

Gut: Advanced Treatments – Part 2

So given these limitations, what are the options available to you as a clinician? So the first is to send the patient to a clinic outside the US that offers FMT. Not all countries have the same restrictions that the US has on FMT; for example, the UK doesn't have the same limitations, and there's a clinic there called Taymount Clinic. I've interviewed the director, Glenn Taylor, twice now for my podcast, so we'll put those in the resources section for this week's content. They have a location near London and they actually just opened a new location as of the time of this recording in the Bahamas.

The pros of the Taymount Clinic are that they're very experienced with FMT, they have a professional staff, they have prescreened donors, they have comfortable accommodation nearby, they will often rotate donors for a particular patient so that you're getting stool isolates, microbiota from five different donors or even more, which increases species diversity, which is a major indicator for gut health.

The cons are that it's definitely not cheap, insurance doesn't cover it, the UK is far away from many patients and the expense of traveling there and staying there in addition to the expense of the procedure itself can be prohibitive, of course. Unfortunately, it really comes down to ... if you want to send your patients to a clinic, this is the one that I know of that has the most experience. The Centre for Digestive Diseases in Australia is an option too, but only for people who live in Australia. They used to treat overseas patients, but they're no longer doing that. If you are in Australia and you live in Australia, that's still a possibility, and I think it may even be covered by the healthcare system, which is amazing. Probably some of our Australian participants in ADAPT would know the answer to that, so if you're a clinician in Australia, maybe check on the Facebook group. Another clinician in Australia might be able to answer that question.

There is another option, which I've referred to now a couple times, which is to supervise the patient through a DIY home procedure. It's a bit of a legal gray area, but some doctors I know have actually called the FDA and asked about it, and the FDA's response was something along the lines of, "We don't want to know about it, we're not regulating that at this time," so translation: go ahead, knock yourself out. However, it does present a lot of challenges. You have to be set up for pre-screening donors, and then monitoring the donor over time and the patient. It can be difficult to find qualified donors, as I mentioned. The procedure is not likely to be as effective as it would be in a clinic environment like the Taymount Clinic. One possible reason for that is that most of the microbes in stool are anaerobic, which means they need an oxygen-depleted environment to survive, and as soon as a donor passes his stool and then has to bring it from their house to the recipient's house, and then it gets processed in a blender, that's exposure to oxygen that would kill some of the anaerobic bacteria.

Having said that, there are many cases where patients have done DIY-at-home stool transplants, even with recalcitrant antibiotic-resistant *C. diff*, and it saved their lives, so I just want to be clear

that it certainly can work and it has shown a history of working in this situation, but may not be as effective for the reason that I mentioned. It's vivid, as I said, and messy, and some patients are really repulsed by it and have a really hard time doing it, although as I said, that's kind of the smallest concern for most people at this point, but I've decided not to teach this in more detail in this course for all these reasons.

It's really unwieldy, and most clinicians are not going to be able to successfully integrate this into their practice without dedicating a large percentage of their time and their practice to it. There are some clinicians in the US that have done that, like Mark Davis, the Bright Medicine Clinic in Portland, he has a center that does FMT for patients with antibiotic-resistant C. diff. Prior to the FDA ruling, he was treating other patients with other conditions, but he's abiding by the FDA ruling responsibly and so can only accommodate patients with antibiotic-resistant C. diff. So if you do have a patient with that condition, sending the patient to that clinic for FMT is a great idea because Mark Davis is extremely experienced with the procedure and very knowledgeable about it. He's dedicated a significant amount of his time and his resources and his practice to doing that. So you really need to be set up for it, and if you know you want to go in that direction, you can contact Mark Davis, you can join some of the FMT clinician groups and get more involved with them. But I didn't feel like it was applicable to the vast majority of clinicians in this training.

I do have experience, as I mentioned, supervising patients through DIY FMT, and I've also sent several patients to the Taymount Clinic, and so I have a few reflections about my experience with both of those. First, in both cases it can be really effective and produce dramatic results even in the most recalcitrant, so it really is exciting in that respect. I've seen some miraculous turnarounds, patients with intractable constipation for 10 years that started having regular bowel movements literally overnight, after their first DIY treatment. Patients with severe GI issues, fatigue, fibromyalgia, skin issues, improving dramatically. But that said, it's not a panacea. I've also seen patients not only not improve, but I've seen patients get pretty significantly worse. It's not clear yet who is going to get better and who's going to get worse, which is one of the hesitations that I have around this procedure, but some studies have shown that up to 25 percent of patients with inflammatory bowel disease will actually be triggered and have a flare-up when they have an FMT, and I've definitely seen that to be the case in my experience. Some of the patients that had the worst response to FMT were patients with IBD, particularly Crohn's, it seems. If Crohn's is characterized and even ulcerative colitis by an autoimmune attack against commensal bacteria, if you introduce a huge amount of commensal bacteria at once, then that could obviously make the condition worse. So in general, I would say the benefit almost always outweighs the potential consequences if the patient has antibiotic-resistant C. diff, but the calculation is a lot less clear with other conditions at this point.

Last treatment I want to just briefly touch on is helminthic therapy. This is based on the old friends hypothesis, also known as the hygiene hypothesis, which is a very compelling theory with a lot of evidence behind it that suggests that part of what is causing the dramatic rise in autoimmune disease and other immune-related dysfunction is the disappearance of these organisms that we co-evolved with for the vast majority of human history, and they include organisms like Necator

americanus, or hookworm. These organisms have been inhabiting not only human beings but actually mammals for, I think, 350 million years, if I recall.

There's some evidence that the immune system evolved in response to the presence of these organisms, so put another way, there's never been a time in the evolutionary history of mammals up until very recently when we were not colonized by these organisms, and they are thought to play an important role for that reason in tuning and regulating the immune system. The immune system didn't even exist without them, and the argument is that the immune system doesn't even really know how to exist without them. There are studies spanning two decades now that show that reintroducing these organisms into the human host in a safe way, and the studies have shown benefit in doing that with autoimmune disorder, allergies, asthma, and other conditions that involve immune dysregulation.

Pig whipworm, or *Trichuris suis*, has been used for ulcerative colitis in Crohn's, some studies done by Weinstock out of the University of Iowa and a company in Germany called Ovamed that was providing these for those Weinstock studies. I believe Ovamed is still partnered with University of Iowa but is no longer making the pig whipworm available to the general public. The downside of pig whipworm is that they don't colonize the human intestine, so the patient has to keep taking them, and they're quite expensive.

Necator americanus, which is human hookworm, does colonize the human intestine. The reason they can be safely used is that hookworms don't reproduce in the digestive tract, so you don't get a proliferation of hookworm unless the patient is continually exposed to them. So in places like Africa, hookworm can be pathogenic and problematic because kids that are walking barefoot in latrines are continually exposed to more and more hookworm, and they gradually accumulate a higher population of hookworm, and that can cause problems. But a lot of studies have suggested that just maybe 25 to 50 hookworms in the human gut does not cause problems and actually has, like I said, a tuning and regulatory effect on the immune system.

From a clinical perspective, this is interesting, but there's really not much that you can do legally as a clinician to explore this with your patients at this time. Some patients are doing this under the radar. They're ordering the hookworms from places on the internet or they're going down to Mexico, and again, the results vary from miraculous to no change to actually getting significantly worse, so I currently can't recommend helminthic therapy due to a lack of regulation or standardization or even any resource that I can point you to to legally use it as a clinician, but I just want you to be aware of it in case a patient discusses it. It's certainly fascinating and something that I hope sees more development and research but not really practical for use at this time.

Okay, that's it for now, see you next time.