Faecal microbiota transplantation

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Aims

• Why faecal microbiota transplantation (FMT) at NNUH?
• How we set up our service
• Our experience so far
• Next stage
History of FMT

• Bacteriotherapy, faecal transfusion, faecal transplant, stool transplant, faecal enema, and human probiotic infusion (HPI).

• 4th century China (yellow soup, golden syrup)-food poisoning, severe diarrhea

• 1958 first publication Ben Eiseman et al, Colorado, Surgery 1958;44:854-859 (PMC)

• Centre for Digestive Diseases in Sydney, Australia, offering FMT for more than 20 years

• Some baby animals eat their mothers' faeces (coprophagia)
The problem

- UK-20,488 cases (2010), 12000 (2014), 3000 relapses
- USA-100,000 cases, 14,000 deaths
- 1:3 to 1:4 have at least one relapse
- Of these 60% further relapses
- Destruction of gut diversity by antibiotics
**C. difficile** chain of infection

- **Infectious agent**: *C. difficile*
- **Reservoir**: Large bowel
- **Portal of exit**: Faeces
- **Means of transmission**: Faecal-oral
- **Portal of entry**: Ingestion
- **Susceptible host**: Immunocompromised, >65, broad spectrum antibiotic use, healthcare contact
Faecal microbiota transplant for recurrent Clostridium difficile infection
Issued: March 2014
NICE interventional procedure guidance 485
guidance.nice.org.uk/ipg485
NICE Recommendations

• 1.1 Current evidence on the **efficacy** and **safety** of faecal microbiota transplant for recurrent *Clostridium difficile* infection is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.

• 1.2 This procedure should **only** be considered for patients with recurrent *C. difficile* infections that have failed to respond to antibiotics and other treatments.

• 1.3 Clinicians should ensure that a confidential record is kept of the donor and recipient of each faecal microbiota transplant.

• 1.4 NICE encourages further research into faecal microbiota transplant for *C. difficile* infection, specifically to investigate optimal dosage, mode of administration and choice of donor.

• “Implementation of this guidance is the responsibility of local commissioners and/or providers”.
Why FMT?

• Real problem
• Real and lasting solution (improve patient care)
• Break the vicious cycle, Possibility of cure
• Discourage DIY and unregulated practice
• Current CDI treatments not effective—Vanc, Mtz, HNIG, pulsed, tapering, Fidaxomicin, ? Tigecycline
• Existing interest and expertise in *C. difficile*
Evidence-Faecal microbiota transplant (FMT)

Van Nood, N. Eng j, Jan 2013

- Via nasogastric tube, nasoduodenal tube, NJ, rectal enema or via the biopsy channel of a colonoscope
- 42 patients-faecal transplant/ Vancomycin, with a bowel lavage /Vancomycin only. Primary cure rates 81% /23%/ 31% respectively at 10-week follow-up.
- Relapse rates 6%, 54% and 62%
- FMT overall cure rate of 94%
Aim of FMT

• Replace with healthy flora
• Right composition
• Microbial diversity
Stages of FMT

- Pre-screened donor register
- Identify eligible pt
- Notify donor and FMT lab
- Administer donor questionnaire
- Book endoscopy, prep patient
- Prepare donor material
- Infuse FMT
- Store aliquots (donor and recipient)
- Follow up
# Donor exclusion criteria for fecal microbiota transplant

<table>
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<tr>
<th>Absolute</th>
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<tr>
<td><strong>Risk of infectious agent</strong></td>
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<tr>
<td>Known HIV, hepatitis B or C infections</td>
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<td>Known exposure to HIV or viral hepatitis (within the previous 12 months)</td>
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<td>High-risk sexual behaviors</td>
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<td>Use of illicit drugs</td>
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<td>Tattoo or body piercing within six months</td>
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<td>Incarceration or history of incarceration</td>
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<td>Known current communicable disease (e.g., upper respiratory tract infection)</td>
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<td>Risk factors for variant Creutzfeldt-Jakob disease</td>
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<td>Travel (within the last six months) to areas of the world where diarrheal illnesses are endemic or risk of traveler's diarrhea is high</td>
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<td><strong>Gastrointestinal comorbidities</strong></td>
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<tr>
<td>History of inflammatory bowel disease</td>
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<td>History of IBS, idiopathic chronic constipation, or chronic diarrhea</td>
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<td>History of gastrointestinal malignancy or known polyposis</td>
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<td><strong>Factors that can or do affect the composition of the intestinal microbiota</strong></td>
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<td>Antibiotics within the preceding three months</td>
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<td>Major immunosuppressive medications (e.g., calcineurin inhibitors, exogenous glucocorticoids, biological agents, etc)</td>
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<td>Systemic antineoplastic agents</td>
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<tr>
<td><strong>Additional recipient-specific considerations</strong></td>
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<td>Recent ingestion of a potential allergen (e.g., nuts) where recipient has a known allergy to this (these) agent(s)</td>
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<td><strong>Relative exclusion criteria that might be appropriate to consider</strong></td>
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<tr>
<td>History of major gastrointestinal surgery (e.g., gastric bypass)</td>
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<td>Metabolic syndrome</td>
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<td>Systemic autoimmunity (e.g., multiple sclerosis, connective tissue disease)</td>
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<td>Atopic diseases including asthma and eczema, eosinophilic disorders of the gastrointestinal tract</td>
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<tr>
<td>Chronic pain syndromes (e.g., chronic fatigue syndrome, fibromyalgia)</td>
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HIV: human immunodeficiency virus; IBS: irritable bowel syndrome.

NNUH donor screening

- Serum sample for:
  - HIV 1+2 antibodies
  - HTLV I/II antibodies (Ref lab.)
  - Hepatitis A IgM
  - Hepatitis BsAg, cAb,
  - Hepatitis C antibody
  - Hepatitis E antibody (Ref lab)
  - Syphilis ELISA for total antibody
  - CMV/EBV IgG
  - Strongyloides and Entamoeba histolytica serology (Ref lab.)

- NNUH uses Unrelated donors, motivated, well informed

- Stool specimen testing for:
  - Microscopy for Ova, cysts and parasites by concentration
  - Culture for Salmonella, Shigella, Campylobacter, E. coli 0157
  - *C. diff* GDH and Tox A/B
  - Norovirus PCR
  - Screen for extended spectrum beta lactamase producing organisms (ESBLs)
  - Screen for Vancomycin resistant enterococci (VRE)
  - Screen for Meticillin resistant *Staphylococcus aureus* (MRSA)
  - Screen for Carbapenemase producing Enterobacteriaceae (CPE)
Patient prep

- Consent
- Oral Vanc 500mg qds commence 4 days prior to FMT
- Bowel prep day before if possible
- NJ tube insertion
- Slurry infusion
- Can eat 30mins after infusion
- Can go home after one bowel motion
FMT preparation in a dedicated laboratory
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NNUH experience so far

- 1st case Aug 2015
- 12 cases so far
- 11(91%) response (8 wks to 8 months)
- 1 patient’s FMT compromised due to co-admin of needed atbs
- Business case in progress
Side effects from literature -- Minor & infrequent

- Belching, abdominal cramps, tummy pain (Risk is 1 in 5 patients)
- Diarrhoea on the day of the transplant (all patients due to volume of suspension given)
- Infections of the stomach, bowel and the tissue lining the inside of the abdomen (tummy) from commensal organisms (peritonitis or enteritis) within 2 days of having the procedure (Risk 1 in 50 patients).

- **Risks from access route provision**
- Possibility of infection, obesity??
- No serious adverse effect so far in our 12 patients
Patients/ carers ....

Pre-treatment:
- I just want to go back to my wife, she is alone and losing her sight.
- Pt is palliative and difficult to manage due to symptoms
- I want to go to my step father’s funeral
- Care home does not want the pt
- I hate being in isolation. I need my exercises and my rehab
- I was embarrassed at a wedding
- Can’t get carers in
- Symptoms keep coming back

Post-treatment:
- I did not want to flush the toilet, haven't done anything this good for a long time!
- I hadn’t slept through the night for months until last night
- I'll personally come and speak to any patient who is reluctant to take this treatment
Future developments

- Optimum dose, route
- Match donor with recipient
- Super donor
- Any difference based on ribotype e.g. 027?
- Microbial cocktail
- Long term follow up
- Age restriction?
- Use as first line?
Future developments

- Fresh/ frozen
- Stored autologous
- Capsules
- Related/ unrelated donors
- Research, research, research!
- MDRO
- Organ transplant
- Metabolic medicine
- Etc
- Relapses/ re-infection
- Access to out patients and other hospitals
Expanding rapidly

- Now over 500 centers in USA,
- 7 centre in the UK (BMJ 2015)
- open Biome stool bank, USA
- Netherlands stool bank
Conclusion

- 90% efficacy (95% if two FMTs)
- Natural product
- No supply problems
- No direct cost
- No over dose
- No under dose
- No drug reaction
- No drug interaction

- No contraindications
- No age limits
- Logistics and technical considerations
- Reduce antibiotic resistance
- Improve patient care
- Reduce spread in hosp
- Cost effective
ACKNOWLEDGMENT

FMT collaborators
- Institute of food research (IFR)
- Dedicated donors
- Microbiology lab, EPA
- Gastroenterology colleagues/ endoscopy unit
- NNUH Infection control team