of novel forms of multiple-drug resistant organisms (MDROs) in LA County. These can spread easily within and between healthcare facilities and can be very difficult to treat. When you report suspect novel MDROs to Acute Communicable Disease Control (ACDC), we will work with you to prevent their spread.

Contact ACDC at 213-240-7941 within 1 working day

If your facility detects organisms meeting any criteria from any specimen source:

<table>
<thead>
<tr>
<th>Targeted MDRO</th>
<th>Organism(s)</th>
<th>Phenotypic Criteria</th>
<th>Genotypic Criteria</th>
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</thead>
<tbody>
<tr>
<td>Rare carbapenem-producing organisms</td>
<td>Carppenem-resistant (CR) Enterobacteriaceae</td>
<td>Positive mCIM and eCIM test, and/or resistance to one or more new agents</td>
<td>VIM, NDM, IMP, and/or OXA</td>
</tr>
<tr>
<td></td>
<td>CR-Pseudomonas spp.</td>
<td>Positive mCIM test and/or resistance to one or more new agents</td>
<td>KPC, VIM, NDM, IMP, and/or OXA</td>
</tr>
<tr>
<td></td>
<td>CR-Acinetobacter spp.</td>
<td>N/A</td>
<td>KPC, VIM, NDM, IMP, and/or OXA</td>
</tr>
<tr>
<td>Rare vancomycin-intermediate or resistant S. aureus (VISA/VRSA)</td>
<td>Enterobacteriaceae (excluding Proteus, Providencia, Morganella and Serratia)</td>
<td>Colistin MIC ≥24 μg/ml</td>
<td>mcr</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus aureus</td>
<td>Vancomycin MIC ≥24 μg/ml</td>
<td>N/A</td>
</tr>
<tr>
<td>Vancomycin-intermediate or resistant S. aureus (VISA/VRSA)</td>
<td>Enterobacteriaceae (excluding Proteus, Providencia, Morganella and Serratia)</td>
<td>Resistant to all drugs tested on your gram-negative panel(s)?</td>
<td>N/A</td>
</tr>
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<td></td>
<td>N/A</td>
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<tr>
<td>Suspect pan-resistant organisms</td>
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<tr>
<td>Candida auris</td>
<td>G. auris can be misidentified when using traditional methods for yeast identification. Report C. haemulonii as a suspect case.</td>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

* New agents include ceftolozane-atobazolin, tigecycline, telavancin, daptomycin, and linezolid.

For more information on antimicrobial resistance in LA County please visit:

http://publichealth.lacounty.gov/Acd/Diseases/NMDRO.htm
LAC Novel MDRO Response

- Upon receipt of a suspect/confirmed case, LACDPH will:
  - Conduct initial assessment of affected facility to ensure patient is on appropriate level of precautions (Contact vs. Enhanced Standard)
  - Determine patient status and risk for transmission
  - Identify whether transmission may have occurred
  - Educate facility staff on how to prevent transmission
  - Ensure communication of patient infection/colonization status
What LACDPH is Looking For

Implement Contact Precautions for any confirmed or suspected cases

- If resident is colonized and is a ‘low’ transmission risk, consider placing on Enhanced Standard Precautions
- Cohort infected/colonized residents with residents that have no infections/colonizations and are a ‘low’ transmission risk
  - Use LACDPH Infection Control Risk Assessment Guidelines for LTC

Provide resident infection/colonization status upon discharge
LA County Novel MDRO Surveillance Findings

Figure 1D: High risk cases.
High-risk cases were defined as any of the following: assistance for activities of daily living, ventilator-dependent, incontinent, wounds with unmanageable drainage, or unable to maintain hygiene.

67% of N-MDRO cases were considered "High Risk" patients.

Figure 1E: High-risk setting.
High risk settings for N-MDRO transmission are SNFs or long-term acute care hospitals (LTACs). (6 months prior to culture collection date).

53% of N-MDRO cases have stayed in a high risk setting 6 months prior to culture collection date.

Figure 1F: Exposure to healthcare internationally.
Among 51 cases with information available, 19 (37.3%) had international healthcare exposure 6 months prior to culture collection. Healthcare exposure is defined as at least 1 overnight inpatient stay.

Regions:
- Southeast Asia: 4 cases
- The Middle-East: 3 cases
- South Asia: 2 cases
- Mexico: 1 case
- Africa: 1 case

Resistance Mechanism:
- IMP
- NDM
- OXA
- VIM
- NDM+OXA
- OXA+KPC
- MCR-1
Need for Coordinated Approach to Stop Spread

Facilities work together to protect patients.

**Common Approach (Not enough)**
- Patients can be transferred back and forth from facilities for treatment without all the communication and necessary infection control actions in place.

**Independent Efforts (Still not enough)**
- Some facilities work independently to enhance infection control but are not often alerted to antibiotic-resistant or *C. difficile* germs coming from other facilities or outbreaks in the area.
- Lack of shared information from other facilities means that necessary infection control actions are not always taken and germs are spread to other patients.

**Coordinated Approach (Needed)**
- Public health departments track and alert health care facilities to antibiotic-resistant or *C. difficile* germs coming from other facilities and outbreaks in the area.
- Facilities and public health authorities share information and implement shared infection control actions to stop spread of germs from facility to facility.

Photo credit: CDC

[https://www.cdc.gov/vitalsigns/stop-spread/infographic.html#infographic1](https://www.cdc.gov/vitalsigns/stop-spread/infographic.html#infographic1)
Inter-facility Communication is VITAL

http://publichealth.lacounty.gov/acd/docs/FacilityTransferForm.pdf
Remember...

• When in doubt, always contact us!
  – ACDC Phone: 213-240-7941
  – HOU Email: hai@ph.lacounty.gov

• Do not send isolates to LAC Public Health Lab without calling ACDC first

• More information available online:
  – http://publichealth.lacounty.gov/Acd/AntibioticResistance.htm
  – http://publichealth.lacounty.gov/Acd/Diseases/NMDRO.htm
  – http://publichealth.lacounty.gov/Acd/Diseases/CRE.htm
Questions?
WHAT HEALTHCARE FACILITIES CAN DO
It Takes a TEAM to Detect, Report, Contain, and Prevent Novel MDROs

- Infection Preventionists
- Laboratorians
- Clinicians
- Pharmacists
- Nurses
Actions for Infection Preventionists

• Identify colonized and infected residents in the facility
  – Suspect novel MDROs amongst residents with recent healthcare exposure outside the US
    • LAC DPH has criteria available for patients at high-risk for *C. auris*
  – Find out when a patient with an MDRO transfers into your facility.
• Ensure appropriate precautions are strictly adhered to
  – Use LACDPH Infection Control Risk Assessment Guidelines
• Work with EVS to ensure thorough cleaning & disinfection practices
Actions for Clinicians

• Ensure timely, appropriate antibiotic therapy
• Perform hand hygiene ALWAYS: use alcohol-based hand rub or wash hands with soap and water before and after contact with the resident or their environment
• Stay aware of facility and community antibiotic resistance rates
  – LA County Regional Antiibiogram available: http://publichealth.lacounty.gov/acd/antibiogram.htm
Actions for Pharmacists

• Promote antimicrobial stewardship
• Look for novel agents but ensure they are ONLY used when needed
• Track facility and community antibiotic resistance rates
  – LA County Regional Antibiogram available:
    http://publichealth.lacounty.gov/acd/antibiogram.htm
Actions for Microbiologists

• Make sure the lab can accurately identify novel MDROs
  – Our Public Health Lab can provide guidance and/or free testing services, if needed

• Immediately alert clinical and infection prevention staff when novel MDROs are suspected/identified

• Ensure lab reports easy to read, and suppress unnecessary information
Actions for Nurses

• Ask if a resident has received medical care outside the US in the past 12 months
• Wear a gown and gloves when caring for residents with novel MDROs
• Perform hand hygiene ALWAYS: use alcohol-based hand rub or wash hands with soap and water before and after contact with the resident or their environment
• Discontinue devices (i.e., catheters) as soon as no longer necessary
• Alert the receiving facility when you transfer an MDRO-positive resident