C. difficile Prevention:  
A Multifaceted Approach

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Objectives

• Identify recent changes in the epidemiology of Clostridium difficile infection (CDI), including transmission and risk populations
• Describe evidence-based best practices involved in a multifaceted approach to prevention of CDI
• Recognize the problem areas in CDI prevention and discuss possible solutions

The “Syndrome” of Antibiotic-Associated Diarrhea

• Diarrhea is one of the most common complications associated with antibiotic therapy.
• Diarrhea can be caused by a non-specific change in bowel flora or specific components in antibiotics (clavulanate in Augmentin) or a direct motility effect of the antibiotic (erythromycin).
• Clostridium difficile is implicated in 20 to 30 percent of patients with antibiotic-associated diarrhea.
• BUT: CDI can also occur in patients on immunosuppressive drugs or in patients in the community with no antimicrobial exposure.
The Organism

- *Clostridium difficile* is an anaerobic spore-forming gram-positive rod
- Vegetative form: Highly sensitive to oxygen and disinfecting agents
- Spore form: Heat, oxygen stable; resistant to most disinfecting agents except bleach or accelerated hydrogen peroxide
- This organism cannot be cultured from stool in commercial laboratories

The Human/Environmental Reservoir

- *C. difficile* is found in 15 to 70 percent of healthy neonates.
- Some strains are non-toxigenic.
- In healthy adults, intestinal carriage rates of toxigenic *C. difficile* are typically 3 to 8 percent.
- Asymptomatic intestinal carriage rates are higher (approximately 20 percent) among hospitalized adults.
- Strains acquired in health care settings tend to be multidrug-resistant and toxigenic.

A Wide Spectrum of Disease

Simple diarrhea

- Pseudomembranous colitis
- Toxic megacolon
- Sepsis and death

Healthy colon

Pseudomembranous colitis
From the National Vital Statistics Report, 2011

- In 1999, 793 deaths were due to *C. difficile*, compared with 7,476 *C. difficile* deaths in 2008.
- The number of deaths dropped slightly to 7,251 in 2009 and increased to 7,994 in 2011.
- The age-adjusted death rate for this cause in 2011 was 2.4 deaths per 100,000 standard population, an increase of 9.1 percent from the rate in 2010.
- In 2011, *C. difficile* ranked as the 17th leading cause of death for the population aged 65 years and older.
- Approximately 91 percent of deaths from *C. difficile* occurred to people 65 years and older.

New Mexico Mortality Data

![Graph showing mortality data](image)
Outbreak in Canada
• High attributable mortality: 1.2 to 14 percent
• Associated with FQ and cephalosporin use

Described new strain of C. difficile
• Outbreak associated
• FQ resistant
• BI/NAP1/O27

C. Difficile in Previously Low-Risk Populations

• CDI in previously low-risk groups
  – 10 pregnant/post-partum women
  – 23 community dwellers
  – Some patients without antibiotic exposure
• Up to 50 percent of CDI cases may occur outside of the hospital
Changes in Epidemiology of *C. difficile*

As of October 2008, 40 states reported NAP1 strain of *C. difficile*

Percentage of *C. difficile* isolates in Canadian provinces with the BI/NAP1/027 strain in 2005

Other Features of NAP1

- Mortality in reported outbreaks:
  - In a study of 1703 patients, *C. difficile* infection was the attributable cause of death in 117 cases (6.9%) and a contributing factor in an additional 127 deaths (7.5%).

- Hypersporulation:
  - High rate of spore formation, contaminating the environment
  - Resistance to fluoroquinolones

CDC Analysis of 10,342 Cases of CDI from 8 Diverse Geographic Areas, 2010

Charts were reviewed to determine any health care exposure in last 12 weeks - in and output
75 percent of healthcare-associated cases have their onset outside acute care hospitals
Rates of Foodborne Disease in New Mexico, 2011

<table>
<thead>
<tr>
<th>Foodborne Diseases</th>
<th>Number</th>
<th>Rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulism</td>
<td>2</td>
<td>0.7</td>
</tr>
<tr>
<td>Campylobacteriosis</td>
<td>370</td>
<td>17.8</td>
</tr>
<tr>
<td>Cholera</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td>136</td>
<td>6.8</td>
</tr>
<tr>
<td>Giardiasis</td>
<td>150</td>
<td>5.3</td>
</tr>
<tr>
<td>Hepatitis A, acute</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Hemolytic urtic syndrome</td>
<td>15</td>
<td>0.72</td>
</tr>
<tr>
<td>Listeriosis</td>
<td>341</td>
<td>16.4</td>
</tr>
<tr>
<td>Salmonellosis</td>
<td>41</td>
<td>2.1</td>
</tr>
<tr>
<td>Shiga toxin-producing (Esherichia coli) (STEC)</td>
<td>122</td>
<td>5.9</td>
</tr>
<tr>
<td>Typhoid fever (Salmonella typhi)</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>Yersiniae</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>Yersinia pseudotuberculosis</td>
<td>2</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Approximate Rate of CDI in Bernalillo County, 2011-12

- 1,100 cases per 673,460 population

= rate of 163 per 100,000 population per year

i.e., 10-fold that of reported cases of Campylobacter or Salmonellosis.

Data courtesy of Erin Phipps, DVM, Emerging Infections Program, CDC and NMDOH

Not Just Antibiotics: Multiple Identified Risk Factors for CDI

- Diabetes
- Proton-pump inhibitors
- Feeding tube
- GI surgery
- Stool softeners/laxatives
- Immunosuppressive drugs
- H2 blockers
- Age over 70
- Dialysis
- Prior antibiotics—especially fluoroquinolones, cephalosporins, carbapenems and clindamycin
Falling Rates of CDI in the UK:
Rates per 100,000 Bed-Days
(Year Ending March 31)

How did they do it?
Control of *C. difficile* is Multidisciplinary

- Rapid and accurate diagnosis
- Recognition of disease, stratification by severity, and effective treatment
- Isolation of patients with diarrhea
- Environmental cleaning with sporocidal agents
- Correct hand hygiene practice and contact precautions
- Antimicrobial stewardship
- Surveillance and communication of rates
- Communication at discharge and transfer

- Laboratory
- Clinicians
- Nursing
- Environmental services
- All staff and visitors
- Pharmacy, microbiology and clinician partnerships
- Infection preventionists
- Patients
- Staff in-home care and long-term care

Summary of Core Knowledge Areas

- Know the syndrome and risk stratification
- Know the risks
- Understand diagnostic testing
- Use best therapy for the clinical syndrome
- Prevention of transmission
- Managing transitions of care

Physician Education Flyer
The Clinician’s Perspective

- Want rapid, accurate support of a clinical diagnosis
- Not fond of ambiguity
- Need help communicating to patients re: concepts of colonization, increased risk, etc.

Finding a Niche for a New Approach

- Clinicians tend to think of C. difficile in the same context as “stool cultures” for enteric pathogens
- Ask for “culture”
- Ask for “susceptibility testing”
- Want follow-up assurance that treatment has worked as if dealing with Shigella or other enteric pathogens

Core IDSA Guidelines

Diagnosis: What is the best testing strategy to diagnose CDI in the clinical laboratory and what are acceptable options?

- Enzyme immunoassay (EIA) testing for C. difficile toxin A and B is rapid but is less sensitive than the cell cytotoxin assay, so it is a suboptimal alternative approach for diagnosis.
- Toxin testing is most important clinically, but it is hampered by its lack of sensitivity. One potential strategy to overcome this problem is a two-step method that uses EIA detection of glutamate dehydrogenase (GDH) as initial screening and then uses the cell cytotoxicity assay or toxigenic culture as the confirmatory test for GDH-positive stool specimens only.
- Polymerase chain reaction (PCR) testing appears to be rapid, sensitive, and specific and may ultimately address testing concerns. More data on utility are necessary before this methodology can be recommended for routine testing.
- Repeat testing during the same episode of diarrhea is of limited value and should be discouraged.
Why is there no test of cure?

- EIA test for toxin should only be performed in patients exhibiting the effects of toxin, e.g., diarrhea.
- Positive toxins on formed stool are likely to be false positives.
- Antigen (glutaraldehyde dehydrogenase)-and PCR (for gene encoding toxin B)-based tests test for the presence of the organism, not the toxin.
- Asymptomatic carriage is common and may be prolonged.

Questions about Colonization

- Risks vary with the patient
  - Hospitalization in the previous two months
  - Use of antibiotics, chemotherapy, proton-pump inhibitors, or H2 blockers
- What is the prevalence of asymptomatic C. difficile carriage?
  - Approximately 9 percent in one study of patients tested at hospital admission
- How long do patients carry C. difficile?
  - Severely immunocompromised patients have been shown to relapse with the same strain over six months

Evidence-based Cleaning

- Environmental cleaning with bleach or accelerated hydrogen peroxide products* can kill spores, whereas other standard disinfectants cannot
- Limited data suggest cleaning with bleach (1:10 dilution prepared fresh daily) reduces C. difficile transmission
- Use a checklist to make sure all high-touch surfaces are cleaned.

*EPA list as of 8/2012: http://www.epa.gov/oppad001/list_k_clostridium.pdf
How do we get the results we want from our efforts in cleaning?

- Assure the right rooms get cleaned the right way with correct signage and communication with nursing staff
- Use a checklist tool
- Monitor thoroughness of cleaning and use results for continuous training of staff
- Engage patients and families in assuring a safe and clean environment

Key Decisions

- Who cleans what?
- With what?
- For how long? (Contact times)
- When do we use a different product (e.g., for *C. difficile*) and how is this communicated?
- How do we monitor?

Implementing a Cleaning Checklist

- Checklists ensure a culture of reliability
- Interruptions happen constantly in health care: everyone needs help to keep on track and be thorough
Monitoring the Process: UV Marking

Use of a UV marking solution to assess environmental cleaning

Using ATP Monitoring

- A structured list of surfaces is swabbed for ATP reading at the end of all terminal cleans for C. difficile patients
- Feedback to cleaner is instantaneous
- Areas with high readings are re-cleaned
- Data trending software is available

Environmental Contamination Contributes

- Prior Occupant
  - No CDI ⇒ 4.6% CDI
  - Yes CDI ⇒ 11.0% CDI
  - \( P = .002 \)
- Multivariate regression
  - HR 2.35 (1.21-4.54) \( P = .01 \)

Kaplan-Meier curve of Clostridium difficile infection (CDI) development. (\( P < 0.008 \)).
Recommended Education for EMS Personnel

A presentation should be developed for all line staff involved in terminal room cleaning and should:

• Provide an overview of the importance of HAIs in a manner commensurate with their educational level and using as many pictorial illustrations as is feasible.
• Explain their role in improving patient safety through optimized hygienic practice.
• Review specific terminal room cleaning practice expectations.

Call attention to high-touch areas

Toolkit also contains spreadsheet for summary data collection

Surfaces, Chemicals and Tools: Pitfalls

• Surfaces: medical equipment and housekeeping surfaces (high and low touch)
  – May be cleaned by separate groups
• Chemicals: EPA-approved, always dilute and use per manufacturer’s instructions
  – Equipment: always clean per manufacturer’s instructions
• Tools: minimize contamination of bucket solutions, and cross-contamination by rags
The Evidence for Antimicrobial Stewardship

- 33 studies demonstrating cost savings or cost neutrality of programs
- 22 studies examining antimicrobial resistance and *C. difficile* outcomes—14 were able to demonstrate reduction in gram-negative resistance and/or *C. difficile*

Complete Restriction of Fluoroquinolone Use to Control an Outbreak of *Clostridium difficile* Infection at a Community Hospital


Introduction of EHR with Stewardship

- EHR introduced—Reviewed 49 antimicrobial agents
- Increase in:
  - Charts Reviewed 36%
  - Recommendations 98%
  - Accepted Recommendations 124%
- Decrease in:
  - Abx used 28.8% (p<0.0001)
  - Nosocomial MRSA 45.2% (p<0.0001)
  - Nosocomial CDI 18.7% (p=0.07)

The Biggest Challenges

• Adherence to best hand hygiene practice: an easy stream of electronic data helps infection preventionists work on converting health care workers to hand hygiene practice
• Managing transitions of care and flagging high-risk patients

The Power of Feedback

My belief is that health care workers really want to do the right thing, but sometimes they're just not conscious of what they are doing. By providing them with information in a respectful and helpful way about how they're doing, they're going to want to do better.

Elaine L. Larson, PhD, RN, Professor and Associate Dean of the Columbia University School of Nursing, talking about social changes that have an effect on infection prevention.

Skin Contamination is Common

Frequency of *C. difficile* contamination of skin sites of 27 patients with CDI and sterile gloves of after contact with 10 patients

Understanding the Mindset

- Hand hygiene behavior in health care is influenced primarily by inherent practices that have been learned in the community (e.g., when growing up).
- What drives hand hygiene is likely to be predetermined perceptions of what is “clean” (e.g., intact skin or equipment) and what is “dirty” (e.g., feces or a patient identified as having an infection).
- In the hospital, however, “elective” hand hygiene is done after any encounter with the patient or the patient’s surroundings.

Soap and Water is Preferred

Pairwise Comparison of Mean Reduction in C. difficile Colony Count for Hand Hygiene Interventions Used According to Whole Hand Protocol

<table>
<thead>
<tr>
<th>Interventions compared</th>
<th>Mean log reduction (95% CI)</th>
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<tbody>
<tr>
<td>Intervention 1</td>
<td>Intervention 2</td>
</tr>
<tr>
<td>Soap and Water</td>
<td>No hand hygiene</td>
</tr>
<tr>
<td>Warm water and plain soap</td>
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Soap and Water is Preferred

Comparison of Mean Reduction in C. difficile Colony Count for Hand Hygiene Interventions Using Palmer Method

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Hand Hygiene: The Slowest Idea

<table>
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<tr>
<th>Medical Innovation</th>
<th>First Use</th>
<th>Speed of Adoption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia</td>
<td>1846</td>
<td>Within 7 years</td>
</tr>
<tr>
<td>Surgical Antisepsis</td>
<td>1867</td>
<td>Another 30-40 years</td>
</tr>
<tr>
<td>Penicillin</td>
<td>1930</td>
<td>Initially slow, then exploded after 1942</td>
</tr>
<tr>
<td>Oral Rehydration Therapy</td>
<td>1968</td>
<td>1980s</td>
</tr>
<tr>
<td>Hand Hygiene</td>
<td>1847</td>
<td>Still working on it</td>
</tr>
</tbody>
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Spreading Slow Ideas

- Spreading change through going door-to-door and talking to individuals with simple messages
- Community-based teachers
- Make the learner perform the task
- Change the norm
- Point out the discrepancy between teaching and practice, but be supportive


CDI in Acute Care

Patient relapses with severe CDI

Patient transferred out on PPI

Urine sent for culture, which is positive, antibiotics started

Plus: urinary catheter in place

How do we break the cycle?
What Works

• Involving clinicians in developing regional transfer forms
• Engaging providers in long-term care so that they realize which patients are highest risk for relapse
• Making hospitals aware of readmissions for \textit{C. difficile}
• Tracking all multidrug-resistant pathogens e.g., Carbapenemase-resistant Enterobacteriaceae, MRSA with each care transition

For More Information

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