Faecal Microbiome Transplants

Faecal Microbiome Transplant (FMT) is a process whereby faecal bacteria from a healthy, screened donor is put into the colon of the recipient using a simple catheter, this is done by Nurses. Generally speaking, this is done for 10 treatments.

Background

Regarding human health and Faecal Microbiome Transplants there have been thousands of papers published over the last few years linking changes in gut flora composition to allergies, asthma, obesity, cancer, Chronic Fatigue Syndrome, Parkinson's Disease, Irritable Bowel Syndrome and Ulcerative Colitis. This does not mean that this treatment is curative for these conditions but the outcomes from this kind of treatment have been remarkable. These outcomes having been anecdotal, have not yet fed into significant size Randomised Control Studies, so these have yet to be done on the various conditions mentioned using this approach.

Changes in the gut microbiome have also been linked to Inflammatory Arthritis, Multiple Sclerosis and Depression using this approach. This is a full transcript of an article written in The Guardian by Ann Robinson, published on 1st August 2016, this is an excellent overview of how important the gut microbiome is. The article can be accessed using the following link, but we have also put the full text of the article in here because it is such an effective overview.
https://www.theguardian.com/lifeandstyle/2016/aug/01/is-your-gut-making-you-sick

The full text of the Article: "Is your gut making you sick?" Ann Robinson, The Guardian, 1/8/16

A gut full of diverse microbes – bacteria, viruses and fungi – is essential for a healthy mind and body. And evidence is growing that our modern diet, overuse of antibiotics and obsession with cleanliness are damaging the diversity of microbes that live in our guts, contributing to a range of conditions including depression, multiple sclerosis, obesity and rheumatoid arthritis.

Microbes live in our guts, bodily fluids, cavities and skin. For every one of our human cells, there's at least one of them. In an average adult, they weigh in at 1-2kg; similar to our brain. Collectively, they're called the human microbiota and their genes are the microbiome. Only a few microbes cause disease; most are beneficial and live in peaceful symbiotic coexistence in and on our bodies. We need them and they need us. And if our microbes aren't healthy, neither are we.

Microbiome and the diet: *A healthy microbiome protects against obesity, allergies and diseases as bacteria break down food in the colon, providing energy for themselves and useful byproducts for us. These byproducts are essential components of chemicals that affect mood, appetite, metabolism, inflammation and the immune system. Professor Tim Spector of King's College London says that variations in the gut microbiome explain, in large part, why our kids are getting fatter and why some individuals gain more weight than others on the same diet. There is no good evidence that we consume more calories or do much less than*

previous generations, yet people around the world are getting fatter, and Spector says that, while genetics play a part, so does the diversity and types of microbes in the gut.

The gut microbiome is mostly influenced by diet and environment. Babies get their first exposure to bacteria that colonise their guts as they travel down the birth canal. Babies born by caesarean section, as at least a quarter are in the UK, appear to be more prone to obesity. Spector explains that a good diet is a diverse one, with a range of fibre and vegetables including artichokes, leeks, onions and garlic. Polyphenols, found in foods including nuts, seeds, coffee, dark chocolate, red wine, olive oil and berries, are used by microbes as an energy source, with beneficial effects on human immune cells. Foods that nourish the microbiome are called prebiotics, and foods that contain the actual microbes, such as yoghurt and fermented milk called kefir, are called probiotics. Fermented foods, such as sauerkraut, kimchi and miso, are combinations of probiotics and prebiotics, known as synbiotics.

Inflammatory arthritis: *An international consortium of scientists is studying faecal samples from people with inflammatory arthritis, such as rheumatoid arthritis. Bacterial groups that seem to be increased can be isolated and introduced to rodents, triggering the development of arthritis in previously healthy animals. Professor Michael Dustin of the University of Oxford says that the risk of developing rheumatoid arthritis is associated with genetic predisposition and environmental factors. "But it's much easier to modify your microbiota than change your genes," he says. Tests for rheumatoid arthritis can prove positive several years before symptoms appear, so there's a window of opportunity to try to stave off the onset of the condition. Using that time to establish a more protective microbiota is one approach being studied. Dustin says that we still don't know whether dietary changes are enough or whether more radical procedures (such as faecal transplants) are necessary.*

Variations in the gut microbiome explain why our kids are getting fatter and why some individuals gain more weight. (Tim Spector, King's College London)

Diarrhoea: *Changes in the gut microbiome can be very dangerous; people treated with prolonged courses of antibiotics that kill a wide spectrum of bacteria can develop life-threatening diarrhoea due to an overgrowth of Clostridium difficile. Faecal transplants (infusions of donor faeces down a nasal tube or up the rectum into the gut) are used to treat these extremely unwell patients, proving that disruption of the gut microbiome can cause serious illness and restoring it to normal can cure the problem.*

Multiple sclerosis: *About 100,000 people in the UK live with multiple sclerosis (MS), a neurological condition that can cause problems with vision, balance, sensation and movement. Researchers have found specific changes in the microbiome of people with MS that appear to be linked to changes in their immune function. And drug treatment of MS has also been shown to impact on the gut microbiome. Dr David Schley of the MS Society says: "The link between MS and the bacteria living in our intestines is an exciting area of research. Recent studies in mice have indicated that intestinal microbes could influence symptoms. While this early evidence is intriguing, we need to learn more before we can make recommendations over whether people with MS should make changes to their lifestyle or diet."*

Depression: *According to the World Health Organisation, depression is the leading cause of disability worldwide. So, there is a lot of interest in the role of the gut microbiome in preventing and treating it. Professor John Cryan of University College Cork says: "We now know that good brain health depends on good gut health. The gut microbiome affects every aspect of brain functioning and human behaviour." Studies have shown that rats with high levels of bifidobacteria in the gut withstand psychological stress better than those with low levels. And it appears that humans do, too; recent human studies from the Cork group in healthy volunteers show increased brain activity (measured by EEG) and reduced levels of stress (measured by rating scales of anxiety and chemicals in the blood, such as cortisol, that rise in response to stress) when people are given demanding tasks to perform.*

"We know that the more diverse your microbiome, the less likely you are to be frail or have cognitive impairment. And a diverse diet is what drives a diverse microbiome," says Cryan. Microbes from the guts of depressed people have been fed to healthy rats, which then develop depression and anxiety-like behaviours. Other healthy rats, fed microbes from the guts of people without depression, remain well.

"It's an exciting area but we need to find out just how gut bacteria send signals to the brain," says Cryan. "There's no downside to recommending a diverse Mediterranean-style diet that includes lots of fibre and cuts down on emulsifiers, processed foods and artificial sweeteners." Probiotics sold commercially are largely unregulated, are of unknown effectiveness and may not reach the colon alive. "We can't even be sure a lot of them get past the stomach acid," he says. But Cryan thinks that within the next five years we will learn a lot more about which specific bacteria are important and we will be able to test our personal microbiota and supplement deficiencies. "It'll become like getting your cholesterol checked," he predicts.

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What is particularly impressive about the papers on Faecal Microbiome Transplants is that there are no downsides to this treatment, it is completely safe.

Therefore, it is too early to say these are cures, but where patients have had problems which have not responded to standard treatment approaches or where the conventional treatment approaches have been unacceptable, the results have been remarkable.

The key issue regarding the gut microbiome, which consists of hugely complex collections of bacteria, many of them anaerobic (i.e. oxygen will kill them), has a profoundly important effect on the immune system, and several brain-specific mechanisms. These have not been fully worked out but there is a great deal of interest to look into this further, to the extent that The White House has launched a National Microbiome Initiative, and are proposing to spend in the order of half-a-billion dollars on this, looking at being able to understand the vast colonies of bacteria, fungi and viruses that have co-evolved with our bodies, and indeed lands and oceans.

The effect of Probiotics and Prebiotics

This area of self-treatment is now broadly accepted and indeed several methods of improving friendly bacteria in the gut are on supermarket shelves.

However, a review of existing studies found no evidence that taking Probiotics benefits healthy people. Also in 4/7 trials analysed, no effects were observed on the faecal microbiota composition when compared with placebo. (**Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials** *Nadja Kristensen, Thomas Bryrup, Kristine Allin, Trine Nielsen, Tue Hansen, Oluf Pedersen* Genome Medicine2016**8**:52 **DOI:** 10.1186/s13073-016-0300-5)

FMT in Obesity

There have been many cases of obese patients who have had gut microbiome transplants who have subsequently lost weight, there are several papers to back this up. This does not mean that Faecal Microbiome Transplant is a cure for Obesity but the results are most encouraging and indeed interesting. [1,2,3,4,5]

FMT in Clostridium Difficile infections

The only condition for which Faecal Microbiome Transplant has been proven so far is for the condition of recurrent Clostridium Difficile infection. In our view it is likely that further conditions in further studies will begin to attract the kind of proof we have for FMT in Clostridium Difficile infections.

FMT and possible efficacy in Cancer

See: **Sporadic colorectal cancer: microbial contributors to disease prevention, development and therapy** *Julia L Drewes[1], Franck Housseau[1] and Cynthia L Sears British Journal of Cancer* (2016) **115**, 273–280. doi:10.1038/bjc.2016.189 www.bjcancer.com

Donors of FMT Implants

We refine the donor material to get as much of the healthy microbiome as possible, and very little else. Material is processed in an anaerobic (oxygen free) atmosphere. This is because some of the important gut flora die off when exposed to air.

In order to do this a unique and patented laboratory process is used to remove food wastes, mucous, epithelial cells, until the end product is a bacterial colony extract in the form of a pellet. This is then the basis of the implant.

The choice of donor is important and young subjects are chosen who are healthy with no history of antibiotic use and no chronic diseases of any kind.

These donors are examined and have standard laboratory blood tests carried out every three months.

The donors have to observe a high nutrient, high raw food, probiotic and prebiotic-rich diet. These donors are also non-smokers, are of an ideal weight and have an impeccable ‘digestive’ history.

Donors have a naturally occurring slim physique, and they are sound in body, mind and spirit.

If any patient is interested in Faecal Microbiome Transplant, then they should make an appointment to see us and we can then assess whether the use of this approach would be helpful in any particular clinical situation.

Research Evidence:

[1] **An obesity-associated gut microbiome with increased capacity for energy harvest.** *Turnbaugh PJ[1], Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. 2006 Dec 21;444(7122):1027-31.*

[2] Microbial ecology: human gut microbes associated with obesity.
Ley RE[1], Turnbaugh PJ, Klein S, Gordon JI. 2006 Dec 21;444(7122):1022-3.

[3] Therapeutic Potential of Fecal Microbiota Transplantation
Smits LP[1], Bouter KE, de Vos WM, Borody TJ, Nieuwdorp M. Gastroenterology. 2013 Nov;145(5):946-53. doi: 10.1053/j.gastro.2013.08.058. Epub 2013 Sep 7.

[4] Obesity and the human microbiome.
Ley RE[1]. Curr Opin Gastroenterol. 2010 Jan;26(1):5-11. doi: 10.1097/MOG.0b013e328333d751.

[5] Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. *Vrieze A[1], Van Nood E, Holleman F, Salojärvi J, Kootte RS, Bartelsman JF, Dallinga-Thie GM, Ackermans MT, Serlie MJ, Oozeer R, Derrien M, Druesne A, Van Hylckama Vlieg JE, Bloks VW, Groen AK, Heilig HG, Zoetendal EG, Stroes ES, de Vos WM, Hoekstra JB, Nieuwdorp M. Gastroenterology. 2012 Oct;143(4):913-6.e7. doi: 10.1053/j.gastro.2012.06.031. Epub 2012 Jun 20.*

Gastroenterology: The Gut Microbiome in Health & Disease Reflecting the evolution of intestinal microbiome research, the reviews address three themes: (1) basic concepts in the mammalian gut microbiome; (2) gut microbiome and disease, and (3) modification of the gut microbiome to maintain health or treat disease. *Chung Owyang, Gary D. Wu*

Treatment of Ulcerative Colitis Using Fecal Bacteriotherapy The use of human fecal flora to treat gastrointestinal (GI) disorders is not a novel concept, having been practiced periodically for more than 40 years.*Thomas J. Borody, MD, FRACP, FACG, FACP, Eloise F. Warren, BScM, Sharyn Leis, RN, Rosa Surace, and Ori Ashman, MA*

Probiotic Therapy for Ulcerative Colitis In 2009, 2 manuscripts were added to the literature that demonstrated the effectiveness of probiotics in inducing remission in patients with

Ulcerative Colitis. *Martin Floch, MD Journal of Clinical Gastroenterology – Volume 44, Number 4, April 2010*

Fecal Flora Reconstitution for Recurrent Clostridium difficile Infection When the normal colonic flora are altered by antibiotic use, diarrhea is a common sequela. Rates of antibiotic-associated diarrhea (AAD) in outpatient children and adults range up to 30%, and up to 39% for inpatients, depending on the antibiotic administered. *Faith Rohlke, BA, Christina M. Surawicz, MD, MACG, and Neil Stollman, MD, FACP, FACG, AGAF Journal of Clinical Gastroenterology – Volume 44, Number 8, September 2010*

Changes in the Composition of the Human Faecal Microbiota Clostridium difficile-associated disease (CDAD) is the major known cause of antibiotic-induced diarrhea and Colitis, and the disease is thought to result from persistent disruption of commensal gut microbiota. *Khoruts, Alexander MD; Dicksved, Johan PhD; Jansson, Janet K. PhD; Sadowsky, Michael J. PhDJournal of Clinical Gastroenterology: POST AUTHOR CORRECTIONS, 31 December 2009 doi: 10.1097/MCG.0b013e3181c87e02*

Scatalogical Success – Fecal Transplants to Treat Bacterial Infections In a 2009 study published in the *Journal of Clinical Gastroenterology*, researchers found that a single infusion of feces reintroduced beneficial bacteroides — bacteria that are necessary for the body to resist Clostridium difficile infection…*Meredith Melnick @meredithcm Jan. 20, 2011*

Anti-inflammatory properties of the short-chain fatty acids acetate and propionate Inflammatory bowel diseases (IBD), Crohn's disease and ulcerative colitis, are chronic inflammatory disorders of the gastrointestinal tract which withstand strong influence from both genetic and environmental factors…*World J Gastroenterol 2007 May 28; 13(20): 2826-2832 World Journal ofGastroenterology ISSN 1007-9327*

Fecal Microbiota Transplantation for the Treatment of Clostridium difficile Infection Almost all patients treated with donors' fecal infusion experienced recurrent episodes of *Clostridium difficile*-associated diarrhea despite standard antibiotic treatment. Of a total of 536 patients treated, 467 (87%) experienced resolution of diarrhea. *Cammarota, Giovanni MD; Ianiro, Gianluca MD; Gasbarrini, Antonio MD*

Fecal Microbiota Transplantation (FMT) in Multiple Sclerosis (MS) Recent evidence implicates the GI microbiota in the progression of neurological diseases such as Parkinsons Disease 1, Multiple Sclerosis and Myasthenia Gravis 2. We report three patients with MS diagnoses who achieved durable symptom reversal with FMT for constipation. *T.J. Borody, S.M. Leis, J.L. Campbell, M. Torres, A. Nowak, , Centre for Digestive Diseases, Five Dock, New South Wales, AUSTRALIA*

Parkinsons and Faecal Transplant or at least Resolution from Constipation Faecal bacteriotherapy, now termed faecal microbiota transplantation (FMT), has gained prominence in light of the recent epidemic of *Clostridium difficile* infection

(CDI) in North America and Europe. *T.J. Borody, M. Torres, J.L. Campbell, L. Hills, S. Keetheswaran*

Study Suggests Fecal Transplant Could Be Effective Treatment for Crohn's Disease Results of the first FDA-approved study treating patients with Crohn's disease using fecal microbiota transplant (FMT) suggest it could be an effective new treatment. *FDA*

New evidence supports success of fecal transplants in treatment of Clostridium difficile infection Research demonstrates dynamic nature of fecal microbiota *University of Minnesota*

Reduced diversity and altered composition of the gut microbiome in individuals with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome *Ludovic Giloteaux Julia K. Goodrich, William A. Walters, Susan M. Levine, Ruth E. Ley, Maureen R. Hanson Microbiome2016**4**:30* ***DOI:*** *10.1186/s40168-016-0171-4*