Clostridium difficile Infection: Current State of Prevention

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Objectives

• Review the impact, background and changing epidemiology of *C. difficile* and *C. difficile* Infection (CDI)

• Identify specific interventions designed to recognize cases of CDI early then facilitate preventive interventions

• Recognize limitations in our knowledge regarding effectiveness of interventions
Disclosure

• Thanks to Drs. Cliff McDonald and Carolyn Gould with CDC for sharing the CDI Toolkit. Thanks to Dr. Julio Ramirez for the graphics

• Speakers bureau: CareFusion, Sanofi pasteur, MedImmune, Clorox
Scenario

• 76 year old woman admitted to hospital from a long term care facility with a diagnosis of pneumonia. After 4 days of antibiotic treatment, she develops diarrhea. Other symptoms include a temperature of 100.8F, WBC 15.5. Stool sent for C. difficile and was toxin+. 
Impact of *C. difficile*

- CDC estimates that there are >300,000 cases of CDI annually with 15,000-30,000 attributable deaths.

- About half of the cases occur in long-term care facilities

Impact of CDI
Age-Adjusted Death Rate* for Enterocolitis Due to *C. difficile*, 1999–2006

*Per 100,000 US standard population

Pathogenesis of CDI

1. Ingestion of spores transmitted from other patients via the hands of healthcare personnel and environment.

2. Germination into growing (vegetative) form.

3. Altered lower intestine flora (due to antimicrobial use) allows proliferation of *C. difficile* in colon.

4. Toxin A & B Production leads to colon damage +/- pseudomembrane.

Normal Colonic Flora & Mucosa
Pathogenesis of CDI

<table>
<thead>
<tr>
<th>Normal Colonic Flora &amp; Mucosa</th>
<th>Abnormal Flora &amp; C diff Colonization</th>
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## Pathogenesis of CDI

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<tbody>
<tr>
<td><img src="normal_colonic.png" alt="Image of Normal Colonic Flora &amp; Mucosa" /></td>
<td><img src="abnormal%E6%AE%96%E6%B0%91ization.png" alt="Image of Abnormal Flora &amp; C diff Colonization" /></td>
<td><img src="toxins.png" alt="Image of C diff Production of Toxins A &amp; B" /></td>
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### Pathogenesis of CDI

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- **Normal Colonic Flora & Mucosa**: The normal flora and mucosa of the colon.
- **Abnormal Flora & *C diff* Colonization**: The colonization of the colon by abnormal flora and *C diff*.
- ***C diff* Production of Toxins A & B**: The production of toxins A & B by *C diff*.
- **Pseudomembranous Colitis**: The development of pseudomembranous colitis.
## Pathogenesis of CDI

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**Diagram:**
- **Normal Colonic Flora & Mucosa:** Normal flora and mucosa are present, indicating a healthy state.
- **Abnormal Flora & C diff Colonization:** Abnormal flora population and C diff colonization occur, affecting the mucosa.
- **C diff Production of BI NAP Toxin:** C diff produces BI NAP toxin, leading to inflammation.
- **Pseudomembranous Colitis:** Pseudomembranes develop due to the C diff toxin, causing colitis.
Current Epidemic Strain of C. difficile

• BI/NAP1/027, toxinotype III
• Historically uncommon – epidemic since 2000
• More resistant to fluoroquinolones
  – Clindamycin and quinolones recognized as risk factors
  – Higher MICs compared to historic strains and current non-BI/NAP1 strains
• More virulent
  – Increased toxin A and B production
  – Increased sporulation

Risk Factors

• Antimicrobial exposure
• Acquisition of *C. difficile* organism
• Advanced age
• Underlying illness
• Immunosuppression
• Tube feeds
• Use of electronic thermometers
• ? Gastric acid suppression (PPI)
Surveillance:
Categorize Cases by location and time of onset

Admission
Discharge

Day 1
Day 4

2 d

< 4 weeks
4-12 weeks
> 12 weeks

HO
CO-HCFA
Indeterminate
CA-CDI

HO: Hospital (Healthcare)-Onset
CO-HCFA: Community-Onset, Healthcare Facility-Associated
CA: Community-Associated

* Depending upon whether patient was discharged within previous 4 weeks, CO-HCFA vs. CA

Prevention Strategies

• **Core Strategies**
  – Should be first line prevention
  – Some high levels of scientific evidence
  – Demonstrated feasibility

• **Supplemental Strategies**
  – May be implemented in response to epidemic or ongoing transmission
  – Some scientific evidence
  – Variable levels of feasibility
Prevention Strategies: Knowledge Gaps

- Lack of high quality studies
- Implementation of bundles may cloud recognition of what actually works
- What is the situational context in which prevention activities should be applied (e.g., does environmental disinfection prevent CDI transmission during outbreaks)?
- What are the unintended consequences that result from interventions?
Core Prevention Strategies

• Contact Precautions for duration of diarrhea
• Hand hygiene in compliance with CDC/WHO
• Cleaning and disinfection of equipment and environment
• Laboratory-based alert system for immediate notification of positive test results
• Educate about CDI: HCP, housekeeping, administration, patients, families

http://www.cdc.gov/ncidod/dhqp/id_CdiffFAQ_HCP.html
Healthcare Personnel Education

- What is CDI
- Diagnosis and treatment
- Transmission to others
- Isolation
- Hand hygiene
- Environmental cleaning
- Discharge instructions
- When to contact their clinician

- Excellent patient education handout in the APIC Elimination Guide
Patient/Family Education

• What is CDI
• Diagnosis and treatment
• Transmission to others
• Isolation
• Hand hygiene
• Environmental cleaning
• Discharge instructions
• When to contact their clinician

• Excellent patient education handout in the APIC Elimination Guide
Supplemental Prevention Strategies

• Extend use of Contact Precautions beyond duration of diarrhea (e.g., 48 hours)*
• Presumptive isolation for symptomatic patients pending confirmation of CDI
• Evaluate and optimize testing for CDI
• Implement soap and water for hand hygiene before exiting room of a patient with CDI
• Implement universal glove use on units with high CDI rates*
• Use sodium hypochlorite (bleach) – containing agents for environmental cleaning
• Implement an antimicrobial stewardship program

* Not included in CDC/HICPAC 2007 Guideline for Isolation Precautions
Supplemental Prevention Strategies: Rationale for considering extending isolation beyond duration of diarrhea

Supplemental Prevention Strategies:
Consider presumptive isolation for patients with $\geq 3$ unformed stools within 24 hours

- Patients with CDI may contaminate environment and hands of healthcare personnel pending results of diagnostic testing
- CDI responsible for only $\sim 30\text{-}40\%$ of hospital-onset diarrhea
- However, CDI more likely among patients with $\geq 3$ unformed (i.e. taking the shape of a container) stools within 24 hours
  - Information must be shared between shifts and HCP
  - Send specimen for testing and presumptively isolate patient pending results
  - Positive predictive value of testing will also be optimized if focused on patients with $\geq 3$ unformed stools within 24 hours
  - Exception: patient with possible recurrent CDI (isolate and test following first unformed stool)
Supplemental Prevention Strategies:
Evaluate and optimize test-ordering practices and diagnostic methods

• Most laboratories have relied on Toxin A/B enzyme immunoassays
  – Low sensitivities (70-80%) lead to low negative predictive value
• Despite high specificity, poor test ordering practices (i.e. testing formed stool or repeat testing in negative patients) may lead to many false positives
• Consider more sensitive diagnostic methods but apply these more judiciously across the patient population
  – Employ a highly sensitive screen with confirmatory test or a PCR-based molecular assay
  – Restrict testing to unformed stool only
  – Focus testing on patients with ≥ 3 unformed stools within 24 hours
  – Require expert consultation for repeat testing within 5 days

Challenges in Diagnostic Methods

- EIA 70-80% sensitivity and 97% specificity (3% false +)
- Culture >90% sensitivity and 95-97% specificity
- PCR detects organism but not the toxin. Must combine results with clinical context
- Sensitivity- True positives
- Specificity- True negatives
  - 3% prevalence of disease and 3% false positive rate means that half of the positive tests will be false. With a 25% prevalence you will have a 8% false positive.
Challenges in Diagnostic Methods

• Must recognize when to test (not testing formed stool unless specific reasons to do so, defining what is meant by “diarrhea”, and determine how many samples to be tested during a diarrhea episode).

• If diagnostic methods change, it is important that it be known for both infection prevention and clinical decision-making purposes.

• Do not know if testing methods lead to improved patient outcomes
Supplemental Prevention Strategies: Hand Hygiene – Soap vs. Alcohol Hand Rub

- Alcohol not effective in eradicating *C. difficile* spores
- However, one hospital study found that from 2000-2003, despite increasing use of alcohol hand rub, there was no concomitant increase in CDI rates
- Discouraging alcohol hand rub may undermine overall hand hygiene program with untoward consequences for HAIs in general

Supplemental Prevention Strategies: Hand Washing: Product Comparison

<table>
<thead>
<tr>
<th>Product</th>
<th>Log10 Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap Water</td>
<td>0.76</td>
</tr>
<tr>
<td>4% CHG antimicrobial hand wash</td>
<td>0.77</td>
</tr>
<tr>
<td>Non-antimicrobial hand wash</td>
<td>0.78</td>
</tr>
<tr>
<td>Non-antimicrobial body wash</td>
<td>0.86</td>
</tr>
<tr>
<td>0.3% triclosan antimicrobial hand wash</td>
<td>0.99</td>
</tr>
<tr>
<td>Heavy duty hand cleaner used in manufacturing environments</td>
<td>1.21*</td>
</tr>
</tbody>
</table>

* Only value that was statistically better than others

Conclusion: Spores may be difficult to eradicate even with hand washing.

Supplemental Prevention Strategies: Hand Hygiene Methods

• Since spores may be difficult to remove from hands even with hand washing, adherence to glove use, and Contact Precautions in general, should be emphasized for preventing *C. difficile* transmission via the hands of healthcare personnel.

• Have hand hygiene practices make sense to HCP

• Must address hand hygiene needs and impact beyond CDI
Supplemental Prevention Strategies: Glove Use

Rationale for considering universal glove use (in addition to Contact Precautions for patients with known CDI) on units with high CDI rates

• Although the magnitude of their contribution is uncertain, asymptomatic carriers have a role in transmission

• There may be a role for universal glove use as a special approach to reducing transmission on units with longer lengths of stay and high endemic CDI rates

• General benefit in minimizing hand contamination
Supplemental Prevention Strategies: Environmental Cleaning

• Bleach can kill spores, whereas other standard disinfectants cannot
• Limited data suggest cleaning with bleach (1:10 dilution prepared fresh daily) reduces *C. difficile* transmission
• Two before-after intervention studies demonstrated benefit of bleach cleaning in units with high endemic CDI rates
• Therefore, bleach may be most effective in reducing burden where CDI is highly endemic

Supplemental Prevention Strategies: Environmental Cleaning

• Use of hypochlorite for disinfection B-II (moderate evidence to support recommendation, evidence from at least 1 well-designed clinical trial, multiple time-series or from dramatic results from uncontrolled experiment

• in vitro exposure of epidemic C. difficile strains to subinhibitory concentrations of non-chlorine based cleaners significantly increased sporulation capacity

• Current evidence supports the use of chlorine-containing agents (with at least 1,000 ppm available chlorine) to address environmental contamination in areas associated with endemic or epidemic CDI.

• User acceptability, any health/safety concerns, and compatibility challenges must be assessed and addressed.

Supplemental Prevention Strategies:
Environmental Cleaning

Assess adequacy of cleaning before changing to new cleaning product such as bleach

- Ensure that environmental cleaning is adequate and high-touch surfaces are not being overlooked
- Evaluate processes used in cleaning (clean to dirty, products support process)
- One study using a fluorescent environmental marker to assess cleaning showed:
  – only 47% of high-touch surfaces in 3 hospitals were cleaned
  – sustained improvement in cleaning of all objects, especially in previously poorly cleaned objects, following educational interventions with the environmental services staff
- If changing products, ensure staff can be successful with switching and sustaining

Supplemental Prevention Strategies:
Audit and feedback targeting broad-spectrum antibiotics

- Monitoring and feedback a critical element in antimicrobial stewardship programs
- A prospective, controlled interrupted time-series analysis in 3 acute medical wards for the elderly in the UK demonstrated the impact of antimicrobial management on reducing CDI.
  - Introduced a narrow-spectrum antibiotic policy
  - Reinforced using feedback
  - Associated with significant changes in targeted antibiotics and a significant reduction in CDI

Summary of Prevention Measures

Core Measures

• Contact Precautions for duration of illness
• Hand hygiene in compliance with CDC/WHO
• Cleaning and disinfection of equipment and environment
• Laboratory-based alert system
• CDI surveillance
• Education

Supplemental Measures

• Prolonged duration of Contact Precautions*
• Presumptive isolation
• Evaluate and optimize testing
• Soap and water for HH upon exiting CDI room
• Universal glove use on units with high CDI rates*
• Bleach for environmental disinfection
• Antimicrobial stewardship program

* Not included in CDC/HICPAC 2007 Guideline for Isolation Precautions
Process Measurement

• **Core Measures:**
  – Measure compliance with CDC/WHO recommendations for hand hygiene and Contact Precautions
  – Assess adherence to protocols and adequacy of environmental cleaning

• **Supplemental Measures:**
  – Intensify assessment of compliance with process measures
  – Track use of antibiotics associated with CDI in a facility
C. difficile Treatment

- Metronidazole 500 mg po TID
- Vancomycin 125 mg po QID
- Vancomycin > 125 mg po QID
- Vancomycin enema
- Probiotics (e.g., a yeast Saccharomyces boulardii, in conjunction with antibiotics)
- Fecal transplant
- New drugs (e.g., Fidaxomicin, a new class of narrow-spectrum macrocyclic antibiotics)
# Laboratory-identified MDRO or CDAD Event

<table>
<thead>
<tr>
<th><strong>Facility ID:</strong></th>
<th><strong>Event #:</strong></th>
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<tbody>
<tr>
<td><strong>Patient ID:</strong></td>
<td><strong>Social Security #:</strong></td>
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<tr>
<td><strong>Secondary ID:</strong></td>
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<table>
<thead>
<tr>
<th><strong>Patient Name, Last:</strong></th>
<th><strong>First:</strong></th>
<th><strong>Middle:</strong></th>
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<table>
<thead>
<tr>
<th><strong>Gender:</strong></th>
<th><strong>Date of Birth:</strong></th>
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<tr>
<th><strong>Ethnicity (Specify):</strong></th>
<th><strong>Race (Specify):</strong></th>
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## Event Details

<table>
<thead>
<tr>
<th><strong>Event Type:</strong></th>
<th><strong>Date Specimen Collected:</strong></th>
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<table>
<thead>
<tr>
<th><strong>Specific Organism Type:</strong></th>
<th><strong>Specimen Source:</strong></th>
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<tbody>
<tr>
<td>(Check one)</td>
<td></td>
</tr>
<tr>
<td>□ MRSA</td>
<td>□ Location:</td>
</tr>
<tr>
<td>□ MSSA</td>
<td>□ Date Admitted:</td>
</tr>
<tr>
<td>□ VRE</td>
<td></td>
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<tr>
<td>□ MDR-Klebsiella</td>
<td></td>
</tr>
<tr>
<td>□ MDR-Acinetobacter</td>
<td></td>
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<tr>
<td>□ C. difficile</td>
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<thead>
<tr>
<th><strong>Outpatient:</strong></th>
<th><strong>Date Admitted:</strong></th>
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<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
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Preventing Transmission of *Clostridium difficile* in Healthcare Settings

**Performance Improvement**

- Implement an antimicrobial stewardship program that expedites the proper use of antimicrobial agents.
- Educate all staff on the importance of hand hygiene.
- Educate all staff on the importance of hand hygiene.

**Preventing C. difficile**

- Remove gloves and gowns before leaving the room.
- Clean personal protective equipment should be removed before leaving the room with the patient and transported to the designated area.

**Contact Precautions**

- Patients should be placed in contact precautions for 24 hours from the time of positive result or isolation.
- Patients should be placed in contact precautions for 24 hours from the time of positive result or isolation.

**Environment**

- Ensure the environment is free of sick contacts, including patients and healthcare workers.
- Ensure the environment is free of sick contacts, including patients and healthcare workers.

**Patient Care**

- Ensure that all providers follow standard precautions.
- Ensure that all providers follow standard precautions.

**Primary Sources**

- CDC. *Guideline for the Elimination of *Clostridium difficile* in Healthcare Settings, 2018*
- CDC. *Prevention of *Clostridium difficile* Infections in Acute Care Hospitals.* CID 2003;37(Suppl 1):S1-252
- CDC. *Clostridium difficile (CDI) Infections Toolkit. Activity C: ELI Prevention Collaboratives 2009*
Since publication of the Society for Healthcare Epidemiology of America position paper on Clostridium difficile infection in 1995, significant changes have occurred in the epidemiology and treatment of this infection. C. difficile remains the most important cause of healthcare-associated diarrhea and is increasingly important as a community pathogen. A more virulent strain of C. difficile has been identified and has been responsible for more-severe cases of disease worldwide. Data reporting the decreased effectiveness of metronidazole in the treatment of severe disease have been published. Despite the increasing quantity of data available, areas of controversy still exist. This guideline updates recommendations regarding epidemiology, diagnosis, treatment, and infection control and environmental management.

Practical approaches that address CDI in healthcare settings. Epidemiology, diagnosis, surveillance, prevention, frequently asked questions.
Strategies to Prevent *Clostridium difficile* Infections in Acute Care Hospitals

Erik R. Dubberke, MD; Dale N. Gerding, MD; David Classen, MD, MS; Kathleen M. Arias, MS, CIC; Kelly Podgorny, RN, MS, CPHQ; Deverick J. Anderson, MD, MPH; Helen Burstin, MD; David P. Calfee, MD, MS; Susan E. Coffin, MD, MPH; Victoria Fraser, MD; Frances A. Griffin, RRT, MPA; Peter Gross, MD; Keith S. Kaye, MD; Michael Kompas, MD; Evelyn Lo, MD; Jonas Marschall, MD; Leonard A. Mermel, DO, ScM; Lindsay Nicolle, MD; David A. Pegues, MD; Trish M. Perl, MD; Saniyaj Saint, MD; Cassandra D. Salgado, MD, MS; Robert A. Weinstein, MD; Robert Wise, MD; Deborah S. Yokoe, MD, MPH

References

• Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, Pepin J, Wilcox MH; Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). Infect Control Hosp Epidemiol. 2010 May;31(5):431-55.


References


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