MULTIDRUG RESISTANCE ORGANISMS
AND UNDERSTANDING ENHANCED BARRIER PRECAUTIONS

Ashley Jackson, BSMT, MPH, CIC
Clinical Infection Prevention Consultant
February 10, 2021
OVERVIEW

- Discuss the burden of multidrug resistance organisms in healthcare settings
- Discuss the clinical importance of MDROs in long term and congregate care settings.
- Discuss how antibiotic resistance occurs in bacteria and how they are identified
- Identify common multidrug resistance organisms
- Discuss infection prevention measures to prevent MDROs
- Overview of Enhanced Barrier precautions
MULTIDRUG RESISTANT ORGANISMS

- **MDRO**- Organisms that develop resistance to one or more classes of antibiotics. This may result in typical antibiotic regimens not working or becoming less effective.

- Cause infections and/or colonization
- Infections caused by MDROs are:
  - More difficult to treat
  - Require more toxic antibiotics to treat
  - Often have poor patient outcomes
  - Are easily transmitted in healthcare settings
# CLASSES OF ANTIBIOTICS

## Antibiotic Table

<table>
<thead>
<tr>
<th>Class I Penicillins</th>
<th>Class II Cephalosporins</th>
<th>Class III Carbapenems</th>
<th>Class IV Monobactams</th>
<th>GROUP II Class V Aminoglycosides</th>
<th>GROUP III Class VI Quinolones*</th>
<th>GROUP IV Antimetabolites</th>
<th>GROUP V Glycylines</th>
<th>GROUP VI Class IX Tetracyclines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Cefazolin</td>
<td>Imipenem</td>
<td>Aztreonam</td>
<td>Gentamicin</td>
<td>Ciprofloxacin</td>
<td>Trimethoprim-</td>
<td>Tigecycline</td>
<td>Minocycline</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Cefalexin</td>
<td>Meropenem</td>
<td>Tobramycin</td>
<td>Tetracycline</td>
<td>Levofloxacin</td>
<td>Sulfamethoxazole</td>
<td>Tetracycline</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Cefalexin</td>
<td>Doripenem</td>
<td>Amikacin</td>
<td></td>
<td>Moxifloxacin</td>
<td></td>
<td></td>
<td>Doxycycline</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>Cefoxitin</td>
<td>Ertapenem</td>
<td>Netilmicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin</td>
<td>Cefotaxime</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin-</td>
<td>Ceftriaxone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>taxobactam</td>
<td>Ceftazidime</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticarcillin-</td>
<td>Cefepime</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>clavulanate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sulbactam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Resistance to one agent implies resistance to all agents

Other Classes include:
- Glycopeptides: Vancomycin
- Lincosamides: Clindamycin, Lincomycin
- Lipopeptides: Daptomycin
- Macrolides: Azithromycin, Erythromycin
- Polypeptides: Bacitracin, Colistin
- Linezolid (Zyvox)
- Metronidazole (Flagyl)
- Mupirocin (Bactroban)
MDROs cause an increase of mortality, healthcare costs, and length of stays in our healthcare systems.

Estimates of economic costs vary but they ranged as high as 20 BILLION dollars in direct healthcare costs.

https://www.cdc.gov/antibiotic-use/community/about/antibiotic-resistance-faqs.html
RISK FACTORS FOR DEVELOPING A MDRO

- Duration of hospitalization
- High rates of transfer in and between hospitals
- Local institution risk factors
- **Long term care facilities**
- Intensive care units
- High rate of device utilization
- Colonization
- Prior antibiotic use

“Age, comorbid illnesses, invasive medical devices, frequent antibiotic exposure, and dependence on healthcare workers, in the setting of communal living, all serve to increase the risk of nursing home residents becoming colonized or infected with healthcare-acquired bacterial pathogens.”

(Dumyati, et. Al., 2017)
MULTIDRUG RESISTANT ORGANISMS

Cause infections
- More difficult to treat
- Require more toxic antibiotics to treat
- Often have poor patient outcomes
- Are easily transmitted in healthcare settings

Colonization
- Colonization means organisms live on or in the body without having an active infection.
- CDC notes up to 50% of nursing home residents are colonized with MDROs.
- MDRO colonization can increase the individual’s risk for developing an infection.
- ** MDRO-colonized residents serve as a source of transmission to others ***
MDRO colonization can persist for long periods of time (e.g., months) and result in silent transmission.

Common colonization sites for MDROs include:
- Nares
- Axilla
- Groin
- Rectum
HOW DOES ANTIBIOTIC RESISTANCE OCCUR?

• Antibiotic resistance: the ability of bacteria to resist the killing effects of antibiotics.
• Resistant bacteria continue to multiply and can spread resistance to other bacteria.
Examples of How Antibiotic Resistance Spreads

Animals get antibiotics and develop resistant bacteria in their guts.

Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.

Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.

Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.

Vegetable Farm

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

George gets antibiotics and develops resistant bacteria in his gut.

George stays at home and in the general community. Spreads resistant bacteria.

George gets care at a hospital, nursing home or other inpatient care facility.

Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.

Resistant bacteria spread to other patients from surfaces within the healthcare facility.

Patients go home.

Healthcare Facility
MECHANISMS OF RESISTANCE

Germs develop new cell processes that avoid using the antibiotic’s target.

Germs change or destroy the antibiotics with enzymes, proteins that break down the drug.

Germs restrict access by changing the entryways or limiting the number of entryways.

Germs change the antibiotic’s target so the drug can no longer fit and do its job.

Germs get rid of antibiotics using pumps.

TYPES OF MDROS

How do Antimicrobial-resistant Pathogens Emerge?
- Antimicrobial use
- Failure to properly implement infection control practices

Biofilm
- Antibiotics have difficulties penetrating biofilm

[Image of a micrograph showing a biofilm structure with labels for scale and imaging conditions: Acc. V 10.0 kV, Spot Mag. 3.0, Det. SE, WD 20.0 μm, Exp. 1648x]
HOW MDROS ARE IDENTIFIED

- When a specimen (urine, wound, etc.) gets collected, it is sent to the lab to be plated and then incubated so organisms can grow.

- After it grows and a pathogen is determined, it is set up for antibiotic sensitivity testing which is mostly automated.
HOW MDROS ARE IDENTIFIED

Kirby Baur
- Antibiotic impregnated disc
- Zone of inhibition

Minimal inhibitory concentration (MIC) – lowest concentration of drug that still can inhibit microbial growth.

The MIC will determine whether the bacteria is resistant to the tested antibiotic.
OVERVIEW OF MDROS

- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-resistant Enterococcus spp. (VRE)
- Extended spectrum Beta-lactamase producing Enterobacteriaceae (ESBL)
- Carbapenem Resistant *Acinetobacter*
- Carbapenem Resistant Enterobacteriaceae (CRE)
- *Clostridium difficile*
- *Candida auris*
TYPES OF MDROS- MRSA

- Gram positive cocci -resistant to Oxacillin and beta-lactam antibiotics
- *Staphylococcus aureus* - commonly found on the skin or in the noses of healthy people
  - According to CDC:
    - 33% of people are colonized with *Staphylococcus*
    - Only about 2% colonized with MRSA

- MRSA can cause serious infections
  - Wound
  - Blood stream (sepsis)
  - Pneumonia
Can cause blood, urine, and surgical site infections

- *Enterococcus faecalis, Enterococcus faecium*

- Nearly all VRE infections happen in patients with healthcare exposures

- Long term care residents are a risk
Extended Spectrum β-lactamase (ESβL) producing GNR

- Enzyme conferring bacterial resistance to penicillins, first-, second, and third-generation cephalosporins, and aztreonam
Acinetobacter is already a very resistant organism (intrinsically resistance). Resistance to carbapenems further reduces patient treatment options.

Acinetobacter can contaminate healthcare facility surfaces and shared medical equipment. If not addressed through infection control measures, including rigorous cleaning and disinfection, outbreaks in hospitals and nursing homes can occur.
TYPES OF MDROS - CRE

- High mortality - 30-70%
- Double the mortality of MRSA
- Resistant to almost all antibiotics
- Colistin / Tigecycline can be used to treat but these can be toxic
# ENTEROBACTERIACEAE

## Table 1. Genera of Enterobacteriaceae

<table>
<thead>
<tr>
<th>Common Genera of Enterobacteriaceae</th>
<th>Other Genera of Enterobacteriaceae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia</td>
<td>Klebsiella</td>
</tr>
<tr>
<td></td>
<td>Providencia</td>
</tr>
<tr>
<td></td>
<td>Serratia</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>Proteus</td>
</tr>
<tr>
<td></td>
<td>Salmonella</td>
</tr>
<tr>
<td></td>
<td>Shigella</td>
</tr>
<tr>
<td>Alishewanella</td>
<td>Cedexea</td>
</tr>
<tr>
<td>Alterococcus</td>
<td>Citrobacter</td>
</tr>
<tr>
<td>Aquamonas</td>
<td>Cronobacter</td>
</tr>
<tr>
<td>Aranicola</td>
<td>Dickeya</td>
</tr>
<tr>
<td>Arsenophonus</td>
<td>Edwardsiella</td>
</tr>
<tr>
<td>Azotivirga</td>
<td>Erwinia</td>
</tr>
<tr>
<td>Blochmannia</td>
<td>Ewingella</td>
</tr>
<tr>
<td>Brenneria</td>
<td>Grimontella</td>
</tr>
<tr>
<td>Buchnera</td>
<td>Hafnia</td>
</tr>
<tr>
<td>Budvicia</td>
<td>Kluyvera</td>
</tr>
<tr>
<td>Buttiauxella</td>
<td>Leclercia</td>
</tr>
<tr>
<td></td>
<td>Leminorella</td>
</tr>
<tr>
<td></td>
<td>Moellerella</td>
</tr>
<tr>
<td></td>
<td>Morganella</td>
</tr>
<tr>
<td></td>
<td>Obesumbacterium</td>
</tr>
<tr>
<td></td>
<td>Pantoea</td>
</tr>
<tr>
<td></td>
<td>Pectobacterium</td>
</tr>
<tr>
<td></td>
<td>Phlomobacter</td>
</tr>
<tr>
<td></td>
<td>Photorhabdus</td>
</tr>
<tr>
<td></td>
<td>Poodoomamaamaana</td>
</tr>
<tr>
<td></td>
<td>Plesiomonas</td>
</tr>
<tr>
<td></td>
<td>Pragia</td>
</tr>
<tr>
<td></td>
<td>Rahnella</td>
</tr>
<tr>
<td></td>
<td>Raoulzella</td>
</tr>
<tr>
<td></td>
<td>Samsonia</td>
</tr>
<tr>
<td></td>
<td>Sodalis</td>
</tr>
<tr>
<td></td>
<td>Tatumella</td>
</tr>
<tr>
<td></td>
<td>Trabulsiaella</td>
</tr>
<tr>
<td></td>
<td>Wigglesworthia</td>
</tr>
<tr>
<td></td>
<td>Xenorhabdus</td>
</tr>
<tr>
<td></td>
<td>Yersinia</td>
</tr>
<tr>
<td></td>
<td>Yokenella</td>
</tr>
</tbody>
</table>
TYPES OF MDROS - CRE

CRE- Any Enterobacteriaceae resistant to imipenem, meropenem, doripenem, or ertapenem (last resort antibiotics)

OR by production of a carbapenemase (KPC, NDM, VIM, IMP, OXA-48)** demonstrated using a recognized test (e.g. polymerase chain reaction, metallo-β-lactamase test, modified-Hodge test, Carba-NP).

Mechanisms of resistance

- Mediated by plasmids (mobile genetic element)
- Enzymes that inactivate carbapenems
  - *Klebsiella pneumoniae carbapenemase (KPC)*
REPORTING CRE

- Identification of CRE from a clinical specimen associated with either infection or colonization, including all susceptibility results and all phenotypic or molecular test results.

- For the purpose of reporting, CRE are defined as: (1) Enterobacter spp, E.coli or Klebsiella spp positive for a known carbapenemase resistance mechanism or positive on a phenotypic test for carbapenemase production; or (2) Enterobacter spp, E.coli or Klebsiella spp resistant to any carbapenem in the absence of carbapenemase resistance mechanism testing or phenotypic testing for carbapenemase production.
More than half of C. difficile cases among long-term care facility residents happen in those who were recently hospitalized.

From 2011 to 2015, CDC noted decreases in C. difficile cases in people 65 years or older in long-term care facilities.

Although there’s a decrease in healthcare associated C. diff, there hasn’t been a decrease in community acquired C. diff.
Candida auris is an emerging multidrug-resistant yeast (a type of fungus).

- First discovered in 2009.
- It can cause severe infections and spreads easily between hospitalized patients and nursing home residents.
Pan-resistant organisms:

Resistant to all current antibacterial agents

- Acinetobacter
- Klebsiella pneumonia
- Pseudomonas aeruginosa
INFECTION PREVENTION MEASURES

- All MDROs
  - Staff education
  - Risk assessment to identify high risk patients
  - Laboratory notifications/ communication with outside facilities.
  - Hand hygiene
  - **Barrier precautions (Contact or Enhanced barrier precautions)**
  - Antibiotic stewardship
  - Environmental cleaning
  - Cohort residents if necessary
UNDERSTANDING CONTACT AND ENHANCED BARRIER PRECAUTIONS

- CDC implemented Enhanced Barrier precautions for long term care.
- Enhanced barrier precautions does not replace existing guidance regarding use of Contact Precautions for other pathogens (e.g., *Clostridioides difficile*, norovirus) in nursing homes.

WHY CHANGE?

- “Focusing only on residents with active infection fails to address the continued risk of transmission from residents with MDRO colonization, which can persist for long periods of time (e.g., months), and result in the silent spread of MDROs”.
- “With the need for an effective response to the detection of serious antibiotic resistance threats, there is growing evidence that current implementation of Contact precautions in nursing homes is not adequate for prevention of MDRO transmission”.
CONTACT ISOLATION

- **Contact Precautions:**
  - All residents with an MDRO when there is acute diarrhea, draining wounds or other sites of secretions/excretions that cannot be contained or covered
  - On units or in facilities where ongoing transmission is documented or suspected
  - *C. difficile* infection
  - Norovirus
  - Shingles when resident is immunocompromised, and vesicles cannot be covered
  - Other conditions as noted in Appendix A- Type and Duration of Precautions Recommended
  - For Selected Infections and Conditions
  - Gown and gloves upon ANY room entry
  - Room restriction except for medically necessary care
2006 CDC MDRO GUIDELINES
PRECAUTIONS IN LONG-TERM CARE

V.A.5.c.ii.1 "For relatively healthy residents (e.g., mainly independent) follow Standard Precautions making sure that gloves and gowns are used for contact with uncontrolled secretions, pressure ulcers, draining wound, stool incontinence, and ostomy tubes/bags."

V.A.5.c.ii.2. For ill residents (e.g., those totally dependent upon healthcare personnel for healthcare and activities of daily living...) and for those residents whose infected secretions or drainage cannot be contained, use Contact Precautions, in addition to Standard Precautions."

V.A.5.c.iii. For MDRO colonized or infected patients without draining wounds, diarrhea, or uncontrolled secretions, establish ranges of permitted ambulation, socialization, and use of common areas based on their risk to other patients and on the ability of the colonized or infected patients to observe proper hand hygiene and other recommended precautions to contain secretions and excretions.

HICPAC, Management of MDROs in healthcare settings, 2006
RECOMMENDATIONS

RESIDENT CHARACTERISTICS

Five C’s
- Cognitive function (understands directions)
- Cooperative (willing and able to follow directions)
- Continent (of urine or stool)
- Contained (secretions, excretions, or wounds)
- Cleanliness (capacity for personal hygiene)

(Kellar M. APIC Infection Connection. Fall 2010 ed.)

<table>
<thead>
<tr>
<th>Component</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal Protective Equipment (PPE)</td>
<td></td>
</tr>
<tr>
<td>Gloves</td>
<td>For touching blood, body fluids, secretions, excretions, contaminated items; for touching mucous membranes and non-intact skin</td>
</tr>
<tr>
<td>Gown</td>
<td>During procedures and patient-care activities when contact of clothing/exposed skin with blood/body fluids, secretions, and excretions is anticipated</td>
</tr>
<tr>
<td>Mask, eye protection</td>
<td>During procedures and patient-care activities likely to generate splashes or sprays of blood, body fluids, secretions, especially suctioning, endotracheal intubation</td>
</tr>
</tbody>
</table>
ENHANCED BARRIER PRECAUTIONS

- A type of precaution between standard and contact precautions
- Expands the use of PPE beyond situations in which exposure to blood and body fluids is anticipated (i.e. Standard Precautions)
- Refers to the use of gown and gloves during high-contact resident care activities that provide opportunities for transfer of MDROs to staff hands and clothing

As of July 2019, Novel or Targeted MDROs are defined as:

- Pan-resistant organisms,
- Carbapenemase-producing Enterobacteriaceae,
- Carbapenemase-producing *Pseudomonas* spp.,
- Carbapenemase-producing *Acinetobacter baumannii*, and
- *Candida auris*
ENHANCED BARRIER PRECAUTIONS

- 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

Gown and gloves would not be required for resident care activities other than those listed above, unless otherwise necessary for adherence to Standard Precautions. Residents are not restricted to their rooms or limited from participation in group activities.
CONTACT AND ENHANCED BARRIER PRECAUTIONS

- Contact or Enhanced Barrier Precautions:
- Post clear signage on the door or wall outside the room
- Make PPE available immediately outside the room
- Ensure access to alcohol-based hand rub in every resident room (ideally inside and outside)
- Trash can available for PPE disposal
- Periodic monitoring and assessment of compliance
- Provide education to residents, family and visitors
- Adherence to other measures including hand hygiene, environmental cleaning and cleaning, disinfection of medical devices
QUESTIONS?

- Questions are typed in the Q&A box
REFERENCES

CDC. *Implementation of Personal Protective Equipment (PPE) in Nursing Homes to Prevent Spread of Novel or Targeted Multidrug-resistant Organisms (MDROs).* Retrieved from https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html#anchor_1561470277


Kellar M. *APIC Infection Connection.* Fall 2010 ed.


Steider, Katie. The Good, the bad and the resistant: identifying and responding to multidrug-resistant organisms in your facility. Presentation.

Images provided by CDC’s Public Health Image Library: https://phil.cdc.gov/default.aspx