ADVANCES IN FECAL MICROBIOTA TRANSFORMATION

Amanda Bradshaw, MPAS, PA-C
Seattle Children’s Hospital
Seattle, WA

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OBJECTIVES

• Applications for Fecal Microbial Transplant
• Methods involved in Fecal Microbial Transplant
• Outcomes of Fecal Microbial Transplantation
HUMAN MICROBIOME

Microbiome – Referring to the distinctive populations of microorganisms inhabiting a location

“...The ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space.”

Wu and Lewis. CSHL 2013

Weight

Microbiome

Cells

Genes

• 100 trillion microorganisms
• Human gut - 2lbs of bacteria
• Outnumber human cells by a factor of ten
  • Genomes encode around 3 million different genes

Fecal Microbiome

Who’s there?
What are they doing?

Who’s they are varies: your microbiota is plastic and personalized.

What they’re doing is adapting to their environment:
you, your body, and your environment.

Savage, DC. Annu Rev Microbiol 1977; 31:197-128
Diversity within the human fecal microbiome may supply broader insight into the overall health of the individual.

_Hollister, et al. Gastroenterology 2014_

**MICROBIOME AND HUMAN DISEASE**

_Dysbiosis_ – Alterations in the microbiota composition associated with disease

Impacted by:
- Diet
- Antibiotics
- Other

_Wu and Lewis. CGH 2013_

**EFFECTS OF MODIFYING THE DIET ON MICROBIOME**

_Wu, G. Science 334, 105 (2011); 105-108_
MICROBIOME AND HUMAN DISEASE

Described possible associations in the gut for numerous disease processes:
- Infection (Clostridium Difficile)
- Inflammatory Bowel Disease (IBD)
- Cancer
- Metabolic Disorders

C. DIFFICILE PARADIGM

CDI: PATHOGENESIS
Increasing rates of relapsing C. difficile
Cure is common; resurgence is common too!
Nosocomial infection resistance to metronidazole
Flagyl, vancomycin, rifaximin, nitazoxanide, and probiotics

Incidence Rate of CDI

Current Approved FMT Applications

Recurrent C. Difficile Infections

Research Applications:
- IBD
- Obesity
- Antibiotic resistant bacterias
- Graft versus host
FECAL BACTERIOTHERAPY FOR RELAPSING C. DIFFICILE IN A CHILD

2 year old girl – 8 months ordeal
Water diarrhea 1
Treatment
10 days of metronidazole
30 day of vancomycin and lactobacillus gg
Vanco plus rifixamin plus Saccharomyces boulardii plus lactobacillus 99
Re-occurred after 14 days

George Russell, et al Pediatrics 126, number 1, July 2010

FECAL BACTERIOTHERAPY FOR RELAPSING C. DIFFICILE IN A CHILD

Vanco another 2 weeks

Then
Vanco – 2 weeks
Nitazoxanide 3 days then
Vanco 2 weeks then
Rifaxamin 7 days then
Pulsed dose of vanco over 6 weeks
DID NOT WORK! What next!

George Russell, et al Pediatrics 126, number 1, July 2010

FMT AND... IT WORKED

Within 36 hours, abdominal symptoms and diarrhea resolved and did not re-occur during 6 months of monitoring.
**FMT FOR RECURRENT CLOSTRIDIUM DIFFICILE**

![Graph showing percentage cured without relapse for different treatments.](image)

- First Infusion of Donor Feces (n=16)
- Infusion of Donor Feces (overall n=16)
- Vancomycin (n=13)
- Vancomycin with bowel lavage (n=13)

Percentage Cured without Relapse:
- 81.3%
- 93.8%
- 30.8%
- 23.1%

**FMT AND C. DIFFICILE**

**Fecal Microbial Transplant (Transfer)** - Alteration of the gut microbiota by direct transfer of entire communities in the same relative abundance as exists in the healthy donor.

Approximately 90% success rate.

- Wu and Lewis, CGH 2013
- Smits LP, et al. Gastroenterology 2013

**FMT PROCESS**

Typically administered:
- Enema
- Colonoscopy
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- Nasogastric – Infused, then followed with a normal saline flush
- Nasoduodenal
- Nasojejunal
- Capsules

It appears as if all routes are equal.

- Wu and Lewis, CGH 2013
**FMT PROCESS**

- Openbiome – Stool repository
- Donor Screening:
  - HAV antibody (IgM and IgG)
  - HBV Antibody to hepatitis B surface antigen,
  - Antibody to hepatitis B core antigen
  - HCV HCV antibody (RIBA-II)
  - HIV-1 and HIV-2 EIA
  - Treponema pallidum Rapid plasma reagin test
  - Stool Clostridium difficile Toxin A or toxin B (cytotoxin)
  - Enteric bacterial pathogens
  - Selective stool culture
- Ova and parasites Light microscopy

2013 Joint Societal Guidelines for C. Diff

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**IBD AND THE MICROBIOME**

Intestinal microbiota of IBD patients appears to have reduced diversity compared to healthy subjects.

Unclear whether these differences are a cause or consequence of development of IBD.

Smits LP, et al. Gastroenterology 2013

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**FMT IN IBD**

- Will it work
  - Crohn’s disease
  - Ulcerative colitis
- Route
- Dose
- Frequency
- Who is the best donor
**FMT IN CROHN’S DISEASE**

Mild to moderate active disease  
9 Patients  
12-19 years of age  
Medication therapy continued  

Pre-FMT antibiotics  
Nasogastric tube  
Disease activity and microbiome  
Follow up 2, 6, and 12 weeks
**FMT in Crohn's Disease**

7 of 9 patients were in remission at 2 weeks.
5 of 9 patients who did not receive additional medical therapy were in remission at 6 and 12 weeks.
No or modest improvement was seen in patients who did not engraft or whose microbiome was most similar to their donor.

**FMT in Ulcerative Colitis**

Studies suggest remission of disease is possible with multiple FMT’s for a subgroup of patients.


POTENTIAL FUTURE APPLICATIONS

- Metabolic Disorders
- Neuropsychiatric Disorders
- Autoimmune Diseases
- Allergic Disorders
- Tumors

CONCLUSION

- Fecal Microbiome is complex and biologically important in Health and Disease
- Fecal Microbiome modulates us, and we modulate our Fecal Microbiome
- FMT has impressive treatment success in cases of recurrent C. Difficile
- Role of FMT in other disease processes remains to be seen
- Further research is needed to move this discussion forward

REFERENCES


REFERENCES (CONTINUED)


