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Re-establishing the Balance of Nature in C. Diff with Fecal Microbiota Transplant

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Re-establishing The Balance of Nature in C. diff with Fecal Microbiota Transplant

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DISCLOSURE

I have no actual or potential conflict of interest in relation to this program or presentation.
THE CYCLE OF *C. difficile*

Britton R, Young V. Gastroenterology 2014;146.
THE INCREASING PROBLEM OF C. diff INFECTION

C diff- related mortality rates per million population, US, 1999–2004

Lessa FC, et al. CID 2012:55
Redelings MD, et al. EID, 2007
HIGH RATES OF RECURRENT C. DIFF INFECTION

• 20% after initial treatment
• 40% after first recurrence
• 60% after 2 or more recurrences
• High cost of “vancomycin dependent” treatment
  – 125 mg (1 box, 20 ea): $673.99
  – Cost of taper: $2864

McFarland LV. J Med Micro 2005
McFarland LV. J Clin Gastro 2002
Kelly C. JAMA 2009
Walgreens.com
Decreased Diversity of Colonic Microflora in C. Diff Infection

Chang, et al. JID 2008
Fecal Microbiota Transplantation

• Administration of feces from a healthy individual to promote colonization with beneficial gut flora

• *aka*... Fecal bacteriotherapy, Stool transplant, Fecal flora reconstitution

Borody TJ. J Clin Gastro 2004
RANDOMIZED TRIAL SUPPORTING FMT SUSPENDED


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**Graphs:**
- **Percentage Cured without Relapse:**
  - First Infusion of Donor Feces (N=16): 81.3%
  - Infusion of Donor Feces Overall (N=16): 93.8%
  - Vancomycin (N=13): 30.8%
  - Vancomycin with Bowel Lavage (N=13): 23.1%

  *Statistical Significance:
  - P<0.001
  - P=0.008
  - P=0.003

- **Microbiota Diversity**
  - Simpson's Reciprocal Index
  - Comparison:
    - Donors
    - Patients before Infusion
    - Patients after Infusion

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INDICATIONS FOR FMT

1. Recurrent or relapsing CDI
   - At least three episodes of mild-to-moderate CDI and failure of a 6-8 week taper with vancomycin with or without an alternative antibiotic (e.g., rifaximin, fidaxomicin, nitazoxanide)
   - At least two episodes of severe CDI resulting in hospitalization and associated with significant morbidity

2. Moderate CDI not responding to standard therapy (vancomycin) for at least a week

3. Severe (and perhaps fulminant C. difficile colitis) with no response to standard therapy after 48 hours

Suspected Mechanism – Like Resodding

The Good

The Bad

The Reconstituted

Courtesy of Dr. Colleen Kelly
MONITORING FOR SAFETY ISSUES

• No adverse events or infectious complications yet reported

• Risk of infection

• Theoretical risks: allergic, autoimmune, IBD, neurologic, obesity, cancer
SHOULD FDA REGULATE FMT?

• FDA has declared jurisdiction
• Does not wish to “interfere with patient care”
• Consideration of seeking IND approval
• Allowing FMT with standard practices and informed consent for *C. diff* infection
FMT at UMass Memorial for Recurrent *C. diff* Infection

- Outcomes and Data Collection for Fecal Microbiota Transplantation for the Treatment of Recurrent *Clostridium difficile*
- IRB-approved protocol for colonoscopy administration
- Not indicated or acceptable therapy for IBD presently
- Contacts
  - anne.foley@umassmemorial.org
  - randall.pellish@umassmemorial.org
FMT FOR IMMUNOCOMPROMISED (IC) PATIENTS?

• Retrospective case series of FMT in IC patients
  – Overall cure rate was 89%
  – No infections definitively related to FMT
• UMass proposal in discussion
  – Bank stool of solid organ transplant patients prior to transplant
  – Autologous fecal transplant for C. diff infection post transplant
Rationale for FMT in Inflammatory Bowel Disease

- Intestinal microbiota in IBD patients less diverse
  - Studies reporting 25% fewer microbial genes
- Microbiota variations in IBD
  - Reduced *Firmicutes* and *Bacteroides*
  - Increased *Actinobacteria* and *Proteobacteria*
  - Decreased *Feacalibacterium prausnitzii* in Crohn’s
  - Differences a cause or consequence of IBD??
FUTURE DIRECTIONS

• Openbiome.org
• Frozen stool preparations
• Defined, full-spectrum microbiota treatments
• FMT in IBD…not there yet