FMT - The Power of Poop

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DISCLOSURE
No financial relationships to disclose
The Gastroenterologist’s STOOLbox
FOR
*C. diff*, Obesity, Autism, Parkinson’s, Metabolic Syndrome, etc.

FMT for Metabolic Syndrome?

IN THE JOURNALS

**Microbiome Resource Center**

Fecal transplant improves metabolic syndrome in patients with greater initial microbial diversity

October 3, 2017

Fecal microbiota transplantation from lean donors provided short-term improvements in peripheral insulin sensitivity in about half of obese men with metabolic syndrome enrolled in a small clinical trial in the Netherlands.
FMT for Obesity and Metabolic Syndrome?

Treating Obesity and Metabolic Syndrome with Fecal Microbiota Transplantation

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FMT and Obesity

SHORT COMMUNICATION
An opportunistic pathogen isolated from the gut of an obese human causes obesity in germfree mice

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FMT for Insulin Resistance?

BRIEF REPORT

Transfer of Intestinal Microbiota From Lean Donors Increases Insulin Sensitivity in Individuals With Metabolic Syndrome

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FMT for Autism Spectrum Disorders

World Journal of Gastroenterology


DOI: 10.3748/wjg.v22.i1.361

Gut microbiota in autism and mood disorders

Francesca Mangiola, Gianluca Janiro, Francesco Franceschi, Stefano Faguoli, Giovanni Gasbarrini, Antonio Gasbarrini
FMT for Autism Spectrum Disorders?

The Gut Microbiota and Autism Spectrum Disorders

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FMT for Parkinson’s?

Gut Microbes Linked to Neurodegenerative Disease

Bacteria in the intestine influence motor dysfunction and neuroinflammation in a mouse model of Parkinson’s disease.

By Abby Olena | December 1, 2016
FMT and Chemotherapy?

NEWS

Gut bacteria can stop cancer drugs from working

*Presence of particular microbes or enzymes could explain why some treatments are ineffective for certain people.*

By Sara Reardon • 06 June 2017

FMT to Prevent Colon Cancer?

The New York Times  https://nyti.ms/2FAGVxx

HEALTH

Gut Microbes Combine to Cause Colon Cancer, Study Suggests

By GINA KOLATA • FEB. 1, 2018

Two types of bacteria commonly found in the gut work together to fuel the growth of colon tumors, researchers reported on Thursday.

Their study, published in the journal Science, describes what may be a hidden cause of colon cancer, the third most common cancer in the United States. The research also adds to growing evidence that gut bacteria modify the body’s immune system in unexpected and sometimes deadly ways.
FMT in NAFLD?

Cell Metabolism
Gut Microbiome-Based Metagenomic Signature for Non-invasive Detection of Advanced Fibrosis in Human Nonalcoholic Fatty Liver Disease

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In Brief
Loomba et al. reveal how a panel of gut microbiome biomarkers can be used as a non-invasive test to accurately diagnose advanced fibrosis in patients with non-alcoholic fatty liver disease.

FMT for Ulcerative Colitis?

IBD patients with uveitis show distinct microbiome signature, suggesting gut-eye axis

Patients with inflammatory bowel disease who develop uveitis, a common extra-intestinal manifestation of IBD affecting the eye, showed a unique gut microbiome signature compared with IBD patients without uveitis, according to new research presented at the American Uveitis Society Meeting.
History

- 4<sup>th</sup> century – food poisoning and severe diarrhea was treated with “yellow soup” in China (oral administration of a fecal suspension) (Ge Hong)
- 16<sup>th</sup> century – fecal products were used for diarrhea, fever, pain, vomiting & constipation (Li Shizhen)
History cont.

- 17th century veterinary medicine (enema and oral administration) “transfaunation”
- 1958 Eiseman used fecal enemas for pseudomembranous colitis

Reported Improvement

- C. diff
- IBS
- IBD
- Pouchitis
- Hepatic encephalopathy
- Metabolic syndrome/Obesity/T2D
- ITP
- CVHD
- Sepsis
- Parkinson
- Multiple sclerosis
- Dystonia
- Mood disorders
- Chronic fatigue syndrome
Dysbiosis

- The loss of balance between the cells of a human organism and the bacterial cells that inhabit it.

The Lesion

- Intestinal Dysbiosis
- In healthy adults the predominant microbiota are:
  - Bacteroidetes
  - Firmicutes
  - Actinobacteria
  - Proteobacteria
Dysbiosis

- 30-50% reduction in biodiversity of intestinal microbiota in IBD
- Obesity/Metabolic Syndrome
  - Less *Bacteroides* & more *Firmicutes*
- IBD
  - Less *Bacteroidetes* and *Firmicutes* and more *Acinobacteria* and *Enterobacteria*

Human Bacterial Genome

- 90% of the bacteria in humans reside in the colon
- Previously estimated to be 100 billion \((10^{14})\) bacteria
- Recent studies suggest 40 billion \((10^{11})\) bacteria
- 1000 different species - primarily anaerobic bacteria
C. diff Recurrence Rates

- 15 – 30% after initial treatment
- 40% chance after second treatment
- 65% chance after third treatment

CDI Patients

- Decreased microbiome diversity
- Less
  - Bacteroides
  - Firmicutes
- High levels of
  - Proteobacteria
  - Verrucomicrobia
**Clostridium difficile**

- 1996 – 98,000 cases
- 2003 – 178,000
- Current – 500,000-700,000 cases annually in the US
- Case fatality rate >3% (29,000 deaths)
- Annual cost $3.2 billion

**Active Ingredients in FMT for CDI**

- Sterile filtrates are as effective as fresh feces
- Filtrates contain: bacterial debris, proteins, antimicrobial compounds, metabolic products and microbial DNA
- Bacteriophages, bacteriocins, DNA fragments that stimulate host responses

Gastroenterology 2017;152:799-811
Fecal Microbiota Transplantation (FMT)

- 50 grams of donated stool is mixed with 200 mL of diluent (water, milk yogurt, nonbacteriostatic saline, etc.)
- Efficacy of fresh and frozen are similar
- 92% of RCDI patients are cured with FMT (range 81-100%) proof of principle

OpenBiome

- Donor screening cost $5,000
- 4% of potential donors are accepted (Tufts University students)
- As of 2017 they had provided over 30,000 treatments
- Co-founder Carolyn Edelstein (cousin with C. diff)
OpenBiome Preparations

FMT LOWER DELIVERY
For colonoscopy, sigmoidoscopy, or enema
Item: FMT50
Price: $495 per dose (1 bottle)
Visibility: 6 months at -20°C, 12 months at 80°C

FMT UPPER DELIVERY
For nasoenteric/gastric tube or EGD
Item: FMT10
Price: $495 per dose (1 bottle)
Visibility: 6 months at -20°C, 12 months at 80°C

FMT CAPSULE G3
For oral administration
Orders of capsules are capped at three units
Item: FMTcapG3
Price: $495 per dose (1 bottle = 30 capsules)
Visibility: 6 months at -20°C, 12 months at 80°C
Includes 2 vent test capsules to assess patient’s swallowing ability
Physician orientation required before first order

OpenBiome Poop Bank

MAKE YOUR CONTRIBUTION HERE
THANK YOU FOR YOUR DEPOSIT

RECEIVE PAYMENT HERE
AMOUNT
$ 40.00
SELECT TYPE OF PAYMENT
CASH CHECK CREDIT CARD

Campbell 15
Interesting **Moonlighting** Job

**The Washington Post**

**Speaking of Science**

You can earn $13,000 a year selling your poop

*By Rachel Feltman  January 29, 2015*

You can donate blood, plasma, eggs, and sperm. Why not poop? Yes, your feces are perhaps your greatest untapped monetary resource. Thanks to a nonprofit organization called OpenBiome, you can cash in to the tune of $13,000 a year -- and save lives while you’re at it.
EPIC FMT Order Sets

FMT Consent

The doctor has explained the benefits of the procedure(s) to me. I understand there is no guarantee that I will achieve those benefits.

I understand that unknown things may happen during this procedure. Because of that, a different procedure may be needed. Therefore, I authorize the doctor, associates, or assistants to perform any procedure(s) needed to best take care of me.

The doctor has explained to me that there are risks with this procedure. It is possible that unexpected things may happen. These might include, but are not limited to:

- Transfer of infectious organisms contained in stool (bacteria, viruses, fungi, parasites)
- Allergic reactions to components (antigens) contained in the donor stool
- Complications related to the insertion of the tube or scope, such as potential tear of the lining of the intestinal tract or aspiration of stool into the lungs (inhaled it into the airway)
- Fears, bloating, abdominal discomfort, constipation, diarrhea, nausea, vomiting
- Rare risk for developing of autoimmune disorders (e.g. rheumatoid arthritis, Sjogren’s Syndrome, thrombocytopenia purpura)
- For those with inflammatory bowel disease (IBD), a low risk of flare

Possible alternatives for recurrent CDI have been explained to me. This includes not having this procedure at all. Other alternatives might include, but are not limited to, various antibiotic options or surgery and I understand the risk and benefits of the alternative treatments. I understand that any condition could improve, worsen or stay the same with each of the alternative treatment options, including FMT.
FMT Pearls

- Administration by colonoscopy, enteroscopy, naso-jejunal tube, enema, and capsule have similar efficacy
- The volumes are different for upper (30 mL) (30 capsules) and lower (250 mL) administration
- There is a trend toward improved outcomes with larger volumes

FMT Pearls

- FMT via colonoscopy is the preferred route of administration
- No antibiotics before or after FMT
- Large volume prep decreases the number of persistent spores
- Loperamide the morning of the procedure
- PPI therapy prior to upper FMT
Neuropsychiatric Disorders and the Gut

- 66 human subjects, randomized, double blind, placebo-controlled study
- Probiotic therapy \((Lactobacillus \text{ and } Bifidobacterium)\)
- Anger-hostility, depression, somatization & global severity index we all lower \((p<0.05)\)


FMT & Neuropsychiatric Disorders

- Case series of multiple sclerosis patients who underwent FMT and followed for up to 15 years
- All 3 experienced progressive neurologic improvement and regained their ability to walk
- 2 had restoration of urinary function
- 1 disease progression halted

*Am J Gastroenterol* 2011; 106: S352
**Autism Spectrum Disorder**

- *Clostridium* species are increased in the feces of autistic children compared to non-ASD children
- ASD symptoms resolved after FMT in two children
- 5 ASD children improved after being administered cultured *Bacteriodes* and *Clostridium*

*Curr Opin Gastroenterol* 2013; 29:79-84.

**Parkinson’s Disease Model**

- Mouse model – predisposed to develop Parkinson-like disorders (adhesive tape and beam studies)
- In a germ-free environment fewer motor deficits and reduced accumulation of misfolded protein aggregates in regions of the brain controlling movement

*Cell* 2016; 167(6): 1469-1480
**Parkinson’s Disease Model cont.**

- Antibiotic treatment had a similar effect as the germ-free environment on motor symptoms.
- Worse symptoms developed in mice raised in a germ-free environment receiving FMT from patients with Parkinson’s disease (no effect on nl).

*Cell* 2016; 167(6): 1469-1480

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**Obesity/Metabolic Syndrome**

- Double-blinded, controlled, and randomized trial - 18 men with metabolic syndrome.
- FMT with either their own feces or feces from lean men.
- Non-placebo group: increased peripheral and hepatic insulin sensitivity & microbial diversity.

*Gastroenterology* 2012; 143: 913-916.
Weight Gain After FMT

- 32 year-old female w/ recurrent CDI
- Donor 16 year-old daughter 140-170 lbs (BMI 26.4)
- Recipient baseline weight 136 lbs
- 16 mos after FMT recipient weighed 170 lbs (BMI 33)
- 35 mos after FMT 177 lbs (BMI 34.5)

[https://academic.oup.com/ofid/article-abstract/2/1/ofv004/1461242 Open Forum Inf Diseases]

Missouri Adolescent Twin Study

- 1 MZ & 3 DZ pairs
- Discordant for obesity
- FMT into germ free mice
- Total body and fat mass increased and obesity-associated phenotypes were transmissible (uncultured and cultured)

*Science* 2013; September 6; 341(6150)
**Missouri Adolescent Twin Study cont.**

- When mice transplanted with the flora from the obese twin were co-housed with mice transplanted with flora from the lean twin, the adiposity phenotype did not develop (coprophagia).

**Obesity**

- **THEORY:** The microbiome’s digestive efficiency
- Diet accounts for 57% of the structural variation in the mouse gut microbiome
- Other important factors: gender, diet, circadian rhythms, feeding pattern, etc.
T2D Subjects

- Metformin increases
  - Enterobacteriaceae (*Escherichia, Shigella, Klebsiella, Salmonella*)
- Metformin decreases (*Clostridium* and *Eubacterium*)

T2D cont.

- One week of vancomycin in obese men with metabolic syndrome reduced peripheral insulin sensitivity
- Farm industry exploitation of this strategy for decades
Alternative Titles For This Presentation

- Bacteriotherapy using fecal flora
- Messing with movements
- Manipulating human motions
- Capsule FMT – A tough pill to swallow
- Bacterial re-POOPulation of the gut
- FROM THE BATHROOM TO THE BEDSIDE

A GI Magic Box?
Apothecary Case
A Step Back?

The GI STOOLbox of the Future-Microbial-Based Therapeutics

Figure 4. Gut Microbiota and Specific Commensals as Potential Preventive or Therapeutic Agents. Clinical studies are indicated in blue, and preclinical (mouse) studies in red.

From the Bathroom to the Bedside—Exercise Caution in Extrapolating Basic Findings