Multi-Drug Resistant Organisms (MDROs)

Multi-Drug Resistant Organisms (MDRO)

Infection Prevention & Control
Boot Camp For Long-Term Care Facility
Infection Preventionists

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
- Explain the role of the laboratory in alerting nursing staff when an MDRO has been identified so appropriate precautions can be implemented
- Discuss how MDROs are transmitted in long-term care (LTC) facilities

3 Categories of Concerned Threats

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

Urgent – Serious – Concerning

Urgent Threat	Serious Threat	Concerning Threat
1. *Clostridium difficile* 2. CRE 3. Drug-resistant *Neisseria gonorrhoeae*	1. Multi-drug resistant *Acinetobacter* 2. ESBL 3. Drug-resistant (DR) *Campylobacter* 4. VRE 5. MRSA 6. Drug-resistant *Streptococcous pneumoniae* (SP) 7. Drug-resistant *Tuberculosis* 8. DR *Psuedomonas aeruginosa* 9. DR Shigella 10. DR *Salmonella Typhi* 11. DR non-typoidal *Salmonella*	1. Vancomycin-resistant *Staphylococcus aureus* (VRSA) 2. Erythromycin-resistant *Group A Streptococcus* 3. Clindamycin-resistant *Group B Streptococcus*

Antibiotic Resistance Threats in the United States, 2013. http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf

MINIMUM ESTIMATES OF MORBIDITY & MORTALITY FROM MDRO INFECTIONS[3]

MDRO	INFECTIONS INCLUDED IN CASE/DEATH ESTIMATES	ESTIMATED ANNUAL NUMBER OF CASES IN U.S.	ESTIMATED ANNUAL NUMBER OF DEATHS IN U.S.
MRSA	Invasive infections (both healthcare & community)	80,000	11,000
VRE	Healthcare-associated infections (HAI) in hospitalized patients (not in long term care)	20,000	1300
ESBL	HAI caused by *E.coli* (EC) and *Klebsiella pneuoniae* (KP) with hospital onset	26,000	1700
CRE	HAI caused by EC & KP with onset in hospital patients	9300	610
***Streptococcus pneumoniae* (SP) (full resistance to clinically relevant drugs)**	All infections	1,200,000	7000

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

[1] Centers for Disease Control. Healthcare infection control practices advisory committee (HICPAC) MDRO Guideline. http://www.cdc.gov/hicpac/mdro/mdro_2.html

BACKGROUND

- 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
- Global problem-bugs without borders
- Many forms of resistance spread quickly

[2] Centers for Disease Control. Antibiotic Resistance Threats in the United States. 2013. http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

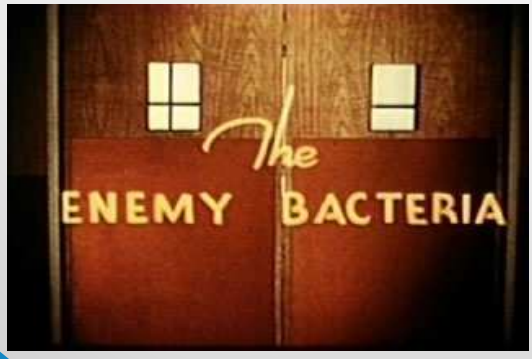
Multi-Drug Resistant Organisms (MDROs)

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



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*)

Multi-Drug Resistant Organisms (MDROs)

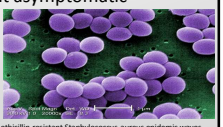
Mechanisms of Antibiotic Resistance

- Drug destruction by enzyme within organism (inactivation of drug)
- Alteration of drug receptor/target sites
- Decreased drug permeability or active efflux of the antibiotic
- Chromosomal drug resistance occurs by spontaneous mutation in the gene locus that controls susceptibility to a drug

[3] Medscape. Insights into Antibiotic Resistance Through Metagenomic Approaches. http://www.medscape/.com/viewarticle/715178_2

MRSA

- *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



[4] Chatterjee SS, Otto M. Improved understanding of factors driving methicillin-resistant Staphylococcus aureus epidemic waves. Clinical Epidemiology.2013;:205-217.https://www.ncbi.nlm.gov/pmc/articles/PMC3707418/

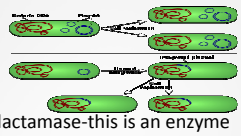
VRE

- Vancomycin Resistant *Enterococcus* (*faecalis* or *faecium*)
- *Enteroccci* 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)

[5] Centers for Disease Control. Healthcare associated infections - https://www.cdc.gov/HAI/organisms/vre/vre.html

Multi-Drug Resistant Organisms (MDROs)

ESBL



- Extended-spectrum beta lactamase-this is an enzyme developed by the organism
- Mostly found in gram negative organisms *enterobacteriacea* 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 H_2O molecule (called hydrolysis) e.g., penicillins and cephalosporins

[6] DeBusscher J, Zhang L, Buxton M, et al. Persistent extended-spectrum B-Lactamase urinary tract infection. Emerging Infectious Diseases 2009. November. http://wwwnc.cdc.gov/eid/article/15/11/09-1465

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 happens 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

[7] Cunha BA, Bronze MS, et al. Acinetobacter. Medscape. http://emedicine.medscape.com/article/215691-overview

Multi-Drug Resistant Organisms (MDROs)

Background

- The first case of Carbapenem-resistant *Enterobacteriaceae* (CRE) was identified in the U.S in 2001 in North Carolina[a]
- 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[a]
- According to LAC Public Health CRE is endemic in LA County
- Mortality rates from CRE may be as high as 50%[8,9]
- Limited treatment options for treating CRE infection[8,9]

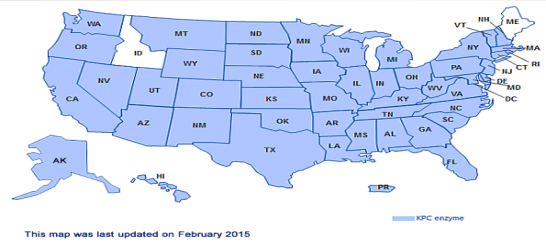
[a] Carbapenem-resistant Enterobacteriaceae (CRE) Control and Prevention Toolkit. http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/cre-toolkit/creindex.html

[8] Watkins RR, Bonomo RA. Increasing prevalence of carbapenem-resistant Enterobacteriacea and strategies to avert a looming crisis. Expert Review of Anti-Infective Therapy 2013;11(8):543-545 http://www.tandfonline.com/doi/pdf/10.1586/eri.13.42

Background (continued)

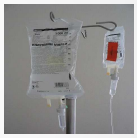
- Experts believe the main reasons for increase in this resistant strain of organism is due to[9]:
  - Over-use or inappropriate use of antibiotics
  - Poor hygienic conditions and lack of adequate environmental cleaning and disinfection
  - Organisms contain mobile genetic material (plasmids) that contain antibiotic (ATB) resistance genes (easily transferred to other organisms)
  - Travel

CRE Cases Reported to CDC by February 2015



Centers for Disease Control and Prevention. Healthcare-Associated Infections (HAI). Tracking CRE. http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html.

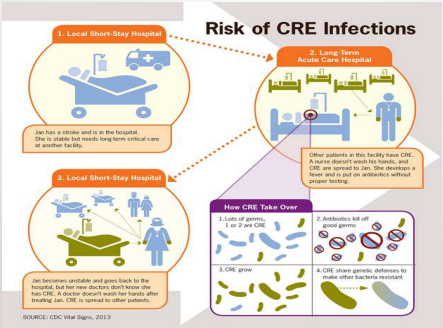
WHO IS AT HIGH RISK FOR CRE[8,10]?



- Most often seen in patients who:
  - Are elderly [8]
  - Are immuno-compromised
  - Have poor functional status[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

[10] Carbapenem-resistant Enterobacteriacea in Healthcare Settings. http://www.cdc.gov/hai/organisms/cre/

HOW EASY IS IT TO GET CRE?



CDC TOOLKIT FOR CRE[8,11]

- 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

[11] Facility Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE). November 2015 Update- CRE Toolkit.

CDC TOOLKIT FOR CRE[8,11] (continued)

- Screening of CRE patients and contacts
- Active surveillance testing
  - Looking at non-clinical or non-identified cases of CRE
  - 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
  - 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[8,10]
  - Review micro results in your facility for preceding 6-12 months (once CRE detected)[8,11]
  - Get involved with Public Health in CRE collaboratives[8,11]
- Establish communication tools (Inter-facility Transfer Form)[11]

Microsoft Office 2013 Clipart

Microsoft Office 2013 Clipart

POSITIVE CRE RESULTS: WHAT NOW?

Educate

- Positive clinical cultures[11]:
  - Resident is symptomatic:
    - Isolate
    - Physician will treat
- Positive surveillance culture or point-prevalence culture[11]:
  - 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)

CLOSTRIDIUM DIFFICILE

BACKGROUND

- CDC reports that 94% of *Clostridium difficile* infection(CDI) cases had recent exposure to a healthcare setting[12]
- According to CDC estimates, *Clostridium difficile* (CD) causes more than 60% of the 23,000 patient deaths from antibiotic resistant organisms annually[13]
- Within past decade, we have seen patient mortality from CDI skyrocket more than 400% with the emergence of hypervirulent strains of CDI (NAP1)[14]
- CD is the #1 urgent threat bacteria, according to CDC
- Annual economic costs of CDI estimated at up to $20 billion in the U.S. alone[15]

12 Szymczak T. Clostridium difficile prevention; expanding our awareness & prevention efforts
13 Jarvis, WR, et al. National point prevalence of Clostridium difficile in U.S. healthcare facility in patients. AJIC, May 2009
14 Centers for Disease Control-Antibiotic resistant threats in the U.S., 2013. http://www.cdc.gov/drugresistance/threat-report
15 Kyle L, et al. Healthcare costs and mortality associated with nosocomial diarrhea due to CDI. 2002;34:346-53

CLOSTRIDIUM DIFFICILE

- CD is a gram positive anaerobic bacillus that produces toxins (toxin A and B)
  - Toxins irritate the intestines and causes diarrhea
  - Can cause toxic megacolon and death
- Hypervirulent CD strain-BI/NAP1/027
- CD produces spores that can survive on the environment for months (up to 5-6 months)
- Most common cause is use of antibiotics
  - Diarrhea can develop up to 8 weeks after antibiotic therapy

[16] APIC Implementation Guide. Guide to preventing *Clostridium difficile* infections. 2013. http://www.apic.org/Resource_/TinyMceFileManager/Guidelines/CDI/CDI-IMPLG-FINAL.pdf

TRANSMISSION[16]

- Transmission is through fecal-oral route
- Can be transmitted through environmental surfaces or contaminated equipment
- Spores continue to shed after CDI is resolved
- Experts estimate that 20% of LTC residents who have CDI can remain colonized

RISK FACTORS FOR CDI

- Elderly individuals
- Age-related immune senescence
- Comorbidities
- Recent hospitalization or extended stay in a healthcare facility
- Recent use of antibiotics
- Use of proton pump inhibitors (PPI)
- Immuno-suppressive medications
- Vitamin D deficiencies
- Crohn's Disease or irritable bowel disorders

[17] Ghose C. Clostridium difficile infection in the twenty-first century. Emerging Microbes and Infections (2013) 2, e62; doi:10.1038/emi.2013. Published September 18, 2013. http://www.nature.com/emi/journal/v2/n9/full/emi201362a.html

CLOSTRIDIUM DIFFICILE INFECTION DEFINITION

- McGeer's Criteria for *Clostridium difficile* infection, both criteria 1 and 2 must be present:
  - One of the following criteria:
    - Diarrhea: 3 or more liquid or watery stools above what is normal for the resident within 24-hour period
    - Presence of toxic mega-colon (documented by x-ray)
  - One of the following diagnostic sub-criteria:
    - Stool sample with positive results for toxins
    - Pseudomembranous colitis identified during endoscopic exam or surgery

[18] Stone N, et al. Surveillance definitions of infection in long-term care facilities: Revisiting the McGeer criteria, Infection Control & Hospital Epidemiology, Volume 33, October 2012.

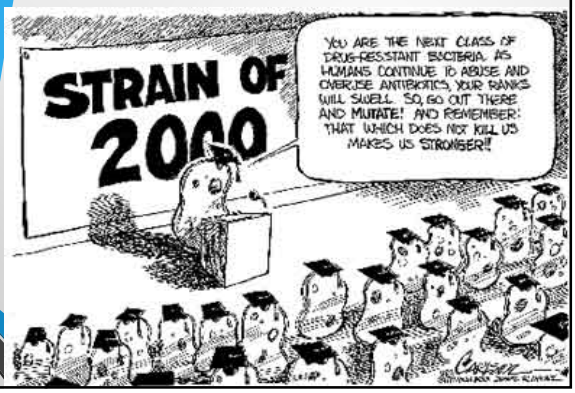
Multi-Drug Resistant Organisms (MDROs)

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

19 Lister P, Wolter DJ, Hanson ND. Antibacterial-resistant Pseudomonas aeruginosa: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clinical Microbiology Review 2009:October-22(4):582-610. https://pubs.asm.org/jcm/article/PMC2772362

Bacteria Continue to Mutate



New Delhi Metallo-beta-lactamase 1

- 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 the 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

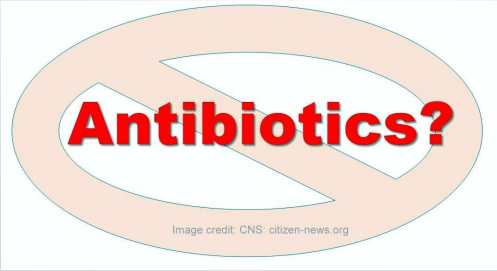
[iii] Rasheed JK, Kitchel B, Zhu W, et al. New delhi metallo-B-lactamase-producing enterobacteriacea, United States. Emerging Infectious Diseases Volume 19 (6):June 2013. http://wwwnc.cdc.gov/eid/article/19/6/12-1515

MCR1-*ECHERICHIA COLI*

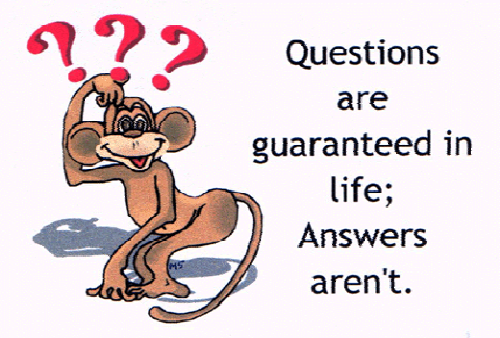
- First case identified in Pennsylvania May 2016
  - Found in *Echerichia coli* (*E. coli*) in urine
- Second case identified in New York in June 2016
  - This patient had undergone surgery within past year
- Plasmid-mediated resistance gene in *E. coli* to Colistin
  - **This is the last-resort drug 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)

[21] Sheng- Riley MM. The emergence of mcr-1in humans and animals: What IPs need to know. Prevention Strategist Fall 2016;Vol9(3):pp 46-49

JUDICIOUS USE OF ANTIBIOTICS



ANY QUESTIONS??



Multi-Drug Resistant Organisms (MDROs)

Four Core Actions to Fight MDRO Infections[3]

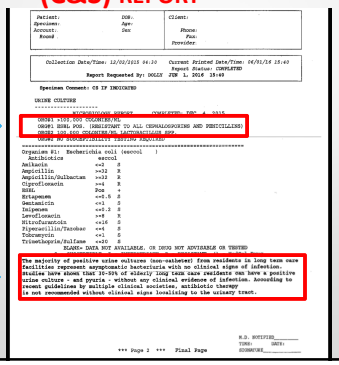
- Preventing infections and preventing the spread of resistance (Infection control practices)
- Tracking resistant bacteria (surveillance activities)
- Improving the use of antibiotics (stewardship program)
- Promoting the development of new antibiotics and developing new diagnostic tests for resistant bacteria (e.g. PCR tests with more timely turnaround-time)

Both Clipart purchased from Adobe Stock June 2016

Sample of a urine culture & sensitivity (C&S) report

Message Alert For MDRO

Message alert to consider UTI vs ASB



Patient: DOB:
Specimen: Age:
Account: Sex
Room

Client:
Phone:
Fax:
Provider:

Collection Date/Time: 12/02/2015 04:30 Current Printed Date/Time: 06/01/16 15:40
Report Status: COMPLETED
Report Requested By: DOLLS JUN 1, 2016 15:40

Specimen Comment: CS IF INDICATED

URINE CULTURE

MICROBIOLOGY RESULT COMPLETED: DEC 4, 2015

ORD#1 -191,000 COLONIES/ML
ORG#1 ESBL POS. (RESISTANT TO ALL CEPHALOSPORINS AND PENICILLIN)
ORG#1 >10,000 COLONIES/ML LACTOBACILLUS SPP.

ORG#1 NO SUSCEPTIBILITY TESTING REQUIRED

Organism #1: Escherichia coli (escoli)

Antibiotics	escoli	
Ampicillin	>32	R
Amoxicillin	>32	R
Amoxicillin/Sulbactam	>32	R
Ciprofloxacin	>4	R
ESBL	Pos	+
Ertapenem	<=0.5	S
Gentamicin	<=1	S
Imipenem	<=0.3	S
Levofloxacin	>4	R
Nitrofurantoin	<=16	S
Piperacillin/Tazobac	<=4	S
Tobramycin	<=1	S
Trimethoprim/Sulfame	>=20	S

PLEASE: DATA NOT AVAILABLE, OR DRUG NOT ADVISABLE OR TESTED

The majority of positive urine cultures (non-catheter) from residents in long term care facilities represent asymptomatic bacteriuria 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.

M.D. NOTIFIED_____
TIME: DATE:
SIGNATURE_____

*** Page 2 *** Final Page