Clostridium difficile Infection
CDI

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05/21/2013
Question

Outbreak investigation…
Threat preparedness…

Are they related?
Answer

• Two essential public health roles in emergency preparedness
  – Prevent epidemics and spread of diseases
    – Routine outbreak investigation and public health surveillance
  – Respond to disaster (disaster outbreaks) and assist community in recovery
    – What type of outbreaks after natural disaster (Derecho storm?)
    – What type of outbreaks → public health threat? Why?

• TP grant → funds → requirement → performance measures
What do you need to do?

- Routine PH surveillance & outbreak investigation
- Building relationship with your partners ….who?
- Know & communicate with your neighbors (counties/other states)
- Learn about the real public health threats
- Learn outbreak investigation steps
- Learn what measures to recommend to control outbreaks:
  - appropriate infection control measures
  - measures to control environmental contamination
- Communicate information
Objectives

- Review microbiology and epidemiology of *Clostridium difficile*
- Review risk factors for transmission
- Discuss testing methods and diagnosis
- Review surveillance for *C. difficile*
- Discuss preventive strategies
C. difficile: Microbiology

- Gram positive spore forming bacillus (rods)

- Obligate anaerobe

- Part of the GI Flora in
  - 1-3% of healthy adult
  - 70% of children < 12 months

- Some strains produce toxins A & B

- Toxins-producing strains cause C. diff Infection (CDI)
C. difficile: Background

- Most common cause of HAI in U.S.

- A common cause of nosocomial antibiotic-associated diarrhea (AAD) (20-30%)

- Most common infectious cause of acute diarrheal illness in healthcare settings

- The only nosocomial organism that is anaerobic and forms spores

- CDI → occur in low risk populations
**CDI: Impact**


CDC/SHEA Train the Trainer
## CDI: Impact

<table>
<thead>
<tr>
<th>Type</th>
<th>Number of annual cases</th>
<th>Cost</th>
<th>Number of annual deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital-onset, hospital acquired (HO-HA)</td>
<td>165,000</td>
<td>$ 1.3 B</td>
<td>9000</td>
</tr>
<tr>
<td>Community-onset hospital acquired (CO-HA)</td>
<td>50,000</td>
<td>$ 0.3 B</td>
<td>3000</td>
</tr>
<tr>
<td>[4 weeks of hospitalization]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing home-onset</td>
<td>263,000</td>
<td>$ 2.2 B</td>
<td>16,500</td>
</tr>
</tbody>
</table>
**C. difficile**: Transmission

- **Fecal – oral route**
  - Contaminated hands of healthcare workers
  - Contaminated environmental surfaces.
    - Survive for up to 5 months on environmental surfaces

- Person to person in hospitals and LTCFs

- **Reservoir**:
  - Human: colonized or infected persons
  - Contaminated environment

- Infective dose is < 10 spores
CDI: Pathogenesis

Step 1 - Ingestion of spores transmitted from other patients

Step 2 - Germination into growing (vegetative) form

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

Step 4 - Toxin B & A production leads to colon damage +/- pseudomembrane
CDI Pathogenesis

- Admitted to healthcare facility
- C Diff exposure & acquisition
- Antimicrobials
- Colonized no symptoms
- Infected Symptomatic
CDI: Risk Factors

- Exposure to antimicrobials (prior 2-3 months)
- Exposure to healthcare (prior 2-3 months)
- Infection with toxigenic strains of C. difficile
- Age > 64 years
- Underlying illness
- Immunosuppression & HIV
- Chemotherapy (immunosuppression & antibiotic-like activities)
- Tube feeds and GI surgery
- Exposure to gastric acid suppression meds ??
- CDI in low risk populations
Changing CDI Epidemiology
Current Epidemic Strain of *C. difficile*

- Increase incidence and severity of CDI in the U.S.
- Emergence of CDI in low risk populations → Severe disease
- Current epidemic Strain → BI/NAP1/027, toxinotype III
  - Historically uncommon – epidemic since 2000
- More resistant to fluoroquinolones
- Produces extra toxin called binary toxin
- More virulent
  - Increased toxin A and B production (16 and 23 times)
  - Change in binding domain of toxin B → increase adherence to the gut wall
  - Increased sporulation → increase survival
## Antimicrobials Predisposing to CDI

<table>
<thead>
<tr>
<th>Very commonly related</th>
<th>Less commonly related</th>
<th>Uncommonly related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin</td>
<td>Sulfa</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Macrolides</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Carbapenems</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Other penicillins</td>
<td>Chloramphicol</td>
</tr>
<tr>
<td>Fluoroquinolons</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Among symptomatic patients with CDI:
  - 96% received antimicrobials within the 14 days before onset
  - 100% received an antimicrobial within the previous 3 months
- 20% of hospitalized patients are colonized with *C. diff*
Clinical Manifestations

• Toxin-producing strains of *C. difficile*:
  – Asymptomatic carriers = Colonized
  – Symptomatic (ill)
    - Mild or moderate diarrhea
    - Pseudo membranous colitis that can be fatal

• Exposure ➔ CDI
  - Median time of 2-3 days

• Risk of developing CDI after exposure ranges between 5-10 days to 10 weeks
CDI: Symptoms

- Watery diarrhea (≥ 3 unformed stools in 24 or fewer consecutive hours)
- Loss of appetite
- Fever
- Nausea
- Abdominal pain and cramping
## CDI: Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Testing Toxins</strong></td>
<td>• Detects toxin A or both A &amp; B</td>
<td>Less sensitive</td>
</tr>
<tr>
<td></td>
<td>• Rapid (same day)</td>
<td>63-94%</td>
</tr>
<tr>
<td></td>
<td>• Inexpensive</td>
<td>Non specific</td>
</tr>
<tr>
<td>Tissue culture cytotoxicity assay</td>
<td>Provides specific and sensitive results for <em>C. diff</em> 67-100%</td>
<td>-Detect toxin B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Technical expertise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-24-48 hours</td>
</tr>
<tr>
<td><strong>Organism ID</strong></td>
<td>Rapid, sensitive, may prove useful as a triage or screening tool</td>
<td>Not specific, toxin testing required to verify diagnosis</td>
</tr>
<tr>
<td>Glutamate Dehydrogenase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCR</td>
<td>Rapid, sensitive, detects presence of toxin gene</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special equipment</td>
</tr>
<tr>
<td>Stool culture</td>
<td>Most sensitive test available when performed appropriately</td>
<td>False-positive results if isolate is not tested for toxin labor-intensive; requires 48–96 hours</td>
</tr>
</tbody>
</table>
Best Strategy for *C. difficile* Testing

- Testing should be performed only on (symptomatic patients) diarrheal stool
- Testing asymptomatic patients is not indicated
- Do not retest if the initial test was negative
- Testing for cure is not recommended
Best Strategy for \textit{C. difficile} Testing

- For clinical use: two-step testing
  - Screen $\rightarrow$ EIA detection of GDH
  - Follow $\rightarrow$ cytotoxicity assay or toxigenic culture to confirm
- Gold standard $\rightarrow$ stool culture $\rightarrow$ toxigenic culture assay
- Toxin is very unstable, degrades at room temperature, and undetectable within 2 hours (false negative results)
CDI Surveillance: Case Definition

Commonly used case definitions

- CDC (NHSN)
  - Infection Surveillance
  - Lab surveillance (ID or event)

- Case definition (SHEA/IDSA)
  - Clinical: presence of diarrhea 3 or more unformed stools in 24 or fewer consecutive hours)
  
  AND

  - Laboratory: A stool test result positive for toxigenic *C. diff* or its toxins
    OR colonoscopic / histopathologic findings demonstrating evidence of pseudomembranes

SHEA- ADSA, 2010
CDI Surveillance: Case Definition

**McGeer case definition for LTCFs**

- Both 1 & 2 should be present
  1. GI sub criteria
     - Diarrhea: 3 or more liquid or watery stools above what is normal for the resident within a 24-h period
     - Presence of toxic megacolon (abnormal dilatation of the large bowel, documented radiologically)
  2. One of the following diagnostic subcriteria
     - Positive stool sample yields a positive laboratory test result for
     - Pseudomembranous colitis is identified during

- It is important to differentiate primary from recurrent episode of CDI
Lab Event (ID) - CDC

- A case of CDI = positive test result that is not duplicate for *C. difficile* toxin A and/or B, or a *toxin-producing C. difficile* organism detected by culture or other laboratory means performed on a stool sample.

- A duplicate positive test from the same patient and location within the past two weeks.

- Recurrent CDI: Any Lab ID >2 weeks ≤8 weeks after the most recent one.

- New CDI: Any Lab ID Event >8 weeks after the most recent one or with no previous Lab ID Event documented for that patient.

- Uses: time, location, new cases, recurrence, prevention strategies.
Lab Event (ID) - CDC

Lab Event “Diagnosis”

- Duplicate
- 2 weeks
- 2-8 weeks
- Recurrent CDI
- Same Illness
- More than 8 weeks
- Or never had CDI
- New CDI
### CDI Surveillance

- **Surveillance definitions of CDI by time of onset:**

<table>
<thead>
<tr>
<th>Case Classification</th>
<th>Case Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare facility (HCF)-onset, HCF-associated CDI</td>
<td>Onset &gt; 3 days of admission (on or after the 4th day)</td>
</tr>
<tr>
<td>Community-onset, HCF-associated CDI</td>
<td>Community onset or within 48 hours of admission and within &lt; 4 weeks of the last discharge</td>
</tr>
<tr>
<td>Community-associated CDI</td>
<td>Onset in the community but within more that 12 weeks of last discharge</td>
</tr>
</tbody>
</table>
Time Line for Surveillance Definitions of 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. Onset defined in NHSN by specimen collection date
CDI Surveillance: Recommendations

- Minimum: surveillance → HCF-onset, HCF-associated to
  - Detect outbreaks
  - Monitor patient safety
- Rate of HCF-associated CDI (number of cases per 10,000 patient-days)
- Compare your rates with other facilities
- In outbreaks → stratify rates by patient location in order to target control measures
CDI Outbreaks

Outbreak definition:
• Three or more epidemiologically linked CDI cases occurring in the same area/unit of the facility within a period of seven days or less OR
• Occurrence of facility-acquired CDI in excess of what is normally expected

• What do you want to know?
  ▪ Date of onset
  ▪ Facility acquired
  ▪ Meet case definition
    ▪ Clinical picture
    ▪ Lab confirmation
  ▪ Infection control measures
Is CDI Reportable in WV?

• Currently
  – Individual cases are not reportable
  – Outbreaks of CDI are reportable

• New reportable disease rules → effective in July, 2013
  – CDI → Lab event → reportable to NHSN
  – Outbreaks of CDI are reportable
• A 31 YO 14 weeks pregnant with twins → ED → 3 weeks of intermittent diarrhea, then 3 days of cramping and watery, black stools 4-5 times/day

• Hx of trimethoprim-sulfamethoxazole exposure for a UTI 3 months ago

• Stool → positive for *C. difficile* toxin → admitted, treated metronidazole and discharged

• Readmitted the next day for 18 days with severe colitis and was treated with metronidazole, cholestyramine, and oral vancomycin, improved and discharged

• 4 days later she was readmitted with diarrhea and hypotension, had a spontaneous abortion

• Aggressive resuscitation and subtotal colectomy, patient died → the 3rd day

• Histopathologic exam of the colon → megacolon & pseudomembranous colitis.
CDI Pathogenesis

- Antimicrobial stewardship
- Antimicrobials
- C Diff exposure & acquisition

Colonized no symptoms

Optimizing Environmental cleaning and Hand Hygiene

Admission to healthcare facility

Infected Symptomatic

Shorten hospital stay
Antimicrobial Stewardship

• Regardless of setting, ~ 50% antibiotic use is “inappropriate”
Antimicrobial Stewardship

• Recommendations:
  ➢ Minimize → frequency and duration of antimicrobial therapy
  ➢ Decrease the number of antimicrobial prescriptions
  ➢ Targeted antimicrobials should be based on the local epidemiology and the *C. difficile* strains
  ➢ Restrict the use of cephalosporin and clindamycin
  ➢ Audit and feedback targeting broad-spectrum antibiotics
Prevention Strategies

Core

• High level of scientific evidence
• Demonstrated feasibility

Supplementary

• Some scientific evidence
• Variable level of feasibility
Prevention Strategies: Core

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

**Tip:** Routine identification of colonized patients for infection control purposes is not recommended and treatment of such identified patients is not effective
Prevention Strategies: Supplemental

- Extend contact precautions beyond duration of diarrhea (48 hours)
- Presumptive isolation for symptomatic patients
- 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
Preventive Strategies: Contact Precautions

Core
- Gloves/gowns on room entry
- Private room (preferred) or cohort with dedicated commodes
- Dedicated equipment
- Maintain for duration of diarrhea
- Measure compliance

Supplemental
- Extend use of contact precautions beyond duration of diarrhea
- Presumptive isolation
- Universal glove use on units with high CDI rates
- Intensify assessment of compliance
Preventive Strategies: Hand Hygiene

Core
- HH based on CDC or WHO guidelines
- Soap and water preferentially in outbreak or endemic settings
- Measure compliance

Supplemental
- Soap and water for HH before exiting room of a patient with CDI
- Intensify assessment of compliance

Conclusion: Spores may be difficult to eradicate even with HH absolute adherence with glove use
Environmental Contamination
Rationale for Universal Glove Use

Preventive Strategies: Environmental Cleaning

Core
- Cleaning and disinfection of equipment and environment
- Consider sodium hypochlorite in outbreak or endemic settings
- Routinely assess adherence to protocols and adequacy of cleaning

Supplemental
- Reassess adequacy of room cleaning and address issues
- Use sodium hypochlorite (bleach) – containing agents
Preventive Strategies: Environmental Cleaning

- Identify and remove environmental sources of *C. diff*

- Routine environmental screening for *C. diff* is not recommended

- Ensure that environmental cleaning is adequate and high-touch surfaces are not being overlooked

- If possible, use the environmental markers to assess cleaning after education
# Infection Prevention and Control Isolation Compliance Checklist

Date and Time of Observation ____________________________  Observer ____________________________  Precaution/Isolation Type ____________________________

<table>
<thead>
<tr>
<th>Unit</th>
<th>Room #</th>
<th>Compliance with Hand Hygiene Practices</th>
<th>Person Observed (HCW or visitor)</th>
<th>100% Compliant with isolation?</th>
<th>Yes or No</th>
<th>Identify variance by PPE or Signage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ABHR Soap + H₂O</td>
<td>1 = Physician  2 = RN  3 = Transporter  4 = PA  5 = Respiratory RX  6 = Nursing assistant  7 = Rehab  8 = Lab  9 = Dietary  10 = Housekeeping  11 = Other HCW  12 = Visitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1  2  3  4  5  6  7  8  9  10  11  12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 8.1.** Infection Prevention and Control Isolation Compliance Checklist. Source: Loretta Litz Fauerbach, Shands at the University of Florida.
Table 10.2. Environmental checklist using sodium hypochlorite for daily cleaning when *C. difficile* is involved.

**Clostridium difficile ENVIRONMENTAL CHECKLIST USING SODIUM HYPOCHLORITE**

**FOR DAILY CLEANING - ROOM OBSERVATIONS:** Please review a sample of 5 patients per week (1 patient per day) with known or suspected *C. difficile*.

<table>
<thead>
<tr>
<th>Instruction</th>
<th>Component</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>At start, perform hand hygiene.</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Put on PPE.</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disinfect w/ hypochlorite-based disinfectant, high-touch surfaces.</td>
<td>Door knobs/handles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Door surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bed rails</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Call button</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Phone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overbed table &amp; drawer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Countertop</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Light switches</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Furniture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arms of patient chair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seat of patient chair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All other miscellaneous horizontal surfaces</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Window sills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bedside commode</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medical equipment (e.g., TV controls)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spot clean walls with disinfectant cloth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disinfect w/ hypochlorite-based disinfectant:</strong></td>
<td><strong>BATHROOM, including:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bathroom door knob</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Toilet horizontal surface/seat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Toilet lever/flush</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Faucets (at sink)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bathroom handrails</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sink</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tub/shower</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mirror</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Damp dust:</strong></td>
<td>Overhead light (if the bed is empty)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TV &amp; stand</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clean:</strong></td>
<td>Lights</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clean floor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dust mop tile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wet mop tile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hand sanitizer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paper towels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Soiled curtains</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>For terminal cleaning, damp dust:</strong></td>
<td>Bed frame</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mattress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Remove bed with clean linen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Replace as needed:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pillows, mattresses, pillow covers, mattress covers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other:</strong></td>
<td>Empty trash &amp; replace liner</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Discard dust cloths, N/A</strong></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Change mop heads after each isolation room:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Remove PPE before exit:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Perform hand hygiene:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any significant areas not mentioned above (please describe):

This room looks clean and ready for use:

Sign-off by Environmental Services employee cleaning the room:

Sign-off by TBD, based on your hospital process for cleaning room:

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Preventive Strategies: Summary

- Surveillance
- Microbiologic identification
- Contact precautions
- Hand hygiene
- Environmental cleaning
- Antimicrobial stewardship
- Education → HCWs, patients, visitors, families
- Administrative support
Resources

- APIC: Guide to Preventing *Clostridium difficile* Infections (2013)

- SHEA/IDSA Compendium of Recommendations

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Supplement Article: SHEA/IDSA Practice Recommendation

Strategies to Prevent *Clostridium difficile* Infections in Acute Care Hospitals

*SHEA-IDSA Guideline*

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)

Prevention of *Clostridium difficile* Infection (CDI) Massachusetts CDI Prevention Collaborative; Carolyn Gould, MD MSCR; L. Cliff McDonald, MD

SHEA HAI training program, May 2011
Questions / Discussion