Multi-Drug Resistant Organisms: a Primer on CRE/CP-CRE, C. auris, ESBL & CRAB

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Disclosures

- Work funded by CDC grant
- Conflicts of interest
Learning Objectives

- Understand what is an MDRO
- Review antibiotics and bacterial resistance
- Identify sources of MDRO’s
- Review bacterial resistance mechanisms
- Identify Current CDC MDRO threat levels
- COVID-19 impact on U.S. MDRO’s
- Review ESBL, CRE, CRAB and C.auris
- Learn about next steps to mitigation
Setting the Table
What is a MDRO

MDRO Definition:

• For epidemiologic purposes, MDROs are defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents.

• Multi-Drug-Resistant-Organism

Common Examples

• Methicillin-Resistant Staphylococcus aureus (MRSA)
• Vancomycin-Resistant Enterococcus (VRE)
• Extended Spectrum Beta-Lactamases (ESBL)
• Carbapenem-Resistant Enterobacterales (CRE)
Antibiotics and Resistance

• Penicillin was discovered in 1928 by Alexander Fleming
  • First resistance identified in 1940 in *Staphylococcus*
• Penicillin became commercially available in 1943
• After the discovery of each new antibiotic, there is acknowledgement of resistance alongside the discovery
• Bacteria know how to fight back, and they do so very quickly and efficiently
# Bacterial Resistance Timeline

<table>
<thead>
<tr>
<th>Antibiotic Approved or Released</th>
<th>Year Released</th>
<th>Resistant Germ Identified</th>
<th>Year Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>1941</td>
<td>Penicillin-resistant <em>Staphylococcus aureus</em>²⁰, ²¹</td>
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<td></td>
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<td>Penicillin-resistant <em>Streptococcus pneumoniae</em>³⁰</td>
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<td>Penicillinase-producing <em>Neisseria gonorrhoeae</em>³²</td>
<td>1976</td>
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<td>Vancomycin</td>
<td>1958</td>
<td>Plasmid-mediated vancomycin-resistant <em>Enterococcus faecium</em>²¹</td>
<td>1988</td>
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<td></td>
<td></td>
<td>Vancomycin-resistant <em>Staphylococcus aureus</em>³⁴</td>
<td>2002</td>
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<td>Amphotericin B</td>
<td>1959</td>
<td>Amphotericin B-resistant <em>Candida auris</em>³⁵</td>
<td>2016</td>
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<tr>
<td>Methicillin</td>
<td>1960</td>
<td>Methicillin-resistant <em>Staphylococcus aureus</em>³⁶</td>
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<tr>
<td>Extended-spectrum cephalosporins</td>
<td>1980 (Cefotaxime)</td>
<td>Extended-spectrum beta-lactamase-producing <em>Escherichia coli</em>³⁷</td>
<td>1983</td>
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<tr>
<td>Azithromycin</td>
<td>1980</td>
<td>Azithromycin-resistant <em>Neisseria gonorrhoeae</em>³⁸</td>
<td>2011</td>
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<tr>
<td>Imipenem</td>
<td>1985</td>
<td><em>Klebsiella pneumoniae</em> carbapenemase (KPC)-producing <em>Klebsiella pneumoniae</em>³⁹</td>
<td>1996</td>
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<tr>
<td>Ciprofloxacin</td>
<td>1987</td>
<td>Ciprofloxacin-resistant <em>Neisseria gonorrhoeae</em>³⁰</td>
<td>2007</td>
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<tr>
<td>Fluconazole</td>
<td>1990 (FDA approved)</td>
<td>Fluconazole-resistant <em>Candida</em>²¹</td>
<td>1988</td>
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<tr>
<td>Caspofungin</td>
<td>2001</td>
<td>Caspofungin-resistant <em>Candida</em>²³</td>
<td>2004</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>2003</td>
<td>Daptomycin-resistant methicillin-resistant <em>Staphylococcus aureus</em>³⁵</td>
<td>2004</td>
</tr>
<tr>
<td>Ceftazidime-avibactam</td>
<td>2015</td>
<td>Ceftazidime-avibactam-resistant KPC-producing <em>Klebsiella pneumoniae</em>²⁴</td>
<td>2015</td>
</tr>
</tbody>
</table>

Where do MDRO’s Come From? (page 1)

**Reservoirs**
- Food sources
- Agricultural animals and plants
- Companion animals
- Water / Soil
- Plumbing – drains (biofilms)

Thanner et al. mBIO 2016.
Where do MDRO’s Come From? (page 2)

**Reservoirs**

- Asymptomatic carriers – transmission or environmental contamination
- Selected during treatment: not just the infection, but entire microbiome
- Topical antibiotics & colistin resistance

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**Where the organisms can infect the body**

- Skin/soft tissue
- Lungs
- Bloodstream
- Urinary tract

**How antibiotic-resistant bacteria take over**

...antibiotic-sensitive bacteria are killed and antibiotic-resistant bacteria become dominant.

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Thanner et al. mBIO 2016.
Bacterial Resistance to Antimicrobials

• Resistance is not new or unexpected, it’s a natural phenomenon associated with DNA replication/transcription errors

• Three fundamental mechanisms of antimicrobial resistance. All DNA based.
  1. Enzymatic degradation of antibacterial drugs
  2. Alteration of bacterial proteins that are antimicrobial targets
  3. Changes in membrane permeability to antibiotics
Plasmid Mediated Resistance

- Plasmids harbor genes coding for antibiotic resistance and virulence factors.
- This allow bacteria to survive a hostile environment, and resist treatment.
- Examples:
  - *Pseudomonas aeruginosa* can become more mucoid
  - *K. pneumonia* with a KPC enzyme can resist most antibiotics
- Most CRE’s are resistant due to having a plasmid
CDC Serious Threats

These germs are public health threats that require prompt and sustained action:

- **DRUG-RESISTANT CAMPYLOBACTER**
- **DRUG-RESISTANT CANDIDA**
- **ESBL-PRODUCING ENTEROBACTERIACEAE**
- **VANCOMYCIN-RESISTANT ENTEROCOCCI**
- **MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA**
- **DRUG-RESISTANT NONTYPHOIDAL SALMONELLA**
- **DRUG-RESISTANT SALMONELLA SEROTYPE TYPHI**
- **DRUG-RESISTANT SHIGELLA**
- **METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS**
- **DRUG-RESISTANT STREPTOCOCCUS PNEUMONIAE**
- **DRUG-RESISTANT TUBERCULOSIS**

COVID-19 U.S. Impact on Antimicrobial Resistance

**Serious Threats Impact**

- Antifungal-resistant *Candida*, overall 12% increase, and 26% increase of Hospital-onset cases
- ESBL’s, overall 10% increase in cases and 32% increase in Hospital-onset cases
- *Pseudomonas aeruginosa* counts stable, but saw a 32% increase in Hospital-onset cases

COVID-19 U.S. Impact on Antimicrobial Resistance

**Urgent Threat Impact:**

- Carbapenem-resistant *Acinetobacter*, overall 35% increase, and 78% in Hospital-onset cases
- *C. auris*, 60% increase in cases to 754 cases in 2022. Newest report is now 3,270 cases, as 200% increase
- Carbapenem-resistant Enterobacterales, overall stable, but 35% increase in Hospital-onset cases

https://www.acpjournals.org/doi/10.7326/M22-3469
Extended-Spectrum Beta-Lactamase (ESBL) Enterobacterales
What is a ESBL?

- Some Enterobacterales can produce enzymes called extended-spectrum beta-lactamases (ESBLs). ESBL enzymes break down and destroy some commonly used antibiotics, including penicillins and cephalosporins, and make these drugs ineffective for treating infections.
ESBL-producing Enterobacteriaceae (a family of different types of bacteria) are a concern in healthcare settings and the community. They can spread rapidly and cause or complicate infections in healthy people.
Why are ESBL Bacteria Considered Epidemiologically Important?

• ESBL-producing Enterobacteriaceae often cause infections in otherwise healthy people. About one-quarter of patients with these infection had no known underlying health conditions.

• Antibiotic options to treat ESBL-producing Enterobacteriaceae infections are limited. Healthcare providers often have to use intravenous (IV) carbapenem antibiotics to treat infections that used to be treated with oral antibiotics.

Current CDC ESBL Statistics

• CDC and partners are working to assess and address why cases of ESBL-producing Enterobacteriaceae have increased since 2012.

ESBL Identification

- Standard microbiology testing, for organisms with susceptibilities
- ESBL will show resistance to 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} generation cephalosporin's

Enterobacterales (\textit{E. coli, K. pneumoniae, K. oxytoca, or P. mirabilis} only):

<table>
<thead>
<tr>
<th></th>
<th>Ceftriaxone, Cefotaxime, or Ceftazidime</th>
<th>Cefoxitin</th>
<th>Cefepime</th>
<th>Presumed Beta-lactamase</th>
<th>Beta-lactam treatment options</th>
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<tr>
<td>Susceptibility</td>
<td>I or R</td>
<td>I or R</td>
<td>S</td>
<td>AmpC</td>
<td>Cefepime or carbapenems</td>
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<tr>
<td>Susceptibility</td>
<td>I or R</td>
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<td>AmpC and ESBL</td>
<td>Carbapenems</td>
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<td>S</td>
<td>S</td>
<td>ESBL</td>
<td>Carbapenems</td>
</tr>
</tbody>
</table>

https://www.idstewardship.com/5-important-things-know-extended-spectrum-beta-lactamases-esbl-insights-clinical-microbiologist/
How to Test for ESBL

The Microbiology lab is your new best friend!

• Platforms your lab might have for susceptibilities
  • Automated susceptibilities testing (AST)
  • Kirby-Bauer disk diffusion
  • E-tests
  • Molecular testing, looking for CTX-M gene
**Escherichia coli**

<table>
<thead>
<tr>
<th>AUTOMATED SUSCEPTIBILITY</th>
<th>Breakpoint</th>
<th>S.I.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>&lt;=4 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanic</td>
<td>4/2 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>&lt;=2 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>2/1 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>&lt;=1 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>&lt;=1 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefepime</td>
<td>&lt;=0.5 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>&lt;=0.5 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&lt;=0.5 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>&lt;=4 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&lt;=0.5 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>&lt;=0.125 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>&lt;=1 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Imipenem</td>
<td>&lt;=0.25 ug/mL</td>
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<td>Levofloxacin</td>
<td>&lt;=1 ug/mL</td>
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<tr>
<td>Meropenem</td>
<td>&lt;=0.125 ug/mL</td>
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</tr>
<tr>
<td>Moxifloxacin</td>
<td>&lt;=1 ug/mL</td>
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</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>&lt;=2/4 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>&lt;=1 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1 ug/mL</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>1/19 ug/mL</td>
<td>Susceptible</td>
</tr>
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**Escherichia coli** (ESBL)

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<tr>
<td>Ampicillin</td>
<td>&gt;16 ug/mL</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>16/8 ug/mL</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>&gt;16 ug/mL</td>
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<tr>
<td>Cefazolin</td>
<td>&gt;32 ug/mL</td>
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</tr>
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<td>Cefepime</td>
<td>&gt;16 ug/mL</td>
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<td>Ceftazidime</td>
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<td>Ceftriaxone</td>
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<tr>
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<td>&gt;8 ug/mL</td>
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<td>Tobramycin</td>
<td>1 ug/mL</td>
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</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>&lt;=0.5/9.5 ug/ml</td>
<td>Susceptible</td>
</tr>
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</table>
How Common are ESBL Infections?

- Almost half of ESBL-producing Enterobacteriaceae infections occur in people who have not had recent inpatient healthcare exposure or an invasive medical procedure. These infections are called community-associated infections.
Who is Most Likely to get a ESBL Infection?

• These infections most commonly occur in people with exposure to healthcare, including those in hospitals and nursing homes. However, unlike many other resistant germs, ESBL-producing Enterobacterales can also cause infections in otherwise healthy people who have not been recently been in healthcare settings. In healthy people, this often means urinary tract infections.

• ESBL germs have also been identified in people returning to the United States after traveling abroad, especially to places where these germs are more commonly found.

https://www.cdc.gov/hai/organisms/ESBL.html
Carbapenem-resistant Enterobacterales (CRE)
What is a CRE or CP-CRE?

Enterobacterales that test resistant to at least one of the carbapenem antibiotics or produce a carbapenemase (an enzyme that can make them resistant to carbapenem antibiotics) are called CRE.

**Common Plasmids:**
- *K. pneumoniae* carbapenemase (KPC)
- New Delhi Metallo-beta-lactamase (NDM)
- Verona Integron-Encoded Metallo-beta-lactamase (VIM)
- Imipenemase (IMP)
- Oxacillinase-48 (OXA-48)

**Carbapenem Antibiotics**
- Doripenem
- Ertapenem
- Imipenem
- Meropenem

In the United States, CRE are generally associated with healthcare settings, and approximately 30% of CRE carry a carbapenemase. These carbapenemase genes are often on mobile genetic elements, which can be easily shared between bacteria, leading to the rapid spread of resistance.
Why are CP-CRE Considered Epidemiologically Important?

• CRE organisms are often resistant to multiple classes of antibiotics, substantially limiting treatment options.

• Infections caused by these organisms are associated with high mortality rates among hospitalized patients, up to 50% in some studies.

• Many CRE produce carbapenemases, which can be transmitted from Enterobacteriales to other germs, facilitating spread of resistance.

• Enterobacteriales are a common cause of infections in both community and healthcare settings. Although CRE is currently primarily associated with inpatient healthcare settings, it has the potential to spread to community settings.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html
Current CDC CRE Statistics

• Containment strategies have prevented further spread of some types of CRE in the United States, but continued action is needed.

CRE and Carbapenemase Identification

CRE Identification

• Enterobacterales that test resistant to at least one of the carbapenem antibiotics on microbiology sensitivity report

Carbapenemase Identification

• Phenotypic tests for carbapenemase production
• Molecular assay for the presence of a carbapenemase gene

https://www.cdc.gov/hai/organisms/cre/technical-info.html#:~:text=Types%20of%20CRE-,How%20does%20CDC%20define%20CRE%3F,carbapenem%20antibiotics)%20are%20called%20CRE.
## CRE Example

### Escherichia coli

<table>
<thead>
<tr>
<th>AUTOMATED SUSCEPTIBILITY</th>
<th>DISK DIFFUSION Breakpoint</th>
<th>S.I.R.</th>
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<tr>
<td>Amikacin</td>
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<td>Ciprofloxacin</td>
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<td>Doripenem</td>
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<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>&gt;4 ug/mL</td>
<td>Resistant</td>
</tr>
<tr>
<td>Meropenem</td>
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<tr>
<td>Nitrofurantoin</td>
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<td>Tetracycline</td>
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</tbody>
</table>

### PCR Testing
- NDM-1
How to Test for CRE

• Clinical laboratories can perform phenotypic tests for carbapenemase production (e.g., CarbaNP, mCIM, and mCIM with eCIM) or molecular assays for the presence of a carbapenemase gene.

• Carbapenemase testing is available through the AR Lab Network. This testing includes phenotypic testing for carbapenemase activity and molecular identification of the five carbapenemases most frequently identified in CRE: KPC, NDM, VIM, OXA-48-type, and IMP.

https://www.cdc.gov/hai/organisms/cre/technical-info.html#Common
How Common are CRE Infections?

- In 2017, CRE caused an estimated 13,100 infections in hospitalized patients, and 1,100 estimated deaths in the United States [Source: 2019 AR Threats Report].

- NDM, VIM, and IMP are less commonly identified in CRE in the United States relative to KPC. Since the AR Lab Network began testing in 2017, only about 10% of carbapenemases identified have been metallo-β-lactamases (MBLs).

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html
Who is Most Likely to get a CRE Infection?

• Healthy people usually do not get CRE infections—
• Patients in hospitals and long-term care facilities like skilled nursing facilities and long-term acute care hospitals.
• Patients whose care requires devices like ventilators (breathing machines), urinary (bladder) catheters, or intravenous (vein) catheters
• Patients who are taking long courses of certain antibiotics
• Patients with weakened immune systems
• Healthcare-related risk factors include requiring help with most activities of daily living, like toileting and bathing, exposure to an intensive care unit, and mechanical ventilation.
• Several antibiotics have been associated with getting CRE, including carbapenems, cephalosporins, fluoroquinolones, and vancomycin.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html
What Can Clinicians do to Prevent CRE Transmission?

• Know if patients with CRE are admitted to your facility and stay aware of CRE infection rates in your facility.
• When you transfer a patient with CRE, use an inter-facility transfer form to alert the receiving facility during the transition of care.
• Ask if a patient has received medical care somewhere else, including another facility or other countries.
• Screen patients who have had an overnight stay in a healthcare facility outside the United States in the prior 6 months for the presence of carbapenemase-producing CRE. Free admission screening is available through the AR Lab Network. Contact your HAI coordinator for more information on accessing AR Lab Network testing.
• Whenever possible, place patients currently or previously colonized or infected with CRE in a private room with a bathroom and dedicate noncritical equipment (e.g., stethoscope, blood pressure cuff) to CRE patients.
• Wear a gown and gloves when caring for patients with CRE.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html
What Can Clinicians do to Prevent CRE Transmission?

• Perform hand hygiene—use alcohol-based hand rub or wash hands with soap and water before and after contact with patient or their environment.

• Make sure labs immediately alert clinical and infection prevention staff when CRE are identified. If your laboratory does not perform testing for carbapenemases, talk to your HAI coordinator about getting isolates tested through the AR Laboratory Network.

• Prescribe and use antibiotics appropriately.

• Discontinue devices like urinary catheters as soon as no longer necessary.

• When a patient with an unusual type of carbapenemase-producing CRE is identified in your facility, work with public health to prevent spread, including following guidance to assess for ongoing transmission.

https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html
Carbapenem-Resistant *Acinetobacter baumannii* (CRAB)
What is a CRAB?

- *Acinetobacter* is a group of bacteria (germs) commonly found in the environment, like in soil and water. While there are many types, the most common cause of infections is *Acinetobacter baumannii*, which accounts for most Acinetobacter infections in humans.
- When resistant to multiple antibiotics, they’re multidrug resistant.
- Carbapenem-resistant *Acinetobacter* are usually multidrug-resistant.
- *Acinetobacter baumannii* can cause infections in the blood, urinary tract, and lungs (pneumonia), or in wounds in other parts of the body. It can also “colonize” or live in a patient without causing infections or symptoms, especially in respiratory secretions (sputum) or open wounds.

https://www.cdc.gov/hai/organisms/acinetobacter.html
Acinetobacter bacteria can survive a long time on surfaces. Nearly all carbapenem-resistant Acinetobacter infections happen in patients who recently received care in a healthcare facility.
Why are CRAB Considered Epidemiologically Important?

• Carbapenem-resistant *Acinetobacter* cause pneumonia and wound, bloodstream, and urinary tract infections. These infections tend to occur in patients in intensive care units.

• Carbapenem-resistant *Acinetobacter* can carry mobile genetic elements that are easily shared between bacteria. Some can make a carbapenemase enzyme, which makes carbapenem antibiotics ineffective and rapidly spreads resistance that destroys these important drugs.

• Some *Acinetobacter* are resistant to nearly all antibiotics and few new drugs are in development.

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat
Why are CRAB Considered Epidemiologically Important?

• Treatment options for infections caused by carbapenem-resistant *Acinetobacter baumannii* are extremely limited. There are few new drugs in development.

Current CDC CRAB Statistics

• In 2017, carbapenem-resistant *Acinetobacter* caused an estimated 8,500 infections in hospitalized patients and 700 estimated deaths in the United States.

CRAB Identification

- Standard microbiology identification and sensitivities
- Molecular testing to look for a carbapenemase gene
How to Test for CRAB

• Testing in the Antibiotic Resistance Laboratory Network (AR Lab Network) during 2019 found that carbapenemase genes were detected in 83% of CRA isolates tested. These carbapenemase gene-positive CRA (CP-CRA) are divided into two categories based on the type of gene present:
  • Most CP-CRA possess genes for carbapenemases that have been specifically identified among *Acinetobacter* species. These more common genes make OXA-23-like, OXA-24/40-like and OXA-58-like oxacillinases. Because these genes were detected frequently, they are not targeted for routine molecular testing.
  • A small proportion of CP-CRA possessed mobile genes that encode carbapenemases (KPC, IMP, NDM, VIM, OXA-48-like) found often in other gram-negative bacteria, such as Enterobacterales. These genes are amplifying the problem of resistance and are targeted for further molecular testing.

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat
Who is Most Likely to get a CRAB Infection?

- *Acinetobacter* infections typically occur in people in healthcare settings. People most at risk include patients in hospitals, especially those who:
  - are on breathing machines (ventilators)
  - have devices such as catheters
  - have open wounds from surgery
  - are in intensive care units
  - have prolonged hospital stays

- In the United States, *Acinetobacter* infections rarely occur outside of healthcare settings. However, people who have weakened immune systems, chronic lung disease, or diabetes may be more susceptible.
How are CRAB Germs Spread or Transmitted?

- *Acinetobacter* can live for long periods of time on environmental surfaces and shared equipment if they are not properly cleaned.
- The germs can spread from one person to another through contact with these contaminated surfaces or equipment or though person to person spread, often via contaminated hands.

https://www.cdc.gov/hai/organisms/acinetobacter.html
What Can Clinicians do to Prevent CRAB Transmission?

- When available, house patients infected or colonized with CRAB in single patient rooms. If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence).

- Use gown and gloves (e.g., Contact Precautions in Acute Care settings and Enhanced Barrier Precautions in long-term care settings for patients/residents who are infected or colonized with CRA). Consider empiric use of these precautions for patients transferred from high-risk settings.

- Review facility infection prevention and control practices and provide staff with feedback, particularly for:
  - Hand hygiene adherence
  - Personal protective equipment donning and doffing and adherence
  - Environmental cleaning and disinfection

https://arpsp.cdc.gov/story/cra-urgent-public-health-threat
Candida auris
What is a *Candia auris*?

- *Candida auris (C. auris)* is an emerging multidrug-resistant yeast (a type of fungus). It can cause severe infections and spreads easily between hospitalized patients and nursing home residents.
- First identified in 2009 in Asia
- More than 1 in 3 patients with invasive *C. auris* infection (for example, an infection that affects the blood, heart, or brain) die

https://www.cdc.gov/fungal/candida-auris/index.html
Candida auris (C. auris) is an emerging multidrug-resistant yeast (a type of fungus). It can cause severe infections and spreads easily between hospitalized patients and nursing home residents.
Why are *C. auris* Considered Epidemiologically Important?

CDC is concerned about *C. auris* for three main reasons:

- It is often multidrug-resistant, meaning that it is resistant to multiple antifungal drugs commonly used to treat *Candida* infections.

- It is difficult to identify with standard laboratory methods, and it can be misidentified in labs without specific technology. Misidentification may lead to inappropriate management.

- It has caused outbreaks in healthcare settings. For this reason, it is important to quickly identify *C. auris* in a hospitalized patient so that healthcare facilities can take special precautions to stop its spread.

https://www.cdc.gov/fungal/candida-auris/index.html
Current CDC *C. auris* Statistics

In 2021, cases reached a count of 3,270 with an active infection and 7,413 that showed the fungus was present but hadn’t caused an infection. Infection counts were up 95% over the previous year, and the fungus showed up on screenings three times as often. The number of cases resistant to medication also tripled.

https://www.acpjournals.org/doi/10.7326/M22-3469
Number of *C. auris* clinical cases through December 31, 2022

There have been 5,654 clinical cases and 13,163 screening cases since 2013.

- **0 clinical cases and at least 1 screening case**
- **1 to 10**
- **11 to 50**
- **51 to 100**
- **101 to 500**
- **501 to 1000**
- **1001 or more**

C. auris Identification

It is difficult to identify.

• *C. auris* can be misidentified as a number of different organisms when using traditional phenotypic methods for yeast identification such as VITEK 2 YST, API 20C, BD Phoenix yeast identification system, and MicroScan.

https://www.cdc.gov/fungal/candida-auris/identification.html
# When to suspect *C. auris*

<table>
<thead>
<tr>
<th>Identification Method</th>
<th>Organism <em>C. auris can be misidentified as</em></th>
</tr>
</thead>
</table>
| Vitek 2 YST*                                | *Candida haemulonii*  
*Candida duobushaemulonii*                                                                        |
| API 20C                                      | *Rhodotorula glutinis* (characteristic red color not present)  
*Candida sake*                                                                                     |
| API ID 32C                                   | *Candida intermedia*  
*Candida sake*  
*Saccharomyces kluveri*                                                                           |
| BD Phoenix yeast identification system       | *Candida haemulonii*  
*Candida catenulata*                                                                                 |
| MicroScan                                   | *Candida famata*  
*Candida guilliermondii*  
*Candida lusitaniae*  
*Candida parapsilosis*                                                                            |
| RapID Yeast Plus                            | *Candida parapsilosis*                                                                                |

https://www.cdc.gov/fungal/candida-auris/identification.html
How to Test for *C. auris*

- Diagnostic devices based on matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) can differentiate *C. auris* from other *Candida* species, but not all the reference databases included in MALDI-TOF devices allow for detection.

- Molecular methods based on sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA also can identify *C. auris*.

- The GenMark ePlex Blood Culture Identification Fungal Pathogen (BCID-FP) Panel and BioFire FilmArray BCID2 have been FDA approved as molecular tests for *C. auris* identification in positive blood cultures.

- AR Lab Network

https://www.cdc.gov/fungal/candida-auris/identification.html
How Common are *C. auris* Infections?

- In 2019 CDC reported 476 clinical cases
- 2015 to 2017 saw a 318% increase in reported cases
- 754 estimated cases in 2020
- 3270 estimated cases in 2021

Case counts continue to rise quickly, along with colonization screening cases.

While not as common as a ESBL, or CRE, *C. auris* is rising the fastest among the CDC urgent threats

https://www.cdc.gov/media/releases/2023/p0320-cauris.html
Who is Most Likely to get a *C. auris* Infection?

- People who are very sick with invasive medical devices
- Long or frequent stays in Hospitals and Long-term-care facilities and nursing homes
- Long term antibiotic use or antifungals
- People who weakened immune systems
- Patients who received medical care in foreign countries

https://www.cdc.gov/fungal/candida-auris/index.html
How are *C. auris* Spread or Transmitted?

- *C. auris* can spread in healthcare settings through contact with contaminated environmental surfaces or equipment, or from person to person.
- *C. auris* can be transmitted in healthcare settings and cause outbreaks.
- It can colonize patients for many months.
- It can persist in the environment and on surfaces.
- Withstands some commonly used healthcare facility disinfectants.

https://www.cdc.gov/fungal/candida-auris/index.html
What Can Clinicians do to Prevent *C. auris* Transmission?

- Quickly identify any patient with colonization or active infection based on their risk factors, and implement precautions
- Adherence to hand hygiene
- Appropriate use of Transmission-Based Precautions based on setting
- Cleaning and disinfecting the patient care environment, daily and terminal cleaning using Products with EPA-registered claims for *C. auris* (List P)
- Use disposable equipment, or dedicated equipment
- Communicate patient *C. auris* status when patient transferred
- Screening for high-risk patients

https://www.cdc.gov/fungal/candida-auris/index.html
Addressing MDRO’s: Next Steps
Antimicrobial Resistance: 5 Things to Know

1. Antimicrobial resistance occurs when germs defeat the drugs designed to kill them, called antibiotics or antifungals.

2. Antimicrobial resistance can affect people at any stage of life. Infections caused by resistant germs are difficult—sometimes impossible—to treat.

3. You can take steps to reduce your risk of getting an infection.

4. Talk to your healthcare provider or veterinarian about whether antibiotics or antifungals are needed.

5. Tell your healthcare provider if you recently traveled to or received care in another country. Antimicrobial resistance has been found in all regions of the world.

https://www.cdc.gov/drugresistance/about/5-things-to-know.html#:~:text=Antimicrobial%20resistance%20occurs%20when%20germs,at%20any%20stage%20of%20life.
MDRO Identified, Now What?

- Confirm if the patient has an active infection or is colonized, ensure the proper treatment course has been selected.
- Place patient in transmission-based precautions or enhanced barrier precautions.
- Look for other cases. Is this just one, or are there others?
- Report the case to public health as needed or required.
- Ensure good hand hygiene practices are in place.
- Ensure proper cleaning and disinfection is occurring.
Hand Hygiene

Use an Alcohol-Based Hand Sanitizer

- Immediately before touching a patient
- Before performing an aseptic task (e.g., placing an indwelling device) or handling invasive medical devices
- Before moving from work on a soiled body site to a clean body site on the same patient
- After touching a patient or the patient’s immediate environment
- After contact with blood, body fluids or contaminated surfaces
- Immediately after glove removal

Wash with Soap and Water

- When hands are visibly soiled
- After caring for a person with known or suspected infectious diarrhea
- After known or suspected exposure to spores (e.g. B. anthracis, C difficile outbreaks)

https://www.cdc.gov/handhygiene/providers/index.html
Environmental Cleaning and Disinfection

• Environmental cleaning is part of Standard Precautions, which should be applied to all patients in all healthcare facilities.

• Clean with an EPA registered disinfectant with the proper/needed kill claims for the MDRO in question

• Clean high touch surfaces regularly

• Launder linens at high temperature

• Ensure staff are properly trained with competencies

• Audit cleaning processes to ensure compliance

https://www.cdc.gov/hai/prevent/resource-limited/index.html
PPE

Standard precautions say to use PPE as needed based on the risk of exposure

- Gloves
- Masks (ear loop, surgical, N-95)
- Gowns
- Eye protection (glasses, goggles, face shields)

- Follow correct donning and doffing sequences
- Always perform hand hygiene after removal of PPE

https://www.cdc.gov/hai/prevent/ppe.html
Standard Precautions

• Perform hand hygiene
• Use PPE whenever there is an expectation of possible exposure to infectious material
• Follow respiratory hygiene/cough etiquette principles
• Ensure proper patient placement
• Properly handle and clean and disinfect patient care equipment and instruments/devices
  • Clean and disinfect the environment appropriately
• Handle textiles and laundry carefully
• Follow safe injection practices
• Ensure healthcare worker safety including proper handling of needles and other sharps

https://www.cdc.gov/infectioncontrol/basics/standard-precautions.html
Transmission Based Precautions

**Contact Precautions**
- Patient placement
- Use needed PPE correctly
- Limit transport and movement of patients
- Use disposable or dedicated patient-care equipment
- Prioritize cleaning and disinfection of the rooms

**Droplet Precautions**
- Source control: put a mask on the patient
- Ensure appropriate patient placement
- Use PPE appropriately
- Limit transport and movements of patients

**Airborne Precautions**
- Source control
- Patient placement in Airborne Infection Isolation room (AIIR)
- Restrict susceptible healthcare personnel from entering room
- Use PPE appropriately
- Limit transport and movement of patients
- Immunize susceptible persons as soon as possible following unprotect contact

https://www.cdc.gov/infectioncontrol/basics/transmission-based-precautions.html
Enhanced Barrier Precautions

- Enhanced Barrier Precautions (EBP) are an infection control intervention designed to reduce transmission of resistant organisms that employs targeted gown and glove use during high contact resident care activities.

- EBP may be indicated (when Contact Precautions do not otherwise apply) for residents with any of the following:
  - Wounds or indwelling medical devices, regardless of MDRO colonization status
  - Infection or colonization with an MDRO.

Examples of high-contact resident care activities requiring gown and glove use for **Enhanced Barrier Precautions** include:

- Dressing
- Bathing/showering
- Transferring
- Providing hygiene
- Changing linens
- Changing briefs or assisting with toileting
- Device care or use: central line, urinary catheter, feeding tube, tracheostomy/ventilator
- Wound care: any skin opening requiring a dressing

https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html
Acute Care Setting Prevention

- Always follow Standard Precautions
- Implement Transmission Based Precautions based on organism
  - Contact Precautions (MDRO, ESBL, CRAB, CRE, C.auris)
  - Droplet Precautions (Respiratory viruses)
  - Airborne Precautions (TB, Chickenpox, Measles)
- Leave precautions in place until discharge, or per CDC Appendix A, or per internal policy guidance
Post Acute Care Setting Prevention

• Always follow Standard Precautions
• Enhanced Barrier Precautions for residents with MDRO infection or colonization
• Contact Precautions: All residents infected or colonized with MDRO in the following situations
  • Acute diarrhea, draining wounds, other site excretions or secretions that are unable to be covered or contained
  • For a limited time period as determined in consultation with public health authorities, on units or in facilities during the investigation of a suspected or confirmed MDRO outbreak
  • When otherwise directed by public health authorities
  • All residents who have another infection (e.g., C. difficile, norovirus, scabies) or condition for which Contact Precautions is recommended in Appendix A (Type and Duration of Precautions Recommended for Selected Infections and Conditions) of the CDC Guideline for Isolation Precautions

https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html
Outbreaks

• Healthcare Facility contacts Local Public Health for assistance
• Epidemiologist gathers initial information and provides consultation on case finding, lab testing and infection control
• Team works on-site and help gather additional information from interview, case/chart review, observations and environmental sampling as needed
• Analyze information to identify risk factors for infection and help develop control measures
• Recommend new or revised measure and steps to prevent more patients from becoming infected or harmed
• Health department and facility implement recommendations and check to ensure the control measures are working

Individual Prevention

- Maintain good hygiene, wash hands regularly, maintain good health
- Proper use of antibiotics
- Clean your environment
Communication is Key

Patient Transfers Between Healthcare Locations

- Implement systems to designate patients known to be colonized or infected with a targeted MDRO and to notify receiving healthcare facilities and personnel prior to transfer of such patients within or between facilities

https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html
Public Health Departments and MDROs

Take Steps Now! Public health departments should lead coordination.

- Identify the health care facilities in the area and how they are connected.
- Dedicate staff to improve connections and coordination with health care facilities in the area.
- Work with CDC to use data for action to better prevent infections and improve antibiotic use in health care settings.
- Know the antibiotic resistance threats in the area and state.

SOURCE: CDC Vital Signs, August 2015.
Public Health Departments

• Understand the prevalence or incidence of MDRO in their jurisdiction by performing some form of regional surveillance for these organisms.

• Increase awareness among healthcare facilities of the regional prevalence of MDRO and prevention strategies and initiatives.

• Provide a standardized form for facilities to use during patient transfers, especially between hospitals and long-term care facilities.

• Consider including MDRO infections on your state’s Notifiable Diseases List.

• Include a range of facility types when developing regional MDRO prevention projects.

• Be a resource for healthcare facilities on appropriate infection prevention measures and antimicrobial stewardship

What CDC is Doing: Investments and Action

Since 2016 Congress has appropriated $160 million in investments to for the CDC to fight antimicrobial resistance.

- State level funding
- Healthcare programs to reduce MDRO and HAI’s
- Community actions (education, data, testing, research)
- Environmental Actions (water and soil)
- Food Supply Actions (lab capacity, innovation, data sharing)
- Global Action (collaborating with global partners, investing)
- Lab Capacity Action (expansion of testing and AR Lab Network)
- Innovative Action (research)

CDC Antimicrobial Resistance Laboratory Network

CDC’s Antimicrobial Resistance Laboratory Network (AR Lab Network), established in 2016, provides nationwide lab capacity to rapidly detect antimicrobial resistance and inform local responses to prevent spread and protect people. It closes the gap between local capabilities and the data needed to combat antimicrobial resistance in the U.S.

Core Testing by all regional labs

- Molecular testing to detect colonization of carbapenem-resistant Enterobacterales (CRE).
- Detection of new and emerging threats, like novel carbapenemase genes, and ability to detect changes in known threats, like methicillin resistant Staphylococcus aureus.
- Fungal susceptibility of Candida species to identify emerging resistance. Identification and colonization screening to detect and help prevent spread of Candida auris (C. auris).
- Perform expanded susceptibility testing to determine if new drugs or drug combinations will be effective to treat patients infected with especially rare resistant pathogens.
- Isolates may be used for the CDC and FDA AR Isolate Bank and WGS projects.

https://www.cdc.gov/drugresistance/ar-lab-networks/domestic.html
We have work to do!

Questions?

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.
Resources

- CDC Antibiotic Resistance Threats in the U.S., 2019
- https://www.acpjournals.org/doi/10.7326/M22-3469
- https://www.cdc.gov/hai/organisms/ESBL.html
- https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html
- https://www.cdc.gov/hai/organisms/acinetobacter.html
- Infection Preventionists Fact Sheet
- Laboratory Staff Fact Sheet
- Identification of C. auris
- Screening for C. auris
Additional Resources

- https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html
- https://www.cdc.gov/drugresistance/biggest-threats.html
- https://www.cdc.gov/hai/outbreaks/index.html
- https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html