Epidemiology and Prevention of *C. difficile* and Multidrug-resistant Organisms

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Objectives

- Review the prevalence and risk factors for *C. difficile* infection (CDI) and multidrug-resistant organisms (MDROs)
- Describe emerging antibiotic resistance (AR) threats and lessons learned from the CDC containment efforts
- Identify strategies to detect and prevent the spread of AR pathogens in nursing homes
What’s in a name? Introducing *Clostridiodes difficile*

Reclassification of *Clostridium difficile* as *Clostridioides difficile* (Hall and O’Toole 1935) Prévot 1938.

Lawson PA¹, Citron DM², Tyrrell KL², Finegold SM³.

Abstract

The recent proposal by Lawson and Rainey (2015) to restrict the genus *Clostridium* to *Clostridium butyricum* and related species has ramifications for the members of the genera that fall outside this clade that should not be considered as *Clostridium* sensu stricto. One such organism of profound medical importance is *Clostridioides difficile* that is a major cause of hospital-acquired diarrhea and mortality in individuals. Based on 16S rRNA gene sequence analysis, the closest relative of *Clostridium difficile* is *Clostridium mangenotii* with a 94.7% similarity value and both are located within the family
C. difficile infection (CDI) in older adults

- CDI is the most common cause of acute diarrhea in NHs
- Antibiotics and healthcare exposure are major drivers of C. difficile acquisition and infection
- CDI in older adults can be more severe – higher rates of death and hospitalization

McDonald LC et al Emerg Infect Dis 2006; Simor AS, J Am Geratrc Soc. 2010
CDI with onset in nursing homes

- >100,000 cases of CDI estimated to occur in NHs in a single year
- Up to 75% of residents with NH-onset CDI received antibiotics
  - ~80% occurred within 30-days of hospital discharge
  - 18% were hospitalized
  - 8% died within 30-days of event
C. difficile carriage among nursing home residents

- Enrolled a cohort of residents transferred to a VA nursing facility
  - 110 enrolled and followed up to 6 weeks
  - 5% ineligible because of active CDI at time of admission; 5% not enrolled
- Perirectal swabs for C. difficile culture on admission and weekly
  - 11% detected as asymptomatic carriers on admission
  - 27% acquired C. difficile in the NH within 6 weeks; 90% within first 4 weeks

**Figure 2.** Cumulative percentage of new detection of colonization with toxigenic *Clostridium difficile* for the 85 long-term care facility (LTCF) residents with negative cultures on admission and 1 or more follow-up cultures.
Antibiotics and resistance

- Antibiotics are drugs used to kill bacteria; grouped into classes based on their structure and activity
  - Narrow-spectrum target a few specific bacteria
  - Broad-spectrum can kill a wide variety of bacteria
- **Antibiotic resistance (AR)** = when an antibiotic does not effectively kill a specific bacterial organism
- **Multidrug-resistance** = A term for clinically important antibiotic resistance patterns among bacteria
  - Resistant to a key antibiotic class (e.g., methicillin-resistance)
  - Resistant to multiple antibiotic classes
    - Resistance genes can travel together so acquisition impacts multiple classes of agents
Mechanisms of antibiotic resistance (AR)

- Production of proteins (enzymes) that destroy antibiotics
  - Beta-lactamases
  - Cephalosporinases
  - Carbapenemases
- Altered cell structure
  - Blocks binding and function of antibiotics
  - Changes the targets of antibiotics
- Reduced antibiotic exposure
  - Pump antibiotics out
  - Increase cell barriers to block entry

http://bioinfo.bact.wisc.edu/themicrobialworld/bactresanti.html
## ABC’s of MDROs

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Antibiotic Resistance</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Methicillin-resistant</td>
<td>MRSA</td>
</tr>
<tr>
<td><em>Enterococcus spp.</em></td>
<td>Vancomycin-resistant</td>
<td>VRE</td>
</tr>
<tr>
<td>Enterobacteriaceae (e.g., <em>E coli</em>, <em>Klebsiella</em>)</td>
<td>Cephalosporin-resistant e.g., extended spectrum beta-lactamase</td>
<td>ESBL</td>
</tr>
<tr>
<td>Enterobacteriaceae (e.g., <em>E coli</em>, <em>Klebsiella</em>)</td>
<td>Carbapenem-resistant</td>
<td>CRE</td>
</tr>
<tr>
<td><em>Pseudomonas/ Acinetobacter</em></td>
<td>Resistance to multiple drug classes</td>
<td>MDR</td>
</tr>
</tbody>
</table>
MDRO prevalence in nursing homes (n=18 facilities)

Comparing MDRO prevalence between acute care hospitals and post-acute care facilities

Outbreaks of infection with MDRO follow the flow of colonized patients across institutions

Emergence and regional spread of Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae

Case scenario

- 70 year old admitted from a long-term acute care hospital (LTACH) to nursing home
  - Had complicated hospital history including surgery, prolonged ICU stay, multiple courses of antibiotics
  - Spent 5 weeks in the LTACH for ventilator-weaning, antibiotics and wound care
- On transfer, has tracheostomy, PEG tube, indwelling urinary catheter and partially healing sacral pressure ulcer

*What are this resident’s risk factors for being colonized or acquiring an MDRO?*
Resident risk factors associated with MDROs

<table>
<thead>
<tr>
<th>Common</th>
<th>MDR-GNB</th>
<th>MRSA</th>
<th>VRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional disability</td>
<td>• Long stay, advanced age, large facilities</td>
<td>• Long stay, advanced age, male sex</td>
<td>• Prior hospitalization</td>
</tr>
<tr>
<td>Presence of wounds</td>
<td>• Prior colonization</td>
<td>• Low cognitive status</td>
<td>• Proximity to other colonized individuals</td>
</tr>
<tr>
<td>Presence of urinary catheters</td>
<td>• Presence of feeding tubes</td>
<td>• Prior colonization</td>
<td>• Presence of feeding tubes</td>
</tr>
<tr>
<td>Prior antibiotic therapy</td>
<td>• Bladder dysfunction, fecal incontinence</td>
<td>• Prior hospitalization</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pressure ulcers</td>
<td>• Presence of feeding tubes or intravenous central catheters</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Comorbid conditions such as diabetes, cancer, renal disease, and inflammatory bowel disease</td>
<td>• Urinary incontinence</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pressure ulcers</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Comorbid conditions such as diabetes, pulmonary disease, and heart failure</td>
<td></td>
</tr>
</tbody>
</table>
Case scenario, continued

- On transfer, has tracheostomy, PEG tube, indwelling urinary catheter and large sacral pressure ulcer
- One week into admission, he develops a fever, increased oxygen requirements and increased purulent respiratory secretions; X-ray shows a new infiltrate
- MD sends culture from tracheostomy secretions
  - Grows *Klebsiella pneumoniae*, $>10^5$ cfu

<table>
<thead>
<tr>
<th>Drug</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Amp/Sulbactam</td>
<td>Resistant</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ceftriazone</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>Resistant</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Resistant</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>Resistant</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Trimethoprim/Sulfa</td>
<td>Resistant</td>
</tr>
</tbody>
</table>
Carbapenem-resistance in Enterobacteriaceae (CRE) and other gram-negative bacteria

- Carbapenem antibiotics are reserved for severe, complicated infections with multiple and often resistant bacteria
  - Examples: Imipenem, meropenem, doripenem
  - Considered one of the last lines of defense; “very broad-spectrum”
- Resistance significantly limits treatment options for life-threatening infections
- Carbapenemases are a very concerning resistance mechanism
  - Found on mobile genetic elements which can be easily shared between different bacteria
  - Most common in US: Klebsiella pneumoniae carbapenemase (KPC)
  - Other emerging: New Delhi metallo-beta-lactamase (NDM-1), OXA-48, Verona integron-encoded metallo-beta-lactamase (VIM)
CDC efforts to detect and contain Carbapenemases in the United States

[Map of the United States showing the distribution of Carbapenemases by state.]

https://www.cdc.gov/hai/organisms/cre/trackingcre.html
New CDC Containment Strategy

- Systematic approach to slow spread of novel or rare multidrug-resistant organisms or mechanisms through aggressive response to ≥1 case of targeted organisms
- Response tiers based on pathogen/resistance mechanism

https://www.cdc.gov/hai/outbreaks/mdro/index.html
Containment Strategy
Systematic public health response to slow the spread of emerging AR

Single case of emerging resistance reported to health department

Onsite assessment using standardized tools
State HAI prevention programs provide response capacity in every state

AR Laboratory Network (ARLN): Capacity to detect at 56 state and local public health laboratories

Available through ARLN for carbapenemase-producing organisms

Regular infection control assessments and point prevalence surveys until transmission stops
Challenges with containing MDRO transmission in nursing homes

- Facilities accept patients with longer length of stay and high acuity of care
- Gaps in IPC program infrastructure and practices
  - Lack of staff adherence to hand hygiene and Transmission-Based Precautions
  - Environment and equipment contamination serves as a reservoir for spread
  - Lack of adequate supplies to support infection prevention and control practices
  - Failure to communicate colonization status at transfer

To control the spread of CRE, healthcare facilities should:

- Quantify the magnitude of CRE within the facility
- Identify colonized and infected patients within the facility
- Implement interventions designed to stop the transmission of CRE

*The principles for detecting and preventing CRE apply to many MDROs and CDI*

CRE (or any MDRO) Surveillance: Awareness is key

- Know whether CRE has been detected in your community
  - Contact infection prevention programs of hospitals in your referral network
  - Contact the coordinator of the Healthcare-associated Infections (HAI) program at the state health department
- Know if CRE has been detected from residents receiving care in your facility
  - History of CRE colonization or infection should be communicated at time of admission or transfer
  - Review clinical cultures from your laboratory to see if CRE has been isolated from residents in your facility
- Utilize NHSN to track CRE, other MDROs and CDI in your facility
CRE Prevention Strategies

- Identification
  - Laboratory notification
  - Communication of CRE status during interfacility-transfer
  - Screening contacts of known CRE carriers
  - Active surveillance for CRE colonization

- Prevention of emergence
  - Careful use of invasive medical devices
  - Antibiotic stewardship

- Prevention of spread
  - Hand hygiene
  - Gown and glove use (Contact Precautions)
  - Placement/cohorting of residents and staff
  - Environmental cleaning
  - Chlorhexidine bathing
Bacterial contamination of staff hands prior to hand hygiene in a LTCF

- Cultured the hands of staff immediately after direct care to residents
- Gram negative bacteria were the most common bugs cultured from hands
- Most Gram neg. bacteria live in the GI tract or colonize the urine

Barriers to hand hygiene (HH) adherence in NHs

- Belief that HH guidelines aren’t applicable in long-term care settings
  - 30% wouldn’t change current practices; 20% guidelines impractical
- Lack of access to appropriate HH supplies
  - 16.2% lack of available sink; 27.5% lack of alcohol-based hand rub
- No HH because of glove use
  - 23% nurses, 17% CNAs, 26% other HCWs
- Forgot HH because of workload
  - 35% of nurses, 22% CNAs, 44% other HCWs
- Lack of access to HH feedback and/or education
  - 55% never to rarely received personal feedback on HH practices
  - Other HCWs less often received periodic education on HH (86.8% vs. 92% of nurses and CNAs)

Ashraf MS et al. ICHE 2010; 31(7):758-762
Promoting and monitoring HH practices

Efforts to improve hand hygiene efforts should be multidisciplinary and multimodal, including:

- Ensure accessibility of hand hygiene products and supplies
- Perform a demo with new hand hygiene products before implementation to obtain feedback and support from staff
- Provide reminders and cues to action (e.g., signs) for appropriate HH moments and technique
- Provide feedback on performance data
- Engaging healthcare personnel in discussions to identify HH knowledge gaps and barriers to adherence
- Develop a culture of safety and teamwork

Challenges with gown/glove use for Transmission-Based Precautions in NHs

- Staff concerns about negative impact of gown/glove use on residents
  - Unlikely to change practices if aware of an MDRO
  - Isolation could negatively impact a resident’s well-being
- Lack of private rooms / limited ability to move residents
  - Moving rooms is disrupting to residents and staff
  - Ability to identify carriers to cohort is limited (no active surveillance in most facilities)
- Determining duration of Contact Precautions
  - Don’t want to restrict resident mobility and participation in social events/therapy for prolonged periods
  - Unlikely to document clearance of carriage

Furuno, JP et al. AJIC. 2011; 1-5 epub
MRSA contamination of NH caregiver hands and clothes during common activities

- Evaluated ~950 different interactions between staff and MRSA colonized residents
- Used cultures of gloves/gowns to mimic transmission to hands and clothing
- Assisting with linen change, transfer and personal hygiene had highest likelihood of contamination
- Transmission was increased:
  - Activities were bundled together (e.g., morning or evening care)
  - During care of residents with chronic wounds
Consider a resident-centered approach to gown/glove use

Gown/glove use during care of all high-risk residents, regardless of MDRO status

High risk = presence of indwelling medical devices, chronic wounds, functional dependence, uncontained secretions
A Targeted Infection Prevention Intervention in Nursing Home Residents With Indwelling Devices: A Randomized Clinical Trial

Lona Mody, MD; Sarah L. Klein, PhD; Sanjay K. Saint, MD; Lillian C. Min, MD; Ana Montoya, MD; Bonnie Lansing, LPN; Sara E. McNamara, MPH; Kathleen Symons, BA; Jay Fisch, BS; Evonne Koo, MPH; Ruth Anne Rye, BS; Andrzej Galecki, MD, PhD; Mohammed U. Kabeto, MS; James T. Fitzgerald, PhD; Russell N. Olmsted, MPH; Carol A. Kauffman, MD; Suzanne F. Bradley, MD

**INTERVENTION DETAILS**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Control sites: usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-emptive barrier precautions</td>
<td>Standard Precautions</td>
</tr>
<tr>
<td>Gown and glove use for any intimate care including am and pm care, ADL help</td>
<td>Gown and/or glove use per facility policies</td>
</tr>
<tr>
<td>Active Surveillance and monthly feedback MDRO colonization (surveillance cultures) Infections</td>
<td>Data gathering for outcomes MDRO colonization Infections</td>
</tr>
<tr>
<td>Interactive Education</td>
<td>Education As needed (response to audits, state surveys)</td>
</tr>
<tr>
<td>1. Hand hygiene promotional posters, glo-germ, pre and post hand cultures demonstrations</td>
<td></td>
</tr>
<tr>
<td>2. Personal use hand sanitizers</td>
<td></td>
</tr>
<tr>
<td>3. Interactive Infection Prevention Modules (10 modules, q 2-3 mo)</td>
<td></td>
</tr>
<tr>
<td>4. IP Mini-conference on surveillance</td>
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<tr>
<td>5. Surveillance definition cards to providers</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Number of MDROs/1000 device days</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td><strong>Control</strong></td>
<td><strong>RR</strong></td>
</tr>
<tr>
<td>MRSA</td>
<td>15.1</td>
<td>21</td>
</tr>
<tr>
<td>VRE</td>
<td>7.4</td>
<td>10.3</td>
</tr>
<tr>
<td>CTZ-R GNB</td>
<td>10</td>
<td>16.3</td>
</tr>
<tr>
<td>CIP-R GNB</td>
<td>35.8</td>
<td>46.1</td>
</tr>
<tr>
<td><strong>All MDRO</strong></td>
<td><strong>68.4</strong></td>
<td><strong>93.7</strong></td>
</tr>
</tbody>
</table>

Mody L et al. JAMA Intern Med. 2015 May;175(5):714-23
Presented as oral abstract #1208. IDWeek 2013, San Francisco, CA. Oct 5, 2013
Pros and cons of a resident-centered approach to gown/glove use

PROS
- No longer relying on identification of specific pathogens
- Care planning based on resident needs aligns with principles of “resident-centered care”
- Simplifies messaging to front-line staff
- Enables early implementation of appropriate PPE based on new risks or changing care needs

CONS
- Paradigm shift for facility staff, residents, families and visitors – will require education
- Approach will increase gown/glove use during care of a subset of high risk residents – devices, wounds, complete functional dependence
Gown/glove use to prevent CRE spread

- Identify risk factors among residents identified with CRE colonization/infection
  - Presence of indwelling devices, wounds, ventilator-dependence
  - Functional dependence, incontinence, uncontained secretions
- Consider types of care which may increase transmission of CRE to hands/clothes of healthcare personnel
  - Bathing, dressing, assisting with toileting, changing linens
  - Wound care, device handling, suctioning/oral care
- Use of gown/gloves during direct resident care activities does not prevent individuals from participating in social activities if sites of colonization are covered/contained
Other considerations for implementing Transmission-Based Precautions

- Ensure that all staff receive education on proper use of PPE during resident care
- Communicate to caregivers, families and residents about your facility’s approach to MDRO management
  - Decisions and rationale about gown/glove use during care and room placement should be clearly documented
- Cues to action, monitoring and feedback of adherence to gown/glove use is critical for staff performance
  - Practices at the bedside must align with policies
- Discontinuation of precautions based on resident risk decreasing rather than presence/absence of organism
Take Away Points

- The impact and prevalence of CDI and MDROs is significant in nursing homes
  - As many as 60% of residents are colonized with one or more MDROs on a given day
  - Providers must understand the risk factors for colonization and acquisition
- Public health efforts to contain AR pathogens have increased capacity to detect and respond to emerging threats
  - Implementation of infection control and ongoing surveillance for new cases are critical components of containing resistance
  - Identified challenges with infection prevention and control practices to prevent transmission in post-acute care facilities
- Strategies to prevent MDROs and CDI are multifactorial and may be moving to a more resident-focused, rather than pathogen focused approach
Nursing Homes and Assisted Living (Long-term Care Facilities [LTCFs])

Clinical Staff Information

Nurses, medical providers, and therapists who work in nursing homes and assisted living facilities face a difficult task of managing the complex conditions affecting a person while simultaneously monitoring him/her for signs and symptoms of infections. The resources on this page include guidance documents and web links to resources on the common infections that occur in long-term care facilities and how to prevent them.

The Core Elements of Antibiotic Stewardship for Nursing Homes

National Nursing Home Quality Improvement Campaign C. difficile Fact sheets

Communication Tools

https://www.cdc.gov/longtermcare/staff/index.html
Know your public health HAI prevention partners

State-based HAI prevention

State-based HAI Prevention Activities

SUCCESS STORIES
Many states are showing impressive progress in reducing HAI.

CDC RESOURCES FOR STATES
CDC tools and technical assistance support state efforts to prevent HAI.

Epidemiology and Laboratory Capacity
- Epidemiology and Laboratory Capacity (ELC) Program
- Description of ELC Healthcare-Associated Infection Activities
- Emerging Infections Program

https://www.cdc.gov/hai/state-based/index.html
Thank you!!

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.