Today’s Host

**Morgen Palfrey**, Project Coordinator, Institute for Healthcare Improvement, is the current coordinator for web-based Expeditions. She also contributes to the IHI Leadership Alliance, the Always Project, and works with Strategic Partners in Singapore. Morgen is a member of Work-Life Wellness Team and Diversity and Inclusion Council at IHI, where she and fellow staff members develop strategies for improving the mind and body. Morgen graduated from the University of Florida in Gainesville, FL where she received her Bachelor of Arts degree in Political Science with a concentration in Public Administration.
Audio Broadcast

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1) Click the button on the right hand side of the screen.
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- Phone connection is preferred if you have access to a phone.

WebEx Quick Reference

- Welcome to today’s session!
- Please use chat to “All Participants” for questions
- For technology issues only, please chat to “Host”
- WebEx Technical Support: 866-569-3239
- Dial-in Info: Communicate / Join Teleconference (in menu)
When Chatting...

Please send your message to All Participants

Expedition Director

Diane Jacobsen, MPH, CPHQ, Director, Institute for Healthcare Improvement (IHI) is currently directing the CDC/IHI Antibiotic Stewardship Initiative, NSLIJ/IHI Reducing Sepsis Mortality Collaborative. Ms. Jacobsen served as IHI content lead and improvement advisor for the California Healthcare-Associated Infection Prevention Initiative (CHAIP) and directed Expeditions on Antibiotic Stewardship, Preventing CA-UTIs, Reducing C. difficile Infections, Sepsis, Stroke Care and Patient Flow. She served as faculty for IHI’s 100,000 Lives and 5 Million Lives Campaign and directed improvement collaboratives on Sepsis Mortality, Patient Flow, Surgical Complications, Reducing Hospital Mortality Rates (HSMR) and co-directed IHI’s Spread Initiative. She is an epidemiologist with experience in quality improvement, risk management, and infection control in specialty, academic, and community hospitals. A graduate of the University of Wisconsin, she earned her master’s degree in Public Health- Epidemiology.
Today’s Agenda

- Introductions
- Action Period Assignment
- Debrief
- The Role of Antibiotic Stewardship
- Action Period Assignment

Expedition Objectives

At the end of this Expedition, participants will be able to:

- Explain the impact of the increasing incidence and severity of *C. difficile* on hospitals
- Discuss key approaches to preventing the spread of *C. difficile* in the hospital setting
- Identify and begin improving at least one key process for impacting *C. difficile* in their hospital
Schedule of Calls

Session 1 – Making the Case for Reducing Clostridium difficile Infections (CDI)
Date: Wednesday, June 25, 2:00 – 3:30 PM ET

Session 2 – Rapid Detection and Isolation
Date: Wednesday, July 9, 2:00 – 3:00 PM ET

Session 3 – Symptom Recognition, Precautions, and the Role of the Environment
Date: Wednesday, July 23, 2:00 – 3:00 PM ET

Session 4 – Antibiotic Stewardship
Date: Wednesday, August 6, 2:00 – 3:00 PM ET

Session 5 – The Role of Leadership
Date: Wednesday, August 20, 2:00 – 3:00 PM ET

Session 6 – Transitions and Long-term Care
Date: Wednesday, September 3, 2:00 – 3:00 PM ET

Action Period Assignment

Role of the environment:

- Test a checklist to assess terminal Environmental cleaning:
  - Does your current process/procedure address all the components of the CDC checklist?
  - Request input/feedback on current process from:
    - Environmental Services: current barriers/constraints they encounter in completing terminal cleaning
    - Nursing: are there current constraints

- Incorporate input from Nursing and/or Environmental Services to test a change to your current process
Faculty

Belinda Ostrowsky, MD, MPH, FSHEA did her Internal Medicine Residency at Mayo Clinic, Rochester, MN and Infectious Diseases Fellowship at the Beth Israel Deaconess Medical Center, Boston, MA. During fellowship she completed an MPH and participated in antibiotic resistance research. She was an Epidemiology Service Officer (EIS) at the Centers for Disease Prevention and Control (CDC) working on projects related to healthcare related infections. She is the current director of the Montefiore/Albert Einstein College Antimicrobial Stewardship Program in the Bronx, NY. As the director of the Antimicrobial Stewardship Program (ASP), Dr. Ostrowsky’s interests span the implementation of antibiotic stewardship, infection control and public health. Examples of recent/current projects include: 1) An Agency for Healthcare Research and Quality (AHRQ)/CDC funded multi-center project accessing the role of ASP on C. difficile rates; 2) Developing and studying the impact of prescribing tools to improve empiric antibiotic choices for different prescriber groups (e.g., community acquired pneumonia, emergency room admissions, surgical prophylaxis) and, 3) Accessing the impact of newer rapid microbiological diagnostics on antibiotic prescribing and patient outcomes.

Faculty

Phillip Chung, PharmD, MS completed a general pharmacy residency and a pharmacy residency specialized in infectious diseases at Cleveland Clinic, Cleveland, OH. He is currently Clinical Pharmacy Manager in Infectious Diseases at the Einstein Campus of Montefiore Medical Center and assistant professor of Albert Einstein College of Medicine in the Bronx, NY. His clinical interests include antimicrobial stewardship, antimicrobial pharmacokinetics and pharmacodynamics, antimicrobial resistance, and Clostridium difficile infections.
Faculty

Brian Koll, MD, FACP, FIDSA, Executive Director for Infection Prevention, the Mount Sinai Health System, New York, NY, is a nationally-renowned and award-winning infection prevention expert. He has been featured on CBC Evening News for successful efforts to reduce central line associated bloodstream infections, on World News Tonight for successful efforts to control C. difficile, and in a national public service announcement regarding this disease by the Peggy Lillis Memorial Foundation.

C. difficile Expedition: The Role of Antimicrobial Stewardship

August 6, 2014
Phillip Chung, PharmD, MS
Belinda Ostrowsky, MD, MPH, FSHEA
Does your facility have a formal Antimicrobial Stewardship Program?

- Yes
- No
- Don’t know

Does your facility have written C. difficile guidelines?

- Yes
- No
- Don’t know
Top 5 Issues in Antimicrobial Prescribing & *C. difficile*

1) Formulary Issues
2) Treatment of *C. difficile* (new agents)
3) Role of microbiome
4) Review of antibiotic / medication use (before and after *C. difficile* diagnosis)
5) ASP as part of the solution

What is Antimicrobial Stewardship?

- An antimicrobial stewardship program (ASP) is a systematic approach for developing coordinated interventions to monitor & when necessary, alter current antimicrobial prescribing practices

SHEA/IDSA Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship
http://cid.oxfordjournals.org/content/44/2/159.full.pdf+html
Why ASP for *C. difficile* (CDI)?

- Rates of CDI remain high\(^1\)
- CDI transmission is likely multifactorial\(^2\):
  - Infection control, environment, inter-facility transfer
  - Association with common antimicrobial use
- ASP offers strategies to prevent & control CDI:
  - At several points in prescribing
  - Complementary to other interventions
  - Multi-disciplinary

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1. Elixauser et al. AHRQ at: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb50.jsp

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*C. difficile* Pathogenesis

**Steps**

1. Antibiotic damage
2. CDI healthcare exposure
3. CDI toxin production
4. Toxin hyperproduction
5. Severe sepsis/shock

**Patient Status**

Normal flora

Disruption of flora

*C. difficile* colonization

*C. difficile* colitis

Fulminant colitis

Death from *C. difficile*

---

The Role of Antibiotic in CDI

• Kill intended bacteria

• “Collateral damage” change to microbiome
  – Micro-environment- change mucous / proteins
  – Inhibitory factors
  – Balance bacteria
  – Competition for receptors

The Role of Antibiotic in CDI

• Extent of damage:
  – Spectrum of activity
  – Duration
  – Amount that reaches colon
  – Activity in anaerobic environment
  – Amount excreted in bile
  – Dose
  – Route of administration
Top 5 Issues in Antimicrobial Prescribing & *C. difficile*

1) **Formulary Issues**

2) Treatment of *C. difficile* (new agents)
3) Role of microbiome
4) Review of antibiotic / medication use (before and after *C. difficile* diagnosis)
5) ASP as part of the solution

**Formulary Issues**

- Pharmacy and Therapeutic Committee oversees what (formulary) and how (policy) drugs are used
  - Based on efficacy, toxicity, and cost while limiting redundancy
  - ASP can be a vital part before and after addition of new antibiotics
Formulary Issues in CDI Therapy: The Case of Fidaxomicin

- Enthusiasm over 1st new CDI therapy in 25 years
- Questions: efficacy, incremental benefits, appropriate patients, costs
- ASP gathered stakeholders to review data and discuss place in therapy
- Formulated institutional CDI treatment algorithm
- Presented findings/algorithm to P & T for approval

**CDI Diagnosis**

- 1st episode
  - Mild to Moderate
    - Metronidazole x 10-14 days
  - Severe
    - Vanco PO x 10-14 days

- 1st recurrence
  - Low risk for further recurrence
    - Repeat treatment using initial regimen
  - High risk for further recurrence
    - Consult ID: consider fidaxomicin

- >1 recurrences
  - All severity
    - Consult ID/GI: vanco taper; consider fidaxomicin, fecal transplant

Top 5 Issues in Antimicrobial Prescribing & *C. difficile*

1) Formulary Issues
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**Current CDI Therapy**

- Mild to moderate or non-severe
  - Metronidazole PO: similar efficacy to vancomycin PO
- Severe
  - Vancomycin PO (125mg): superior to metronidazole
- Severe complicated
  - Metronidazole IV + vancomycin PO (500mg)/ vancomycin PR
- 1st recurrence
  - Repeat initial therapy
- Episodes beyond 1st recurrence
  - Vancomycin PO if previously treated with metronidazole
  - Vancomycin taper after completion of therapy
  - Fecal transplant? Newer agent? Alternative therapy?
Comparing Vancomycin Dosing

- Dosing change due to treatment algorithm and ASP
  - >125mg q6h to 125mg q6h
- Patient characteristics
  - Median age ~75 years old
  - 30% with CDI history
  - 40% from LTCFs
  - 55% hospitalized in last 30 days
  - 50% had ABX exposure
  - Median LOS ~20 days
  - 75% considered severe cases
- Implications
  - Lower impact on GI flora and cost saving
  
Chung, et al. ICAAC 2013. Presentation K335

Fidaxomicin

- Approved based on 2 RCTs compared to vancomycin PO
- Exclusion criteria: life-threatening CDI, history of IBD, >1 CDI episode in past 3 months
- Patients: ~65yo, 40% tx’d outpatient, 15% with prior CDI episode
- Implications:
  - Similar efficacy to vanco PO w/ hypervirulent strain
  - Use resulted in less CDI recurrence
  - Use in patients with multiple episodes?
  - What about fulminant CDI?
  - Who would benefit most in face of relative high cost (>2000/course)

Intravenous Immunoglobulins

- Use 1st described in children with multiple CDI episodes
  - IVIG 400mg/kg every 3 wks
  - Diarrhea resolved in 5 of 5 patients after median of 2 doses


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<tr>
<th>Study</th>
<th>Patient(s)</th>
<th>Age</th>
<th>Male</th>
<th>Female</th>
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<th>Days to resolution</th>
<th>Day IVIG started</th>
<th>Cure</th>
<th>Recurrence</th>
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<td>1</td>
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<tr>
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<td>70 (10)</td>
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<td>n/a</td>
<td>M</td>
<td>n/a</td>
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</table>

- Implication: optimal regimen and when to give in disease course is not well established

Top 5 Issues in Antimicrobial Prescribing & *C. difficile*

1) Formulary Issues
2) Treatment of *C. difficile* (new agents)
3) Role of microbiome
4) Review of antibiotic / medication use (before and after *C. difficile* diagnosis)
5) ASP as part of the solution
Probiotics

- *Saccharomyces* or *Lactobacillus* most often used

- Recent meta-analyses showed benefits in reducing
  - ABX-associated diarrhea (AAD) by 42% (RR 0.58, 95% CI 0.50-0.68)
  - CDI by 66% (RR 0.34, 95% CI 0.24-0.49)

- However, more recent studies showed otherwise…
  - Multicenter study comparing lactobacilli/bifidobacteria vs placebo
    - AAD: 10.8% probiotics vs. 10.4% placebo ($p = 0.71$)
    - CDI: 0.8% probiotics vs. 1.2% placebo ($p = 0.35$)
  - Single center study comparing *Saccharomyces* vs placebo
    - AAD: 15.1% probiotics vs. 13.3% placebo ($p = 0.84$)
    - CDI: 2.8% probiotics vs. 2.0% placebo ($p = 1.00$)

- Implications: true effectiveness remains unclear


Fecal Transplant

- First reported in 1958 with pseudomembranous colitis
- Mainly case reports (recurrences)
- Meta-analysis 2013-300 patients- cure rates 85-90%
- RCT Netherlands:
  - Vancomycin regimen, bowel lavage & donor feces via nasoduodenal tube 13/16 (2/3)
  - A standard vancomycin regimen 4/13
  - A standard vancomycin regimen & bowel lavage 3/13
- FDA- declaring biologic/new drug- IND – reconsidered
- Implication: Highly effective- “yuck factor”

“rePOOPulating”- The “poop pill”

• A variation on stool transplant
• Researchers processed feces until only bacteria-encapsulated in 3 layer gelatin capsule
• 27 patients:
  – Ingested 24-34 capsules containing family donated fecal bacteria
  – None had recurrences
  – Advantages: covers more of GI tract, no invasive procedure, more comfortable / acceptable (9.6/10)

Implication: Need more testing, interesting way to “repopulate” gut and decrease recurrent CDI


Top 5 Issues in Antimicrobial Prescribing & C. difficile

1) Formulary Issues
2) Treatment of C. difficile (new agents)
3) Role of microbiome
4) Review of antibiotic / medication use (before and after C. difficile diagnosis)
5) ASP as part of the solution
ASP for CDI

Steps

1. Antibiotic damage
2. CDI healthcare exposure
3. CDI toxin production
4. Toxin hyperproduction
5. Severe sepsis/shock

Patient Status

Normal flora
Disruption of flora
C. difficile colonization
C. difficile colitis
Fulminant colitis
Death from C. difficile

ASP Activities

• Formulary
• Use Before
• Testing
• Use After
• Treatment


What Impact Could Reduced Antibiotic Use have on CDI?

• Recent MMWR¹:
  • Mixed methods, data sources
  • In 323 hospitals, >55% patients received antibiotic
  • 37% prescribing could be improved
  • Wide variety in prescribing
  • Estimated 30% reduction in antibiotic use, could deceed CDI by 26%

¹ CDC. MMWR. Mar 7, 14. 63(09):194-200.
Strategies to Review Antibiotic Prescribing Before CDI

- Review common and high volume antibiotics
- Review antibiotics in CDI cases
- Systemic approach
  - Identify antibiotic prescribing most associated with CDI
- Tailored ASP interventions

ASP Activities Based on Identified Prescribing Issues

<table>
<thead>
<tr>
<th>Issue</th>
<th>ASP Activity (Examples)</th>
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<tbody>
<tr>
<td>Broad empiric regimens</td>
<td>• Upfront restrictions&lt;br&gt;• Ordering screens by syndrome</td>
</tr>
<tr>
<td>Prolonged courses</td>
<td>• Audit &amp; feedback&lt;br&gt;• De-escalation program&lt;br&gt;• Restriction at 72 hours</td>
</tr>
<tr>
<td>Overuse of specific drugs</td>
<td>• Targeted education / distribution local antibiograms&lt;br&gt;• Review allergies&lt;br&gt;• Mandatory ID consults</td>
</tr>
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</table>

Review Medications After CDI Diagnosis

• Antibiotics (short/long term):
  – Are they still needed?
  – Can they be narrowed or the course shortened?

• Other Drugs:
  – Anti-motility agents,
  – Narcotic
  – Laxatives
  – Immunosuppression
Proton Pump Inhibitors (PPI) and CDI

- Data mixed
- 2 studies & editorial in May 2010: “Less is more”1-3
  - Respective cohort: 5 years, 1166 patients
    - Recurrent CDI higher PPI (25.2 vs 18.5%)
    - Many PPI no indications
  - Pharmcoepidemiologic cohort: >100,000 discharges/5 yrs
    - Dose relationship
- FDA warning- PPI & CDI4

- **Practical issues:** Many no indication, associated with VAP, expense, after CDI Dx- stronger case

1-3 Linsky, Arch Int Med 2010, Howell, Arch Int Med 2010; Katz, Arch Int Med 2010

Top 5 Issues in Antimicrobial Prescribing & *C. difficile*

1) Formulary Issues
2) Treatment of *C. difficile* (new agents)
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4) Review of antibiotic / medication use (before and after *C. difficile* diagnosis)
5) **ASP as part of the solution**
ASP as Part of the Solution

**Steps**

1. Antibiotic damage
2. CDI healthcare exposure
3. CDI toxin production
4. Toxin hyperproduction
5. Severe sepsis/shock

**Patient Status**

- Normal flora
- Disruption of flora
- *C. difficile* colonization
- *C. difficile* colitis
- Fulminant colitis
- Death from *C. difficile*

**Interventions**

- ASP
- Inf. Control & Cleaning
- Clinical
- ASP & Lab
- Critical care, GI, ID & Surgery


An Example:
A Cluster of CDI in Heme/Onc Unit

- Multi-disciplinary, including Leadership
- Several issues likely lead to the cluster
- Interventions:
  - **Infection Control**: pre-emptive isolation, vigilance for diarrhea, hand hygiene
  - **Environment**: terminal cleaning, common areas
  - **Lab**: Using data on BI:NAP1, efficient testing
  - **Clinical/Critical Care/ID**: supportive, review other meds / chemo
  - **ASP**: review antibiotic / PPI / Meds - before & after, CDI treatment
Conclusions

- CDI rates remain high
- ASP can help:
  - Formulary
  - Treatment for CDI (role for novel agents)
  - Consider the balance of the microbiome
  - Antibiotic exposures before and after CDI (individuals and in aggregate)
- ASP interventions complement the work of other stakeholders
- Ultimately control of CDI is multidisciplinary

Questions?

Raise your hand

Use the Chat
Action Period Assignment

Test a process to review antibiotic/medication use before and after C. difficile diagnosis:

- Identify the “last 5“ patients diagnosed with C. difficile (one day/week/month, one unit/service, etc.)
- Convene a multidisciplinary review/huddle (to include Physicians and/or Pharmacy reps, Nursing, Infection Prevention, etc.)
- Review AB/PPI/medications before and after C. difficile diagnosis
- Identify any “opportunities“ for:
  - Discontinuing
  - Narrowing or shortening the course

Come prepared to share what you learned

Expedition Communications

- Listserv for session communications: CdiffExpedition@ls.ihi.org
  - To add colleagues, email us at info@ihi.org
  - Pose questions, share resources, discuss barriers or successes
Next Session

**Session 5: The Role of Leadership**
Wednesday, August 20, 2:00 PM – 3:00 PM ET

**Faculty:** Jeremy Boal, MD