Irritable Bowel Syndrome & Fecal Transplantation

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Scope

1. Irritable Bowel Syndrome - Why & What
2. The IBS – Microbiota model of disease
3. Changing the “bug-scape”
4. Fecal Microbiota Transplantation
   - Promises and Perils
   - REANIMATE

The world of Functional Gastrointestinal Disorders (of the lower GI tract)

IBS & our city…

- Prevalence 8.6% by Rome 2 Criteria
- Predominantly < 50yr age
- Higher social economic class
  1. Landed property
  2. >6yrs education
- No difference between sexes
- Constipation (51%) vs Diarrhoea (12%)


Irritable Bowel Syndrome

Diagnosis criteria:

1. Recurrent abdominal pain or discomfort* at least 3 days/month in the last 3 months associated with two or more of the following:
   1. Improvement with defecation
   2. Onset associated with a change in frequency of stool
   3. Onset associated with a change in form (apparence) of stool
* Criterion fulfilled for the last 3 months with symptoms onset at least 6 months prior to diagnosis
* "Discomfort" means an uncomfortable sensation not described as pain
Pathophysiology of IBS
(Various factors involved...)

The Microbial Balance

Our Microflora Evolves

The case for a microbiota-IBS link

IBS symptoms & the Microbiota
Do IBS pts have a different microbiome?

Gut Microbiota and Factors Affecting its Composition

Changing the microbiota-scape
Antibiotics
Rifaximin

“Do you feel better?” with *B. Infantis*

Questions remain…

**Antibiotics**
1. Sledge-hammer “over-kill”?
2. Side-effects eg. *C Difficile* infection
3. Durability of the response

**Probiotics**
1. Which probiotic is best?
2. What is the optimal dose?
3. Durability of response
4. Mechanism of action

An alternative mechanism of action?
Faecal Microbiota Transplantation (FMT)
The new kid on the block?

- Animals

Ancient Medicine
1. “Yellow-Dragon Soup” CHINA
   - Tong-Jin Dynasty 4th Century
   - Ming Dynasty 16th Century

2. Modern Medicine


- REANIMATE

Donor Biologic Screening

- Donor blood tests
  - Screening for: HIV, HCV, HBV, HAV, CMV, HSV, EBV
  - Blood tests for: HIV, HCV, HBV, HAV, CMV, HSV, EBV

- Faecal tests
  - Stool culture
  - Ova, cysts and parasites
  - Isospora x 3 (acid fast)
  - Entamoeba histolytica antitoxin
  - Strongyloides stercoralis antibodies
  - Treponema pallidum antibodies
  - Giardia antigen
  - Clostridium difficile toxin
  - Cryptosporidium antigen
  - E. histolytica antigen

- Faecal Microbiota Transplantation in a Nutshell

- Clostridia Difficile Colitis

- First local ‘poop transplants’

- Don’t pooh-pooh faeces transplant treatment

- New England Journal of Medicine

- Dirodel Infusion of Donor Feces for Recurrent Clostridium difficile

- Donor Screening

- First local ‘poop transplants’
**Faecal Processing protocol**

- **Processing**
  - Approximately 50-60 g fecal material is homogenized in a commercial blender with 250 ml sterile normal saline solution.
  - The slurry is passed through a kitchen type stainless steel strainer to remove larger particulate matter.
  - The resulting material is centrifuged at 6000 x g for 15 minutes and resuspended to approx. half the original volume with sterile saline.
  - Sterile pharmaceutical grade glycerol is added to a final concentration of approx. 10%.

- **Storage**
  - The faecal solution is poured into a 300 ml plastic container and stored at -80°C.
  - Before use, the solution is thawed on ice for up to 4 h, and sterile saline is added to a final volume of 250 ml.

- **Quality Control**
  - One drop of the final thawed suspension is cultured anaerobically, expected to yield heavy mixed growth.

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**“Top-down or Bottom-up?” The Best Route for Stool Delivery**


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**Whose Poop to use?**

- **Related Donor**
  - Less “icky” factor
  - “I’m getting my wife’s stool... part of her now lives in me!”
  - Dysbiosis runs in families and a shared environment

- **Unrelated Donor**
  - 90-92% vs. 70% success rate in CDI eradication (Hamilton et al)

- **Fresh is Better?**
  - 92% Fresh vs. 90% Frozen success rate
  - Ready-to-go poop


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**Beyond C Difficile...**

**FMT in IBS and IBD**

- **Irritable Bowel Syndrome**
  1. Case reports/series
  2. Mainly in IBS-D, some IBS-C/CC
  3. Reports improvement in BM and reduced abdominal pain
  4. Awaiting results of ongoing 2 RCTs

- **Inflammatory Bowel Disease**
  1. Case series
  2. Positive outcomes in Ulcerative Colitis
  3. Promise for use in Crohn’s Disease
  4. Recent data at DDW 2014 from ongoing RCTs were conflicting

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**The Holy Grail for metabolic disorders?**
Therapeutic Potential of FMT

The Genie is now out of the bottle…

The FUTURE 1:
Synthetic Donor Material

RoboGut: The RePOOPulate Project

The FUTURE 2:
-Personalized Microbiota Profiling
-“Bespoke” bacterial top-ups

The FUTURE 3:

- The push for new indications
  1. Evidence for IBD
  2. IBS and FGIDs
  3. Metabolic Syndrome

- Long-term data
  1. Safety data
  2. Durability of the microbioma change
  3. Host-microbiota interactions

“Full Spectrum” Microbiota
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