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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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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
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**


Microbiota Diversity

- 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
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
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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??

*Gastroenterology* 2013;145:946–953
FUTURE DIRECTIONS

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