Novel Approaches for Non-Antibiotic Interventions for Clostridium Difficile Stewardship

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Disclosure

Jason Gallagher
Achaogen: Advisory Board; Allergan: Advisory Board, Speaker’s Bureau; Astellas Pharma, Inc.: Advisory Board, Speaker’s Bureau; Cidara: Consultant; Merck: Advisory Board, Grant Recipient, Speaker’s Bureau; Paratek: Advisory Board; Shionogi: Advisory Board; The Medicines Company: Advisory Board; Theravance: Advisory Board

All other planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.
Objectives

• Compare and contrast different rapid diagnostic tests for Clostridium difficile.
• Evaluate and mitigate medication risk factors for Clostridium difficile.
• Recommend the role of immunomodulatory agents in patient therapy.
• Design an appropriate treatment regimen for a patient with Clostridium difficile.
Patient Case

BM is a 73 y/o female called out from the ICU to the GenMed floor after a 3 day stay for AMS and hypotension. After a rather thorough workup, no definitive source was identified and she was transferred to the floor for further evaluation. She has a PMH of osteopenia.

Vitals:
T 98.8°F, HR 68, BP 92/66 mmHg, RR 18, 98% RA

Chem7 and CBC:

<table>
<thead>
<tr>
<th>135</th>
<th>98</th>
<th>12</th>
<th>100</th>
<th>11</th>
<th>187</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.6</td>
<td>24</td>
<td>1.2</td>
<td>8.7</td>
<td>27</td>
<td>187</td>
</tr>
</tbody>
</table>

Medication Upon Transfer:
- Acetaminophen PO prn
- ASA 81 mg PO daily
- Calcium carbonate 500 mg PO QID
- Ciprofloxacin 500 mg PO twice daily
- Influenza vaccine 0.5 mL IM x 1
- Metronidazole 500 mg PO q8h
- Multivitamins PO daily
- Pantoprazole 40 mg PO daily
DOES BM HAVE RICK FACTORS FOR CLOSTRIDIUM DIFFICILE?

A. Yes
B. No
Background

- *Clostridium difficile* in an anaerobic, spore forming, Gram-positive rod
- Leading cause of health care-associated diarrhea
  - >90% of infections occur in patients with recent (8 weeks) of antibiotic exposure
- Recurrence occurs in ~20% of patients
  - Subsequent courses ↑ difficulty in treating

https://www.cdc.gov/media/releases/2015/p0225-clostridium-difficile.html
Toxin Production

- Toxins A/B
  - Intestinal injury
  - Acute inflammation
- Binary Toxin
  - Increased virulence?
  - Increased recurrence?

Hypervirulent strains
CDC “Urgent Threat”

- ~500,000 cases/year
- ~29,000 deaths/year
- $1-5.4 billion excess medical costs/year

Hypervirulent Strain

- Epidemic strain (NAP1/BI/027)
  - ↑ spore production
  - ↑ toxin A and B (quantity, duration)
  - 3rd toxin: binary toxin
  - ↑ toxin binding to targets, intestinal epithelial adherence
  - ↑ outbreaks, spreading
  - More difficult to treat

# Diagnosis

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
</table>
| 1. Only test watery stools, diarrhea | Strong recommendation  
High quality evidence |
| 2. NAAT are superior to and preferred over toxin A+B EIA | Strong recommendation  
Moderate quality evidence |
| 3. GDH screening can be used in a 2- or 3-step screening algorithm, but sensitivity lower than NAAT | Strong recommendation  
Moderate quality evidence |
| 4. Avoid repeat testing | Strong recommendation  
Moderate quality evidence |
| 5. Avoid testing for cure | Strong recommendation  
Moderate quality evidence |

NAAT: nucleic acid amplification test; EIA: enzyme immunoassay; GDH: glutamate dehydrogenase
## Clostridium difficile RDT

<table>
<thead>
<tr>
<th>Organism</th>
<th>Test Name</th>
<th>Technology</th>
<th>Detection time (h)</th>
<th>Batching</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. difficile</td>
<td>Xpert C. difficile</td>
<td>Multiplex PCR</td>
<td>0.5</td>
<td>No</td>
</tr>
<tr>
<td>C. difficile</td>
<td>Xpert C. difficile/Epi</td>
<td>Multiplex PCR</td>
<td>0.75</td>
<td>No</td>
</tr>
<tr>
<td>C. difficile BI/NAP1/027</td>
<td>Xpert C. difficile/Epi</td>
<td>Multiplex PCR</td>
<td>0.75</td>
<td>No</td>
</tr>
<tr>
<td>C. difficile</td>
<td>Illumigene C. difficile</td>
<td>LAMP</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>C. difficile</td>
<td>BD GeneOhm Cdiff Assay</td>
<td>PCR</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>C. difficile</td>
<td>ProGastro Cd Assay</td>
<td>PCR</td>
<td>3</td>
<td>Yes</td>
</tr>
</tbody>
</table>

RDT: rapid diagnostic technologies

Slide adapted from Karri Bauer
Clostridium difficile RDT in Real Life

- *C. difficile* rate can appear to increase
  - PCR more sensitive
  - Spores can be detected even if not actively infected

- Need strict criteria for testing
  - ≥3 loose stools/24 hours
  - No repeat testing within 7 days
  - Do not use for “test of cure”
Treatment

- **Mild/moderate**: metronidazole 500 mg PO q8h
- **Severe**: vancomycin 125 mg PO q6h
- **Severe/complicated**: vancomycin 500 mg PO q6g
  + metronidazole 500 mg IV q8h
- Missing from the guidelines: fidaxomicin, FMT, bezlotoxumab

FMT: fecal microbiota transplantation

Cohen SH et al. *Infect Control Hosp Epidemiol* 2010;31:431-55
Modifiable Risk Factors

Antibiotic Exposure
High risk:
• Fluoroquinolones
• 3rd and 4th generation cephalosporins
• Clindamycin
• Carbapenems

Exposure to *C. difficile* spores
• Spores can remain viable for months
• Contamination ↑ in rooms of pts with active *C. diff*
• Hands easily contaminated

Gastric Acid Suppression
• Data implicates PPI use
• Need more studies: PPI restriction and ↓ *C. diff*

Additional Risk Factors: older age (≥ 65 years), inpatient stay/healthcare exposure, immunosuppression, low anti-toxin A/B antibody [ ]

# Abx Stewardship – CDI Assessment Tool

## Targeted Assessment for Prevention (TAP) Strategy

<table>
<thead>
<tr>
<th>II. Antibiotic Stewardship for CDI Prevention</th>
<th>Response</th>
<th>Comments (and/or “As Evidenced By”)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does your facility routinely review appropriateness of antibiotics prescribed for treatment of other conditions (e.g., UTI) for patients with new or recent CDI diagnosis?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
<tr>
<td>2. Does your facility educate providers about the risk of CDI with antibiotics?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
<tr>
<td>3. Does your facility educate patients/family members about the risk of CDI with antibiotics?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
<tr>
<td>Does your facility monitor the use of the following antibiotics that are high-risk for CDI:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Fluoroquinolones?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
<tr>
<td>5. 3rd/4th generation cephalosporins?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
<tr>
<td>Does your facility use strategies to reduce the unnecessary use of the following antibiotics that are high-risk for CDI:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Fluoroquinolones?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
<tr>
<td>7. 3rd/4th generation cephalosporins?</td>
<td><img src="yes.png" alt="Radio Button" /> <img src="no.png" alt="Radio Button" /> <img src="unk.png" alt="Radio Button" /></td>
<td></td>
</tr>
</tbody>
</table>

**CDI TAP Facility Assessment Tool V4.0 – Last Updated July 2016**

[https://www.cdc.gov/hai/prevent/tap.html](https://www.cdc.gov/hai/prevent/tap.html) (CDI Facility Assessment Tool)
Non-Restrictive AST on CDI Rates

- Local guidelines, physician letter, pocket guide: awareness and alternatives to 2\textsuperscript{nd} /3\textsuperscript{rd} gen cephalosporins, ciprofloxacin, clindamycin, macrolides
- Non-restrictive AST was more effective than infection control measures in ↓ CDI

AST: Antimicrobial Stewardship

Fluoroquinolone Restriction & CDI

- Respiratory FQ restriction
- System-wide education
- Beta-lactam allergy assessment tool
- RPh competency
- Prospective RPh review for all FQ orders
- No CDI interventions

Shea KM et al. AAC 2017;61:e00125-17

<table>
<thead>
<tr>
<th></th>
<th>Pre-Intervention</th>
<th>Education</th>
<th>Restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td>FQ DOT/1000 PD</td>
<td>41.0 ± 4.4</td>
<td>4.8 ± 3.6</td>
<td></td>
</tr>
<tr>
<td>CDI cases/10,000 PD</td>
<td>4.0 ± 2.1</td>
<td>2.2 ± 1.35</td>
<td></td>
</tr>
</tbody>
</table>
### C. diff Stewardship – More Data!

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carling 2003</td>
<td>• Prospective abx monitoring&lt;br&gt; • ↓ inappropriate IV abx&lt;br&gt; • Guidelines, Rx restrictions, individual MD detailing</td>
<td>• 22% ↓ broad IV abx&lt;br&gt; • C. diff incidence 2.2 → 1.4/1,000 pt days</td>
</tr>
<tr>
<td>Fowler 2007</td>
<td>• ↓ amox/clav use&lt;br&gt; • ↑ benzyl PCN, TMP, amox&lt;br&gt; • Individual MD C. diff/MRSA feedback q8-12 w</td>
<td>• ↓ amox/clav and cepha use&lt;br&gt; • ↑ benzyl PCN use&lt;br&gt; • ↓ C. diff infections with no Δ in MRSA</td>
</tr>
<tr>
<td>Muto 2007</td>
<td>• Educational material&lt;br&gt; • Active C. diff surveillance&lt;br&gt; • ↑ infection control audits&lt;br&gt; • Restrict clinda, CRO, levo, others</td>
<td>• 41% ↓ abx-associated C. diff&lt;br&gt; • Aggregate C. diff rate 7.2 → 3/1,000 pt discharges</td>
</tr>
<tr>
<td>Valiquette 2007</td>
<td>• Educational materials&lt;br&gt; • Alternative abx recommendations&lt;br&gt; • Shorter duration of therapy</td>
<td>• 60% ↓ C. diff incidence&lt;br&gt; • 54% ↓ targeted abx use&lt;br&gt; • ↑ use resp-FQs and pip/tazo</td>
</tr>
</tbody>
</table>

Abx: antibiotic; PCN: penicillin; TMP: trimethoprim; CRO: ceftriaxone; FQ: fluoroquinolone
PPI Stewardship

Howell MD et al. Arch Int Med 2010;170:784-90
# Unnecessary PPI Continuation

<table>
<thead>
<tr>
<th>Reference(s)</th>
<th>Population</th>
<th>Unnecessary Start*</th>
<th>Continued Outside of ICU*</th>
<th>Continued at d/c*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nardino 2000; Parente 2003; Zink 2005</td>
<td>Gen Med</td>
<td>56-75%</td>
<td>-</td>
<td>Up to 55%</td>
</tr>
<tr>
<td>Wohlt 2007</td>
<td>MICU/SICU</td>
<td>-</td>
<td>60%</td>
<td>24.4%</td>
</tr>
<tr>
<td>Murphy 2008</td>
<td>SICU</td>
<td>4.4%</td>
<td>79.3%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Pavlov 2014</td>
<td>MICU/SICU</td>
<td>-</td>
<td>19.1%</td>
<td>-</td>
</tr>
</tbody>
</table>

*Without appropriate indication

# Probiotics

<table>
<thead>
<tr>
<th>Reference</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDSA Guidelines. 2010</td>
<td>No</td>
</tr>
<tr>
<td>Cochrane Review: <em>Use of Probiotics to Prevent C. difficile Associated with Abx.</em> 2013</td>
<td>Yes</td>
</tr>
<tr>
<td>Mexico: <em>Mexican Consensus on Probiotics In Gastroenterology.</em> 2017</td>
<td>Yes</td>
</tr>
<tr>
<td>Susan Davis: <em>Pharmacotherapy 2015;35:1016-25</em></td>
<td>No</td>
</tr>
<tr>
<td>Twitter</td>
<td>No</td>
</tr>
</tbody>
</table>

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Monica Mahoney @mmPharmD - Aug 19
Tweeps! I need your professional opinion. Probiotics for C. difficile ... yay or nay? @SIDPharm @accpinfo @ASHPOfficial @IDSAinfo

*25% Yes*

*75% No*

71 votes - Final results
1-2 Punch: ↓ PPIs and ↑ Probiotics

Study
Implementation of Global Strategies to Prevent Hospital-Onset *Clostridium difficile* Infection: Targeting Proton Pump Inhibitors and Probiotics

Intervention
- C. diff educational campaign
- PPI prospective audit & feedback: orders not approved if not per protocol
- Probiotic bundles added to all abx order sets outside of ICU
  - *Lactobacillus acidophilus, Bifidobacterium lactis, B. longum*

Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>FY14</th>
<th>FY15</th>
<th>Difference</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg PPI use (doses/1000 pt days)</td>
<td>677</td>
<td>581</td>
<td>-96 (14.2%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Avg IV PPI use (doses/1000 pt days)</td>
<td>229</td>
<td>158</td>
<td>-71 (31.1%)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Avg probiotic use (doses/1000 pt days)</td>
<td>97</td>
<td>223</td>
<td>126 (129.6%)</td>
<td>0.0006</td>
</tr>
<tr>
<td># HO-CDI (cases/1000 pt days)</td>
<td>0.49</td>
<td>0.39</td>
<td>-0.1 (20%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Kefir

• Fermented milk with yeast and probiotics
  – Gelatinous white/yellow particles called “grains”
  – “Grains” contain bacteria, yeast, casein, and complex sugars
  – “Grains” ferment the milk
  – Strained prior to consumption/packaging

• 15-20 billion CFUs of probiotics per cup, usually:
  – Bifidobacterium, Lactobacillus, Lactococcus, Leuconostoc, Saccaromyces

http://www.kefir.net; http://lifewaykefir.com
Kefir for *Clostridium*?

### Antibiotic taper

<table>
<thead>
<tr>
<th>Weeks 1-2</th>
<th>Weeks 3-4</th>
<th>Weeks 5-6</th>
<th>Weeks 7-8</th>
<th>Weeks 9-15</th>
</tr>
</thead>
<tbody>
<tr>
<td>M 250mg q6h or V 125mg q6h</td>
<td>M 750mg q72h or V 375mg q72h</td>
<td>M 500mg q72h or V 250mg q72h</td>
<td>M 250mg q72h or V 125mg q72h</td>
<td>150mL TID</td>
</tr>
</tbody>
</table>

### Kefir

150mL TID

Key: M: metronidazole, V: vancomycin

Bakken *CID* 2014;59:858-61
Thirsty for More Kefir?

A Strawberry-Flavored Pearl for *Clostridium difficile* Infection

Kevin W. Garey, PharmD, MS, FASHP
Professor and Chair
Dept. of Pharmacy Practice and Translational Research
University of Houston, College of Pharmacy

Hot Topics in Antimicrobial Stewardship

Tuesday Dec 5, 2017
8am-10am
Chapin Auditorium
Session 238-L01
Probiotics: The Devil is in the Details

- **Product matters**
  - FDA approved product
  - Probiotic strains/amounts

- **Patient selection matters**
  - Reports of systemic infection in immunocompromised
DOES BM HAVE RICK FACTORS FOR CLOSTRIDIUM DIFFICILE?

A. Yes  
B. No

**Patient Case**

BM is a 73 y/o female called out form the ICU to the GenMed floor after a 3 day stay for AMS and hypotension. After a rather thorough workup, no definitive source was identified and she was transferred to the floor for further evaluation. She has a PMH of osteopenia.

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• ASA 81 mg PO daily  
• Calcium carbonate 500 mg PO QID  |
| Chem7 and CBC: | • Ciprofloxacin 500 mg PO twice daily  
• Influenza vaccine 0.5 mL IM x 1  
• Metronidazole 500 mg PO q8h  
• Multivitamins PO daily  
• Pantoprazole 40 mg PO daily |
| 135 | 98 | 12 | 100 | 8.7 | 11 | 187 |
| 3.6 | 24 | 1.2 | 27 | 11 | 187 |
Fast forward 3 years. BM developed *C. diff* during that initial hospitalization and has had 2 recurrences since then. She is hospitalized again, with foul smelling diarrhea that is suspected to be, once again, *C. diff*. Which of the following stand-alone therapeutic interventions could help treat/prevent recurrent *C. diff*?

A. Bezlotoxumab  
B. Fecal Microbiota Transplant  
C. Tlevamer  
D. *C. diff* Vaccine
Toxin Production

- Toxin A
- Toxin B
- Binary Toxin

Toxin binders?

- Toxins A/B
  - Intestinal injury
  - Acute inflammation

- Binary Toxin
  - Increased virulence?
  - Increased recurrence?

Anti-toxin antibodies?

Toxoid vaccines?

Hypervirulent strains
Tolevamer

- Soluble, high-molecular-weight (≥400 kDa) anionic polymer
  - Related to styrenesulfonate (K+ binding)
- Non-covalently bonds *C. difficile* toxin A and toxin B
- Not an antibiotic
- No disruption of gut flora

Johnson S et al. *Clin Infect Dis* 2014;59:345-54
Tolevamer

• 2 Phase 3 trials: 2:1:1
  Tolevamer:Vancomycin:Metronidazole

• Interventions:
  • Tolevamer 9g load (45 mL) x1 then 3g (15 mL) q8h x 14d
  • Vancomycin 125mg PO q6h x 10d
  • Metronidazole 375mg PO q6h x 10d

• Statistically inferior to both, metronidazole and vancomycin

Johnson S et al. *Clin Infect Dis* 2014;59:345-54
Tolevamer

Unanswered Questions:

- Studied as primary therapy - Role for adjunctive therapy to prevent recurrence?

Johnson S et al. *Clin Infect Dis* 2014;59:345-54
Bezlotoxumab

• Fully humanized mAb against toxin B
• Single dose infusion 10 mg/kg IV over 1 hour – **adjunctive therapy only**
  – Metronidazole PO, vancomycin PO (fidaxomicin PO)
• Administer during abx treatment (days 0-14)
• Cost: ~$4500 per 1,000 mg vial
  – CMS NTAP designation

Bezlotoxumab

## Bezlotoxumab

### Post-Hoc Analysis (MODIFY I + II) – 30 Day Hospital Readmission Rates

<table>
<thead>
<tr>
<th></th>
<th>Bezlotoxumab</th>
<th>Placebo</th>
<th>Rate Difference, %</th>
<th>Bezlotoxumab – Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. Readmitted/Total (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All inpatients</td>
<td>27/530 (5.1)</td>
<td>58/520 (11.2)</td>
<td>-6.1 -53</td>
<td></td>
</tr>
<tr>
<td>Age ≥85 y</td>
<td>17/298 (5.7)</td>
<td>43/308 (14.0)</td>
<td>-8.3 -60</td>
<td></td>
</tr>
<tr>
<td>≥1 CDI episode in past 6 mo</td>
<td>11/127 (8.7)</td>
<td>19/122 (15.6)</td>
<td>-6.9 -42</td>
<td></td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>8/138 (5.8)</td>
<td>12/117 (10.3)</td>
<td>-4.5 -33</td>
<td></td>
</tr>
<tr>
<td>Severe CDI</td>
<td>4/113 (3.5)</td>
<td>13/116 (11.2)</td>
<td>-7.7 -69</td>
<td></td>
</tr>
<tr>
<td>027 strain</td>
<td>9/67 (13.4)</td>
<td>14/81 (17.3)</td>
<td>-3.9 -36</td>
<td></td>
</tr>
</tbody>
</table>

NNT = 17

Bezlotoxumab

- Not effective against NAP1/BI/027
- Caution in CHF
- Unanswered Questions:
  - Who to receive? What is “high risk”?  
  - Where to receive? Defer to outpatient?  
  - Benefit over fidaxomicin or FMT? Still unknown
# Toxoid Vaccines – Phase 3 Trials

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Trial</th>
<th>Doses</th>
<th>Patients</th>
<th>Status</th>
</tr>
</thead>
</table>
| Sanofi-Pasteur     | **Cdiffense.**
                   | NCT01887912 | 3 doses: 0.5 mL days 0, 7, 30      | 15,000 adults ≥ 50 years at risk for CDI • 2+ hospital stays • Systemic abx • Anticipated inpatient stay within 2 months | Currently enrolling (8/2013)  |
| Pfizer             | **Clover.**
                   | NCT03090191 | 3 doses                            | 16,000 adults ≥ 50 years at risk for CDI • Systemic abx within 12 weeks • ↑ risk of future healthcare contact | Currently enrolling (3/2017)  |

Good review on Phase 1/2 data: Henderson M et al. *Vaccines* 2017;5:25; doi:10.3390/vaccines5030025
Fecal Microbiota Transplantation (FMT)

- Restoration of gut flora by exogenous transfer of (usually) foreign feces
- Donors:
  - Self vs. related vs. central donor
- Preparation:
  - Fresh vs. frozen vs. synthetic
- Administration:
  - Top-down vs. bottoms-up

Photo courtesy of Maureen Taylor, PA
FDA Approval? (No Poop For You)

- FMT indication may require an FDA IND
  - rCDI failing current therapies? → free flowing FMT
  - All other indications? → file IND for FMT

<table>
<thead>
<tr>
<th>CDI Indication</th>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>First episode</td>
<td>Insufficient evidence, not recommended</td>
<td>Low quality evidence Weak recommendation</td>
</tr>
<tr>
<td>Recurrent</td>
<td>Recommended as treatment for mild and severe rCDI</td>
<td>High quality evidence Strong recommendation</td>
</tr>
<tr>
<td>Refractory</td>
<td>Can be considered as an option</td>
<td>Low quality of evidence Strong recommendation</td>
</tr>
</tbody>
</table>
### Fecal Fixation: Fecal Microbiota Transplantation for Clostridium difficile Infection

#### Does Route Matter?

<table>
<thead>
<tr>
<th>Reference</th>
<th>FMT</th>
<th>Comparator</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Nood 2013</td>
<td>Vanco 500mg PO q6h x 4d then <strong>FMT NG tube</strong> (n=16)</td>
<td>Vanco 500mg PO x 14d q6h (n=13)</td>
<td>81% (94%) vs. 31%</td>
</tr>
<tr>
<td>Cammarota 2015</td>
<td>Vanco 125mg PO q6h x3d then <strong>FMT colonoscopy</strong> (n=20)</td>
<td>Vanco 125mg PO q6h x10d then taper x 3 weeks (n=19)</td>
<td>65% (90%) vs. 26% (63%)</td>
</tr>
<tr>
<td>Hota 2017</td>
<td>Vanco 125mg PO q6h x14d then <strong>FMT enema</strong> (n=16)</td>
<td>Vanco 125mg PO q6h x 14d then taper 4 weeks (n=12)</td>
<td>44% vs. 58%</td>
</tr>
</tbody>
</table>

## Does Preparation Matter?

<table>
<thead>
<tr>
<th>Reference</th>
<th>Investigator</th>
<th>Comparator</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Youngster 2014</td>
<td>Frozen FMT NG tube (n=10)</td>
<td>Frozen FMT colonoscopy (n=10)</td>
<td>60% (80%) vs. 80% (100%)</td>
</tr>
<tr>
<td>Lee 2016</td>
<td>Frozen FMT enema (n=108)</td>
<td>Fresh FMT enema (n=111)</td>
<td>53% (75%, 91%) vs. 51% (91%, 86%)</td>
</tr>
<tr>
<td>Kelly 2016</td>
<td>Donor FMT colonoscopy (n=22)</td>
<td>Autologous FMT colonoscopy (n=24)</td>
<td>91% vs. 63%</td>
</tr>
</tbody>
</table>

**The Poop Scoop:** Colonoscopy > NG tube .... Frozen ≈ Fresh .... Donor > Autologous

FMT General Process

CDI abx for 3-5 days

Discontinue CDI abx 24-48h prior to FMT

Consider bowel lavage prior to FMT

FMT

Follow-up x 8 weeks
Fecally Challenged?

Non-profits collaborating with FDA to provide frozen, screened FMT material

**Open Biome** (Medford, MA)
www.openbiome.org

**AdvancingBio** (Sacramento, CA)
www.advancingbio.org

$485/dose
250 mL

$485/dose
30 mL

$635/dose
30 caps

Stool donations are accepted Tuesdays and Wednesdays from 7 a.m. to 1 p.m. Closed for lunch between 11 a.m.-11:30 a.m.
Fast forward 3 years. BM developed *C. diff* during that initial hospitalization and has had 2 recurrences since then. She is hospitalized again, with foul smelling diarrhea that is suspected to be, once again, *C. diff*. Which of the following stand-alone therapeutic interventions could help treat/prevent recurrent *C. diff*?

A. Bezlotoxumab  
B. Fecal Microbiota Transplant  
C. Tlevamer  
D. *C. diff* Vaccine
In Summary

• CDI is an increasing burden
• Several new agents target rCDI
• CDC and other organizations provide toolkits for CDI
• Best approach involves multi-faceted antimicrobial stewardship interventions
Antimicrobial Stewardship Strategies to Reduce Hospital-Acquired *Clostridium difficile* Infections

Erin McCreary, PharmD, BCPS
Jerod Nagel, PharmD
Tristan Timbrook, PharmD, MBA, BCPS
Lucas Schulz, PharmD, BCPS-AQ, ID
Because Social Media is All the Rage

Got FMT? What do you call it? So far we've got poopsicles 🍦, fecalitini 🍦 & feces pieces 🍦. Others?

Most creative = props from Monica 😞

David Berkowitz @dberkpharmd - Jul 21
Replying to @mmPharmD @real_idpharmd and 9 others
my official title is director of fecal bacteriotherapy

Kurt Wargo @Kurt_Wargo - Jul 21
Replying to @mmPharmD @real_idpharmd and 9 others
Shiitake 🍄

Tim Gauthier @1DStewardship - Jul 21
Kaka capsules... kakacrapoosicles?

Monica Mahoney @mmPharmD - Jul 21
Poop in Polish is "kupa". Kupa Capsules has a better ring to it.

Send in the Kupa troopers!

Jacob Morton @JMIDPharmD - Jul 21
Replying to @dberkpharmd @mmPharmD and 9 others
If you work with several people you could be the poop troop!
Key Takeaways

• Key Takeaway #1
  – Discontinue unnecessary antibiotics

• Key Takeaway #2
  – Discontinue non-indicated gastric acid suppressants

• Key Takeaway #3
  – Evaluate institutional/patient need for rCDI therapies

• Key Takeaway #4
  – Consider rePOOPulation of gut microbiota
Novel Approaches for Non-Antibiotic Interventions for *Clostridium difficile*

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