Multi-Drug Resistant Organisms (MDROs)

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Objectives

At the conclusion of this presentation, participants will be able to:

• Understand which organisms are referred to as multi-drug resistant organisms (MDROs) and are considered to be a threat to residents and our entire healthcare system
• Discuss how to manage residents with MDROs
• Explain the role of the laboratory in alerting nursing staff when an MDRO has been identified so appropriate precautions can be implemented
3 Categories of Concerned Threats³

- The Centers for Disease Control and Prevention (CDC) have prioritized bacteria into 3 categories:

  Urgent – Serious – Concerning

<table>
<thead>
<tr>
<th>URGENT THREAT</th>
<th>SERIOUS THREAT</th>
<th>CONCERNING THREAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. CRE</td>
<td>2. ESBL</td>
<td>2. Erythromycin-resistant Group A <em>Streptococcus</em></td>
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<td></td>
<td>4. VRE</td>
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<td></td>
<td>5. MRSA</td>
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<td>6. Drug-resistant <em>Streptococcus pneumoniae</em> (SP)</td>
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<td>7. Drug-resistant <em>Tuberculosis</em></td>
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<td></td>
<td>8. DR <em>Pseudomonas aeruginosa</em></td>
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<td></td>
<td>9. DR <em>Shigella</em></td>
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<td></td>
<td>10. DR <em>Salmonella Typhi</em></td>
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<td></td>
<td>11. DR non-typhoidal <em>Salmonella</em></td>
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</tbody>
</table>
Minimum Estimates of Morbidity & Mortality from MDRO Infections³

<table>
<thead>
<tr>
<th>MDRO</th>
<th>Infections included in case/death estimates</th>
<th>Estimated annual number of cases in U.S.</th>
<th>Estimated annual number of deaths in U.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>Invasive infections (both healthcare &amp; community)</td>
<td>80,000</td>
<td>11,000</td>
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<tr>
<td>VRE</td>
<td>Healthcare-associated infections (HAI) in hospitalized patients (not in long term care)</td>
<td>20,000</td>
<td>1300</td>
</tr>
<tr>
<td>ESBL</td>
<td>HAI caused by <em>E. coli</em> (EC) and <em>Klebsiella pneumoniae</em> (KP) with hospital onset</td>
<td>26,000</td>
<td>1700</td>
</tr>
<tr>
<td>CRE</td>
<td>HAI caused by EC &amp; KP with onset in hospital patients</td>
<td>9300</td>
<td>610</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> (SP) (full resistance to clinically relevant drugs)</td>
<td>All infections</td>
<td>1,200,000</td>
<td>7000</td>
</tr>
</tbody>
</table>
Defining the Problem

• **MDRO**—multi-drug resistant organisms:
• Microorganisms that are resistant to at least one class of antibiotics or one specific antibiotic
• Present challenges for individual patient management and containment in acute and long term care facilities

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1 Centers for Disease Control. Healthcare infection control practices advisory committee (HICPAC) MDRO Guideline. [http://www.cdc.gov/hicpac/mdro/mdro_2.html](http://www.cdc.gov/hicpac/mdro/mdro_2.html)
• Each year in the U.S., at least 2 million people acquire serious infections with a multi-drug resistant organism (MDRO)

• Almost 250,000 people each year require hospitalization for Clostridium difficile infections alone

• It is estimated about 23,000 people die each year as a direct result of MDRO infections
• Movement of residents between facilities drive antibiotic resistance
• Global problem—bugs without borders
• Many forms of resistance spread quickly
Orange County CDI Collaborative – Facilities

“Connectedness”
**Infection**

- Presence of pathogen
- Organism growth & invasion of host
- Presence of clinical signs & symptoms

**Colonization**

- Presence of microorganism
- No tissue invasion
- Absence of clinical signs & symptoms
The Enemy Bacteria
SIGNIFICANT PATHOGENS

- MRSA (methicillin resistant *Staphylococcus aureus*)
- VRE (vancomycin resistant *Enterococcus*)
- ESBL (extended spectrum beta lactamase)
- ABC (Acinetobacter baumanii complex)
- *Clostridium difficile*
- CRKP (Carbapenem-resistant *Klebsiella pneumoniae*)
  - KPC (*Klebsiella pneumoniae* Carbapenemase)
  - CRE (Carbapenem-resistant *Enterobacteriaceae*)
- NDM1 (New Delhi beta-lactamase)
- mcr1 gene (gene mediated Colistin-resistant *E. coli*)
• *Staphylococcus aureus* is a bacteria carried by healthy people in a variety of body sites (30% on skin, 20-30% in nares)

• One of the most prominent pathogens associated with community, hospital and livestock-associated infections

• Within two years after introduction of Methicillin, resistance was observed

• Transmitted by direct or indirect contact with persons harboring the organism or from the environment

• *Staphylococcus aureus* is a frequent asymptomatic colonizer of humans

• Mild-to-severe skin infections are amongst the most common MRSA related diseases

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• Vancomycin Resistant *Enterococcus (faecalis or faecium)*
• *Enterococci* are commonly found in the intestinal tract of humans
• Can be transmitted through fecal-oral route
• Can cause life threatening infections like endocarditis (heart valves)
• A hearty organism that can survive on environmental surfaces for a long time (5 days to 46 months)

Extended-spectrum beta lactamase-this is an enzyme developed by the organism

Mostly found in gram negative organisms *Enterobacteriaceae* like *E. coli* and *Klebsiella pneumoniae*

This enzyme is carried on plasmids (DNA of the organism) which can be transferred to another organism

This is a mutation whereby an enzyme produced by the organism inactivates certain antibiotics by adding an H₂O molecule (called hydrolysis) e.g., penicillins and cephalosporins

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ACINETOBACTER

- Also called ABC (Acinetobacter baumanii complex)
- This organism is found naturally in the soil and water
- This organism has an inherent resistance to antibiotics
- Outbreaks caused by this organism typically happen in ICUs or sub-acute units
- This organism can live on the skin and can survive on the environment for months
- Acinetobacter infections usually involve organ systems that have a high fluid content, e.g., respiratory tract, urinary tract, peritoneal fluid

CRE NIGHTMARE
next exit
The first case of Carbapenem-resistant *Enterobacteriaceae* (CRE) was identified in the U.S in 2001 in North Carolina.

The director of the CDC, Tom Frieden, has referred to CRE as a “nightmare bacteria”.

According to the CDC, the CRE bacterium are one of the top 3 urgent threats in the US.

According to LAC Public Health CRE is endemic in LA County.

Mortality rates from CRE may be as high as 50%.

Limited treatment options for treating CRE infection.

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Experts believe the main reasons for increase in this resistant strain of organism is due to:

- Over-use or inappropriate use of antibiotics
- Poor hygienic conditions and lack of adequate environmental cleaning and disinfection
- Organisms contain mobile genetic material (plasmids) that contain antibiotic (ATB) resistance genes (easily transferred to other organisms)
- Travel
This map was last updated on February 2015.
WHO IS AT HIGH RISK FOR CRE\textsuperscript{8,10}?

- Most often seen in patients who:
  - Are elderly\textsuperscript{8}
  - Are immuno-compromised
  - Have poor functional status\textsuperscript{10}
  - Have had prolonged stays in healthcare facilities (e.g. intensive care units, long-term acute care hospitals or skilled nursing facilities)
  - Have invasive devices
  - Have had frequent courses of broad-spectrum antibiotics

\textsuperscript{10} Carbapenem-resistant Enterobacteriaceae in Healthcare Settings. https://www.cdc.gov/hai/organisms/cre/
How Easy Is It To Get CRE?

1. Local Short-Stay Hospital
   - Jan has a stroke and is in the hospital. She is stable but needs long-term critical care at another facility.

2. Long-Term Acute Care Hospital
   - Other patients in this facility have CRE. A nurse doesn't wash his hands, and CRE are spread to Jan. She develops a fever and is put on antibiotics without proper testing.

3. Local Short-Stay Hospital
   - Jan becomes unstable and goes back to the hospital, but her new doctors don't know she has CRE. A doctor doesn't wash her hands after treating Jan. CRE is spread to other patients.

How CRE Take Over
1. Lots of germs, 1 or 2 are CRE
2. Antibiotics kill off good germs
3. CRE grow
4. CRE share genetic defenses to make other bacteria resistant

SOURCE: CDC Vital Signs, 2013
• Hand Hygiene
• Contact Precautions
• Education
• Minimizing invasive devices, when appropriate
• Laboratory alert system in place when CRE identified
• Inter-facility communication/identification on admission
• Antimicrobial stewardship
• Environmental cleaning
• Cohorting

• Screening of CRE patients and contacts
• Active surveillance testing
  o Looking at non-clinical or non-identified cases of CRE
  o May be considered for patients coming from a high-risk setting (e.g., ICU) or going to high-risk unit (e.g., subacute)
• Chlorhexadine gluconate (CHG) bathing
  o In Long-term care (LTC), CHG might be used on targeted high-risk residents, or high-risk settings (e.g., sub-acute units)
ADDITIONAL STEPS TO PREVENTION OF TRANSMISSION

• Know CRE trends and prevalence in your community/region and within your own facility\textsuperscript{8,10}
  - Review micro results in your facility for preceding 6-12 months (once CRE detected)\textsuperscript{8,11}
  - Get involved with Public Health in CRE collaboratives\textsuperscript{8,11}

• Establish communication tools (Inter-facility Transfer Form)\textsuperscript{11}
**Positive CRE Results: What Now?**

- **Positive clinical cultures**:  
  - Resident is symptomatic:  
    - Isolate  
    - Physician will treat

- **Positive surveillance culture or point-prevalence culture**:  
  - Resident is asymptomatic:  
    - No ATB should be prescribed  
    - In LTC, may not require isolation (close assessment of resident and surrounding circumstances) refer to your facility policy  
    - Information may be valuable for when resident develops symptoms (earlier implementation of isolation with fewer possible exposures)
**Other MDROs**

*Pseudomonas aeruginosa* has shown be resistant to many antibiotics including carbapenems

- Seldom part of normal flora in humans
- Colonization rates may exceed 50% after hospitalization

- There are multi-drug resistant strains of Tuberculosis (MDR-TB) and with poor compliance to TB drugs can result in extended-drug resistant TB (XDR-TB)

- **Any organism can become an MDRO**
  - If the organism is sensitive to only 2-3 antibiotics this could be considered to be an MDRO

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• It is essential to know when a resident has an MDRO as early as possible
  o Work with your referral sources to provide MDRO information and recent culture results
• Nurses should be trained on how to read culture and sensitivity reports as soon as they are available
• Work with your laboratory provider to develop alert systems when MDRO identified
**Message Alert for MDRO**

Organism #1: *Escherichia coli* (escocol)

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Nalidixic Acid</td>
<td>Pos</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Imipenem</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Piperacillin/Tazobac</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>&gt;20</td>
</tr>
</tbody>
</table>

**Message Alert to Consider UTI vs ASB**

The majority of positive urine cultures (non-catheter) from residents in long-term care facilities represent asymptomatic bacteruria with no clinical signs of infection. Studies have shown that 30-50% of elderly long-term care residents can have a positive urine culture - and pyuria - without any clinical evidence of infection. According to recent guidelines by multiple clinical societies, antibiotic therapy is not recommended without clinical signs localizing to the urinary tract.
- NDM1 is a carbapenamase-producing organism
- Found in *Klebsiella pneumoniae* and *E.coli*
- First found to be associated with exposure to healthcare systems in India or Pakistan
- First reported in Sweden in 2009
- Now cases have been reported in over 15 countries worldwide
- Easily transmissible on plasmids
- From 2009-2011, 9 cases were reported in U.S.
  - 4 cases in California and other cases reported in Illinois, Maryland, Massachusetts, and Virginia

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Mcr1-**Escherichia coli**

- First case identified in Pennsylvania May 2016
  - Found in *Escherichia coli* (*E. coli*) in urine
- Second case identified in New York in June 2016
  - This patient had undergone surgery within past year
- Plasmid-mediated resistance gene in *E. coli* to Colistin
  - **This is the last-resort drug for CRE**
  - Has also been found in other bacteria such as *Salmonella*, *Shigella* and *Klebsiella pneumoniae*
  - This resistant gene has been found in food animals in U.S in June 2016 (pigs)

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21 Sheng- Riley MM. The emergence of mcr-1 in humans and animals: What IPs need to know. Prevention Strategist Fall 2016;Vol 9(3):pp 46-49
**Management of MDROs in LTC**

- Enforce good hand hygiene for **ALL!** (audit)
- Implement Transmission-based Isolation Precautions when MDRO is suspected or confirmed
- Educate staff and visitors on isolation needs
- Validate that precautions are being used properly (audit)
- Cohorting of residents and staff may be needed
- Once MDRO is identified, antibiotic stewardship for that resident is essential
- In LTC, once a resident is colonized consider appropriateness for discontinuation of isolation
• Minimize invasive devices when possible
• In LTC, isolation may need to be individualized for each resident’s situation
• One size does NOT fit all for LTC residents
• Environmental cleaning and disinfecting properly is essential (audit)
  – Not just the environment but all non-critical care equipment that may be used on multiple residents
• Develop good communication between acute care and LTC facilities (inter-facility transfer forms)
• On-going Education!
Core Actions to Fight MDRO Infections

Infection Control
- Preventing infections
- Controlling spread of infections

Tracking
- Surveillance program that tracks bacteria

Antibiotic Stewardship
- Improve use of antibiotics
JUDICIOUS USE OF ANTIBIOTICS

Antibiotics?

Image credit: CNS: citizen-news.org
Questions are guaranteed in life; Answers aren't.