Bringing FMT to Your Practice: How to do it

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The POWER of POOP
promoting safe, accessible fecal microbiota transplant for all who need it

DIY Fecal Transplants to cure yourself of digestive disease
Michael Rost
41,995 views
Fecal Microbiota Transplantation

- Administration of feces (containing entire gut microbial community) from a healthy individual to promote colonization with beneficial flora

- Restore diversity of microorganisms, beneficial anaerobes and butyrate-producing bacteria.
  - Engraftment
  - Augmentation
FMT 101

- Patient selection
- Identify and screen a donor
- Collect and prepare the fecal material
- Administer the donor material to the patient
- Follow up

Patient Selection
Indications

- **Recurrent C. difficile**
  - At least three episodes of CDI and failure of a 6-8 week taper with vancomycin.
  - At least two episodes of severe CDI resulting in hospitalization and associated with significant morbidity.

- **Refractory C. difficile**
  - Moderate CDI not responding to standard therapy (vancomycin) for at least one week.

- **Severe/complicated infection**
  - Patients different & much sicker
  - May require >1 FMT

Consider Alternative Diagnoses

- Post-infectious IBS
- Inflammatory bowel disease
- Bile salt malabsorption
- Lactose intolerance
- Celiac disease
- Giardia infection
- Chronic pancreatitis
- Microscopic colitis
- Factitious diarrhea
Donor Selection and Screening

Donor selection

Donor: often intimate partner, immediate family or household contact
- Not necessarily related
- Volunteer donors

Healthy
- Exclude donors with IBD, autoimmune or atopic conditions, neurologic disease, malignancy, fibromyalgia/chronic fatigue, obesity or features of the metabolic syndrome

“Clean living”
- AABB DHQ: Excludes patients with high risk behaviors, travel, etc.

No antibiotics x 90 days
Donor screening

<table>
<thead>
<tr>
<th>Serologic</th>
<th>Stool</th>
<th>FDA required</th>
<th>Possibly</th>
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<tbody>
<tr>
<td>HIV 1 &amp; 2</td>
<td>Routine bacterial culture</td>
<td>Giardia</td>
<td>CMV</td>
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<td>Hepatitis A, B, C</td>
<td>Ova &amp; Parasites</td>
<td>Cryptosporidium</td>
<td>Human T cell lymphoma virus</td>
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<td>Syphilis (RPR)</td>
<td>C. difficile</td>
<td>Isospora &amp; Cyclospora</td>
<td>EBV</td>
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<td>E. coli O157</td>
<td>Dientamoeba fragilis</td>
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<td>Rotavirus</td>
<td>Blastocystis hominis</td>
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<td>Listeria</td>
<td>Strongyloides stercoralis</td>
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<td>Vibrio</td>
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<td>VRE, MRSA</td>
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<td>Norovirus</td>
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Patient Directed vs. Universal Donor

**Source: family or friend (fresh stool)**

- **Pros:**
  - Patient comfort
  - “Cost”

- **Cons:**
  - Multiple tests
  - Expensive
  - Delays care
  - Physician’s time
  - Unreliable donors

**Source: Stool bank (frozen)**

- **Pros:**
  - Routinely tested, healthy individuals
  - Proven donor track record
  - Efficient

- **Cons:**
  - Must have medical freezer
  - Out-of-pocket cost to patient
  - Institutional and administrative restrictions
**Frozen stool from a bank: OpenBiome Model**

1. Clinician orders fecal preparations from a stool bank
2. Stool bank provides rigorously screened, processed, frozen material
3. The clinicianThaws material and performs FMT

**Donor Assessment**
- 109-point clinical assessment for transmissible infectious diseases and potentially microbiome-mediated conditions
  - E.g. IBD, IBS, depression, anxiety, age, obesity, metabolic syndrome, autoimmune diseases and others

**Stool & Serological Testing**
- Stool testing
  - C. diff toxin PCR, Ova & Parasites, Isospora, Cyclospora, Giardia EIA, Cryptosporidium EIA, H. pylori Ag, Common enteric pathogens (e.g. Salmonella, Shigella, E. coli, Campylobacter, Vibrio, Nm cysts, P. catarrhalis, R. Helicobacter, E. coli, Enterococcus, Staphy. aureus, VRE, Microsporidium)
- Serological testing
  - HIV 1 & 2, HAV, HBV, HCV, HTLV 1 & 2, Treponema pallidum, CBC, LFTs

**Processing, Monitoring & Re-testing**
- 60-day quarantine procedure
- Continuous requalification
- Processing controls
- Filtering & homogenization
- Safety aliquots
- Storage & shipping controls
- Traceability
- 16s rRNA (microbiome) sequencing & characterization

**Preparations**

**Patient**
- Baseline testing
- Continue anti-CDI therapy (vancomycin) until 1-3 days prior to procedure
- +/- Bowel prep
- +/- Loperamide

**Donor**
- Call if any signs of infection between screening and FMT
- Avoid allergens (i.e. nuts) if the patient has allergies
- Osmotic laxative at bedtime prior to donation
- Collect morning stool; +/- keep on ice; used within 6 hours
Preparation & Administration

**Dose**
- Typically 50-100 grams (10-300)
- Single vs. multiple treatments

**Processing**
- Diluents (saline, water)
- Mixing & filter
- Dose volume 50-500 ml

**Route**
- Nasogastric/nasoduodenal tube
- Endoscopic (upper or lower)
- Retention enema

Perskey et al. Am J. Gastroenterol 2000
Aas et al. Clin Infec Dis 2003
Silverman et al. Clin Gastro Hep 2010
Kassam et al. Arch Int Med 2012
Image courtesy of Tom Borody
Administration by lower endoscopy

Infuse at colonoscopy (or sigmoidoscopy) through the biopsy port
Typical dose volume 300-500 mL
Retain material more easily

Enables examination of the colon to rule out other pathology
Crohn’s disease, microscopic colitis, colon cancer

More effective?
91% response vs. 76-79% via gastroscope or ng/d tube
Equally effective in a small, open-label pilot study

Yoon SJ & Brandt L. J Clin Gastroenterol; 2010
Gough E. Clin Inf Dis; 2011

Other routes of administration

Nasogastric or nasoduodenal tube
Less appealing to patients
Requires radiology
Aspiration risk
May be less effective

Retention enemas
Variable patient ability to tolerate
Cannot examine mucosa
Does not reach beyond splenic flexure
May require multiple treatments

Aas et al. 2003; Rubin et al 2012; Van Nood 2013;
Silverman et al. 2010; Kassam et al 2012; Lee et al 2014
Patient Follow-Up

- Retain donor material for 30-60 minutes
- Do not resume vancomycin after the procedure
  - Do not “test for cure.”
- Follow closely for adverse events (AEs) or signs of recurrence
  - Telephone and office contacts
  - 6 month to 1 year for longer-term effects/durability
Common Questions

Regulatory status-U.S.

- **Drug:**
  - “Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease”
  - Biological products are included within this definition

- **Fecal Microbiota = Unapproved drug/biologic**
  - Considered investigational
  - Requires randomized controlled trials, safety/efficacy data

- **Requires Investigational New Drug application (IND) to administer**

http://www.fda.gov
21 CFR 312.2
Enforcement Discretion

- May administer FMT to treat *C. difficile* infection not responding to standard therapies.
  - Must provide informed consent
    - State that FMT is investigational
    - Discuss potential risks

Reimbursement

- Major insurers say nothing or not covered
  - FMT “investigational” & “experimental”

- We charge for consultation and office visit(s)
  - Encounter Level IV or V

- **44705, Preparation of fecal microbiota for instillation, including assessment of donor specimen**
  - The instillation of microbiota is separately reported.
    - For instillation of microbiota by oro-nasogastric tube or enema, use 44799.
    - For endoscopic procedures, diagnosis code: diarrhea, abdominal pain, etc.

- **HCPCS code G0455 includes the work of preparation AND instillation of the microbiota.**
  **Medicare does not pay a separate fee for the installation of the microbiota by nasogastric tube, enema, or by upper or lower endoscopy**
ICD-9 codes for donor specimen

- V01.9 Contact with or exposure to unspecified communicable disease
- V02.3 Carrier or suspected carrier of other gastrointestinal pathogens
- V73.89 Special screening examination for other specified viral diseases
- V73.99 Special screening examination for unspecified viral disease
- V74.5 Screening examination for venereal disease
- V74.9 Screening examination for unspecified bacterial and spirochetal diseases
- V75.8 Screening examination for other specified parasitic infections
- V75.9 Screening examination for unspecified infectious disease

Key Points

- **FMT is very effective for treatment of recurrent Clostridium difficile infection**
  - Nothing else is nearly as effective!

- Careful donor selection is important though stool banks have made this easier

- Methods used to administer FMT may vary depending on the clinical situation
Thank you

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