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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

Establishment of susceptibility

Susceptible microbiota

C difficile spores

Germination

Vegetative C difficile

Disease initiation

Toxin production

Clearance/asymptomatic colonization

Reduced Bacteroides and Firmicutes

Normal microbiota

Antibiotics

Loss of colonization resistance

Recurrence cycle

Recurrence

Recovery

Restoration of colonization resistance

Recurrent disease

CDI treatment (antibiotics)

CDI treatment (fecal transplant)

C difficile infection

Toxin production

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

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
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