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What to do about Aerobic Deficiency Syndrome

Changing microflora: the direct route

What men don't know can kill them: the test they must have

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Changing microflora: the direct route

The exchange that takes place between the bacteria in the gut – genetic, molecular and functional – has profound influences on human health. How we manage this information and apply it in clinical practice has spun out numerous strategies, none more challenging to the average clinician and patient than the idea of faecal transfer. CAM contributing editor Michael Ash, BSc (Hons), DO, ND, FDip ION reports on a controversial therapy proving highly effective against the scourge of C. difficile infection in particular.

Faecal Bacteriotherapy, or Faecal Transplantation, is in essence the transfer of one healthy human’s bacterial colonies – found in their stool sample – to another unhealthy human for the purpose of mitigating an active disease.

Recent findings demonstrate that it is possible to engraft new microbiota from a donor source, resulting in the restoration of gut functionality and improvement in health.

This builds upon decades of case reports and series in which faecal transfers were used to successfully treat refractory and recurrent Clostridium difficile infection.

An answer to non-recovering colitis

Back in 1958 – over 50 years ago – the idea that faecal transplantation may mitigate or resolve the condition called pseudomembranous colitis, caused by a pathogen (we now know this to be Clostridium Difficile (1) growing unopposed on antibiotic treated gastric tissues was explored and written about. (2) A follow-up paper in 1960 gave further insights into its potential as a simple restorative treatment. (3)

In 1958, 4 patients with non-recovering pseudomembranous colitis despite what are described as “heroic” efforts including...
hydration, vasopressors, hydrocortisone, antibiotics and L. acidophilus were in desperation treated with faecal retention enemas using faeces collected from healthy donors with no antibiotic exposure. All 4 recovered in days and were discharged.

The authors noted: “We hope that more complete evaluation of this simple therapeutic measure can be given further clinical trial by others.” They further commented that once “more precise” microorganisms were identified, their administration in “enteric-coated capsules might be both more aesthetic and more effective.”

C. difficile (CD) is now the equivalent killer of patients in the USA to those lost to HIV infection (15–20,000). (4) This simple effective intervention is achieving a greater recognition, but the standard of practice in hospitals for this condition once it has achieved fulminant status is emergent resection of the colon – which apart from the clinical burden in terms of therapy and cost has seen little improvement in outcome figures from that achieved in 1958 at just ~50%. (5) This relapse and loss rate may be improved by using relevant lab markers but patients still suffer from a high rate of mortality. (6)

Over the decades since the 1958 paper more than 200 cases of CD being treated with faecal transfer using either enemas or nasogastric tube administration have been recorded with a quite remarkable successful outcome of ~90% and no apparent ill effects. (7-10)

Current use
So why is this simple, inexpensive and effective strategy still not a standard of care in hospitals? Maybe in the absence of much science (ie appropriate RCT comfort-inducers), the idea probably cannot yet overcome the instinctive avoidance by many clinicians and their patients of something seemingly repulsive. Yet there is no shortage of workable data, just shortage of randomised clinical studies. Albeit that the risk to benefit ratio is heavily in favour, there is a degree of uncertainty about the safety of this innocuous transplantation, never mind that studies on the gut microflora and its role in human health are literally filling journals on a weekly basis. (11)

Borody et al reported positive outcomes in a small trial using faecal transplantation therapy to treat ulcerative colitis (UC). A group of 6 patients with “severe, recurrent symptoms and UC confirmed on colonoscopy and histology were administered retention enemas and repeated this daily for 5 days. A very impressive and complete reversal of symptoms was achieved in all patients by 4 months and all other medication was discontinued. On follow up at 1 and 13 years there was no clinical, colonoscopic, or histologic evidence of UC in any patient.” (12)

Novel ideas
It would seem quite logical that this is an area of investigation for inflammatory bowel diseases, as these are associated with an altered microbial mix in the gastrointestinal tract and subsequent immune discord. (13) Less obvious is the idea that it may alter a generalised condition such as metabolic syndrome and obesity, (14, 15) or a complex but expanding area of diseases referred to as autoimmunity and allergy (15-17), but this has been attracting attract serious discussion. One of the leading researchers Dr Borody from Australia is currently recruiting for patients suffering from Parkinson ‘s disease after he found one of his patients made a recovery after transplantation.

IBS a very common functional disorder has no direct studies on its effects from receiving faecal transplantation but represents an interesting area of possibility. (18)

Probiotics
To date the most appreciated and clinically used manner for influencing the gastric microbial balance or populations has been through the ingestion of probiotics and prebiotics based on the discoveries of the 20th century’s great immunologist Metchnikoff. (19)

However, there is inconsistent evidence of their use as a single therapy in the treatment of conditions such as those described above and consistent outcomes remain difficult to achieve. In part this is due to the unravelling of the role of single strain organisms and their effects on humans as well as the complex logistics of influencing the microbial community in the gut.

Human originating bacteria used in some probiotics may well confer additional immune benefits than those derived from the dairy industry, but both originating organisms are capable of activating microbial associated molecular patterns on dendritic cells and so confer an immunological message to the
adaptive immune cells. (20) It is a formidable task – more than 100 trillion bacteria reside in the colon as well as other organisms and viruses. In addition these cohabitants are uniquely adapted to the gastrointestinal tract and occupy niches in complex communities that resist easy manipulation by medication as well as probiotics.

The result of this has been a gradual understanding of the modest – albeit useful – contribution that a probiotic infusion may make to the bacterial relationships in our inner tube of life. One outcome has also been the now somewhat ensnared notion that, once established, the “fingerprint” of our microflora remains essentially unchanged despite the use of antibiotics and probiotics. This seems to be a compelling concept, especially in terms of the core microbiome and its longevity of occupation, but a recent paper on faecal transplantation suggests that this may need a review. (21)

**Faecal suspensions**

A small group of ten patients undergoing “faecal bacteriotherapy,” or “faecal transplantation” first had their gastrointestinal tract treated with antibiotics and then faecal suspensions collected from healthy donors were administered daily. In this study the first infusion was administered through a colonoscope and subsequent doses were given over a 60-minute period through a nasal jejunal tube or via enemas, suggesting options for clinical settings.

The participant’s microbial concentrations were analysed at 4, 8, and 24 weeks post-infection and then compared with the initial infused donor faecal suspension to determine whether the donor flora had become a stable microbiota of the faeces of the recipients.

The samples revealed that the recipients’ faecal flora changed to reflect that of the donor, indicating the possibility of providing a degree of permanence to the new colonies of bacteria. The authors stated: “This study demonstrates a durable beneficial change in the patients’ bacterial populations of the colon to represent those of the healthy donor’s microbiota. Manipulation of the colonic microbiota to improve its protective and beneficial role represents a promising field of new therapeutic strategies for the treatment of gastrointestinal conditions.”

**Where now?**

Virtually all of this therapy for the purpose of journal publication has been undertaken in hospital settings and researchers have issued warnings regarding the unknown bacterial composition of the donor stool. The application has either been via naso-gastric tube – out of the reach of most practitioners operating from private clinics, or by retention enemas, a long understood mechanism for the introduction of fluids and medications into the colon.

On the basis that the risks to benefits are heavily stacked in the benefits section, one study explored the practicality of having patients administer the enemas at home, using waterised stool samples collected from healthy family members. 7 patients with C. diff were sent home to administer the transplant and follow-up at 14 months revealed 100% success in restoring the GIT to health after a single administration. (22)

The researchers stated: “In this case series faecal transplantation was both well tolerated and efficacious in a group of highly motivated outpatients. No patient required a repeat procedure, and there were no treatment failures despite 3 patients receiving antibiotics in the post-transplant period.”

While unfamiliar to some clinicians, enemas have been used in natural medicine protocols for many years. It is unclear whether the same level of pre preparation is required for a second transplant if required, but this should probably represent the minimum level of investigation when transplanting from an ostensibly healthy patient into one experiencing both functional or pathological GI and systemic illness.

The opportunity for traditional medicine to start to apply the principles ensnired in probiotic therapy, that is the infusion of bacteria rather than antibiotics, is attracting research in the UK where scientists in Manchester are looking at the benefits of freezing a suitable stool specimen and then putting the donor material in a capsule for ingestion.

These crude transplants will eventually make way for what is jokingly referred to as “God’s probiotic” – a pill containing microbes whose potential to fight infections has been scientifically proven. (21)

**References**