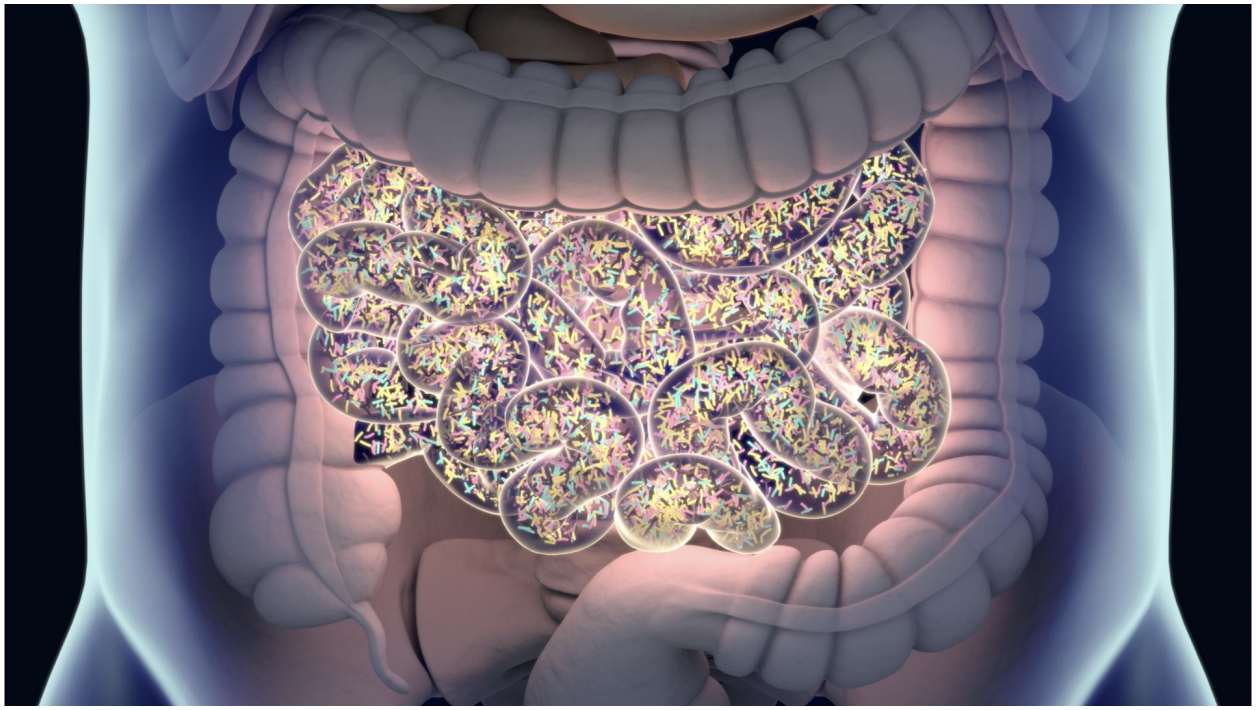
Gut Treatment Protocols: SIBO, Part 7

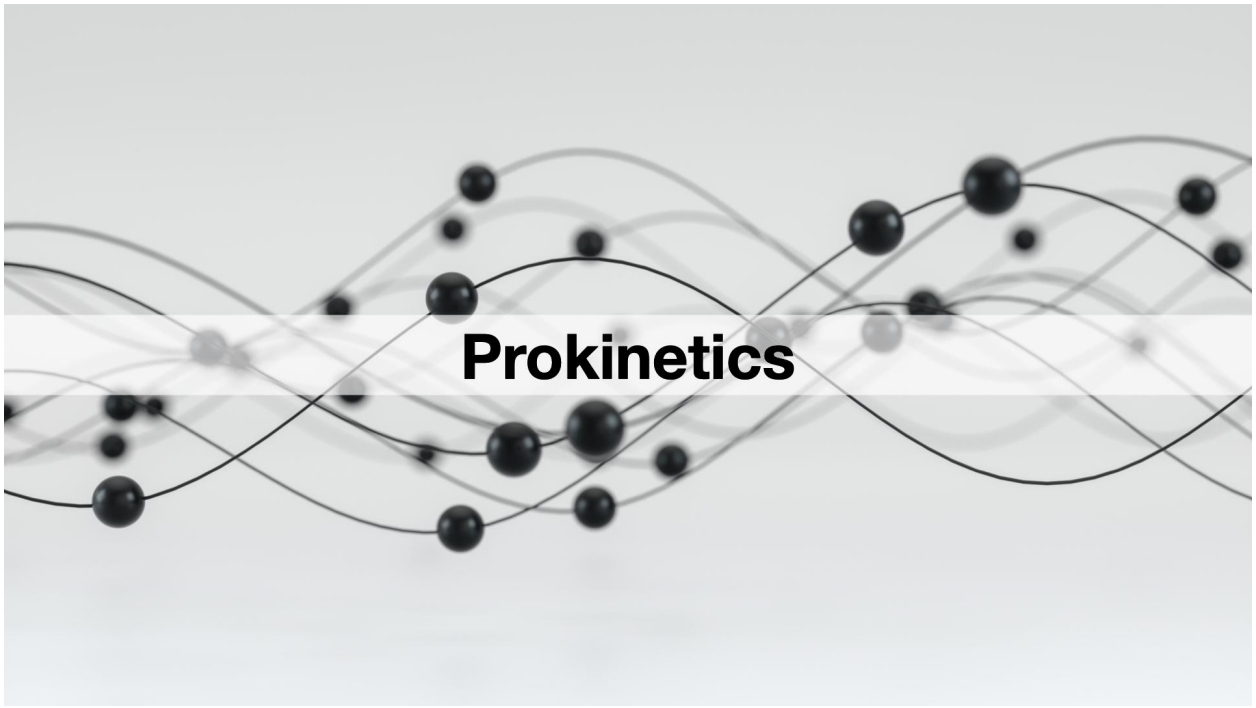
While we're on the topic of recalcitrant and difficult-to-treat SIBO cases, I think it's a good time to discuss treatment options for impaired motility that's connected to post-infectious IBS. Earlier in the program, we talked about the ibs-smart test results and its connection to IBS and SIBO. So when a patient or client has positive anti-vinculin and/or anti-CdtB antibody levels on the ibs-smart test, it indicates some sort of post-infectious gastritis as a likely cause of persistent IBS and/or SIBO and the symptoms associated with those conditions.



If I have a patient [who] has persistent SIBO or IBS that has not responded to initial treatments, gas levels remain high, or they've had [a] known history of food poisoning or their disease timeline corresponds with travel that may have included a foodborne disease incidence, then I will often order the ibs-smart test. At this point, if the ibs-smart test comes back positive, then we pivot treatment slightly and turn our focus on supporting and restoring proper motility of the small intestine and supporting the function of the migrating motor complex [(MMC)].

A reminder that the MMC or intestinal housekeeper, as it is lovingly referred to, is a cyclic and recurring pattern of motility that occurs in the stomach and small intestine during periods of

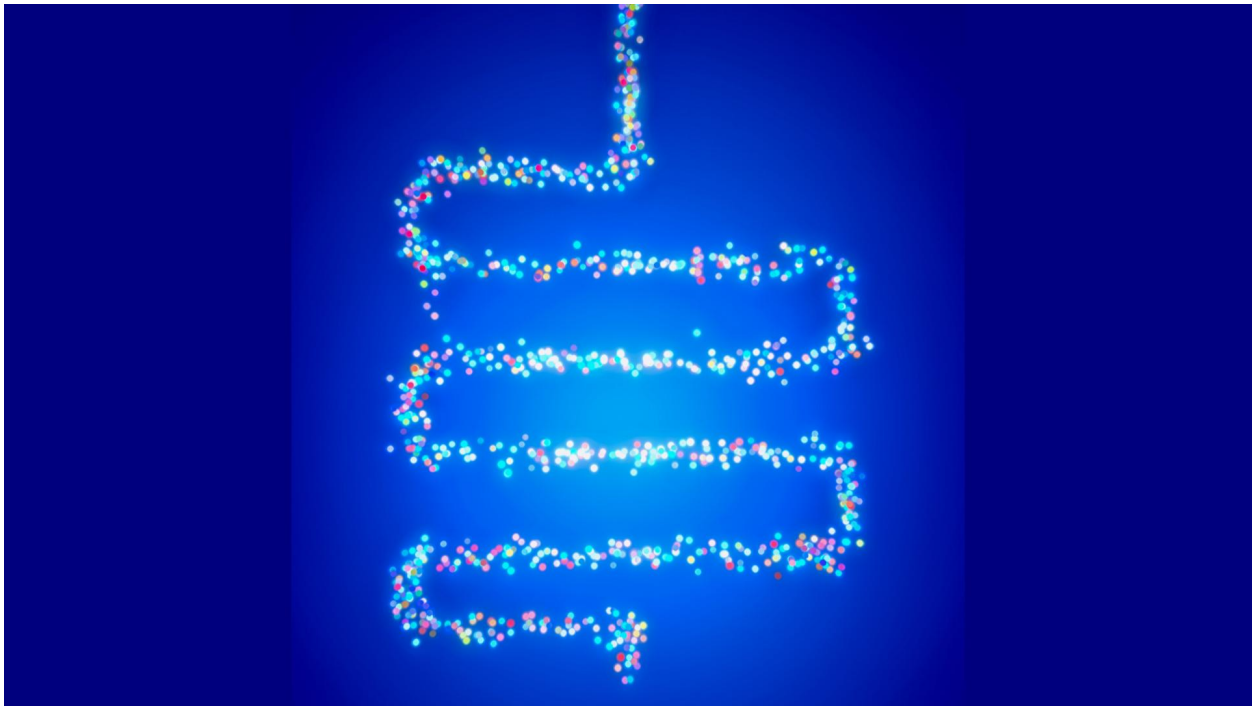
fasting and is interrupted with food consumption. It appears to be controlled by the nervous system and by the secretion of an enteric hormone motilin. Studies have shown that any disruption in the MMC significantly increases the risk of bacterial overgrowth. I think we should talk a little bit more about this and how we can support the MMC and prevent SIBO relapse in practice.



Let's start with prokinetics. There are a variety of ways [you] can go about introducing prokinetic support to your treatment plan. Generally, by the time we have a recalcitrant case of SIBO or persistent IBS and have gotten the ibs-smart test results back, it often feels like the right time to pivot the focus of treatment toward other underlying causes of SIBO anyway. The goal of prokinetics is to stimulate and coordinate [GI] motility, and they do so by increasing transit in the GI tract and also improving the coordination of GI movement downward. They work in a couple of different ways. They're either inhibiting dopamine, which is an inhibitory neurotransmitter in the GI tract that inhibits motility, so prokinetics are inhibiting the inhibitor essentially, or the other mechanism of action is to stimulate acetylcholine, which is a stimulatory neurotransmitter in the [GI] tract.

These are not laxatives. Laxatives are meant to stimulate bowel movements and loosen stool. They are primarily large intestine-focused, as well. So it's important to note that some prokinetics may have a laxative effect at too high of a dose or if the patient doesn't do well with that

particular prokinetic. That may mean you need to change up the prokinetic and make some changes. Examples of prokinetics include metoclopramide, cisapride, domperidone (also known as Motilium), erythromycin in low dose, prucalopride, which is [the] brand Resolor or Resotran, ginger, ginger root, and Iberogast.



The goal of prokinetic therapy, in this case, is to move food, acid, gas, or stool through and out of the GI organs. Also, in addition to moving things down and out, we also want to get the muscles themselves properly contracting. There are a variety of motility disorders that prokinetics are used for, like achalasia, systemic sclerosis, or Hirschsprung's disease and disorders with motility components like gastric esophageal reflux disorder (GERD) and other reflux disease, functional dyspepsia, gastroparesis, which I've mentioned slow stomach emptying that frequently can occur in diabetes, Ehlers-Danlos syndrome, and the two that we focused on for this presentation, SIBO and IBS.

Herbal prokinetics

Prokinetic	Dose
Iberogast	**IBS/dyspepsia:** 20 gtts with meals **SIBO relapse prevention**: 30–60 gtts nightly **Symptom management** 20–30 gtts TID to QID or PRN **Pediatrics**: 10–20 gtts TID-QID
Ginger/Ginger root	**General:** 1000 to 2000 mg daily (up to 6 g QD) **SIBO relapse prevention:** 1000 to 2000 mg QHS **Pediatrics**: 250 mg QHS
Products:	**MotilPro** *(Pure Encapsulations)*, **Motility Activator** (*Integrative Therapeutics*), **SIBO-MMC** (*Priority One*)

Let's start with the herbal prokinetics that I use in practice. I mentioned some of them in the motility and digestion add-on section, but we'll revisit them here quickly. The first one, Iberogast, we've already talked about in the motility support section of this presentation, but as a reminder, it's a nine-herb liquid combination product from Europe, and I find it pretty helpful, more specifically with nausea and dyspepsia, but also helpful for lower GI symptoms, and has been studied for use in IBS. It has a 65 to 80 percent symptom improvement in about 80 percent of patients [who] tried it in studies and in children about 76 percent symptom improvement in 89 percent of the patients in the study. It's safe [for] pregnancy and children.

There have been rare cases of acute hepatitis reported with the use of Iberogast. I've never personally seen this in practice, but you may think about monitoring liver enzymes in patients [who] you have concerns about or patients who are on this for a long term. And you can also see the different dosing here, depending on what you're using the Iberogast for. [For] IBS dyspepsia, you have 20 drops with meals, SIBO relapse prevention is at night, and then symptom management is more consistent throughout the meals or with meals throughout the day. And then the pediatric dosing is listed there, as well.

The other herb is ginger or ginger root. Its site of activity is best for the upper GI and, as you've likely heard, is most famously helpful for nausea and morning sickness, but [it] also can be used for gastroparesis and vomiting and does help with nerve inflammation, and it's anti-inflammatory, particularly through the NF-kappa B pathway. It's safe for pregnancy. I've also listed out the

dosing adjustments based [on] what you might be using it for here. [Use] some caution with ginger burn for patients as taking it with lots of water may help. And some say that the motility activator product actually is a different type of ginger product that's used, and it may be better [tolerated] for people who have that ginger burn. And there [are] some other combination products that I've listed here that we use like MotilPro, Motility Activator, and SIBO-MMC.

2009 **Study**

In addition to herbal prokinetic options, we have pharmaceutical prokinetics that we can use if you're able to prescribe. As I mentioned earlier, there are a handful of prescription options, but I'm going to discuss the three that I'm using most often in practice, and I think they have [a] safer side effect profile and effectiveness. [The] first is low-dose erythromycin (LDE).

You may be asking yourself, why are we mentioning an antibiotic for motility? Well, with a lower dose of 50 to 62.5 milligrams of erythromycin, it's thought to not have any antibiotic effect but does still have some prokinetic effects. The activity is on the motilin receptor, so it's stimulating the stomach and small intestine mostly. It has historically been used for gastroparesis and SIBO relapse prevention. It's well-studied, pretty effective, inexpensive, I think easily available, and tends to have a low side effect profile. As I've mentioned, there [are] no or low antibiotic effects of the low dose. Pimentel also has [shown] a double remission time in patients. Some considerations are that tolerance may be possible or tachyphylaxis when used for long-term or multiple times per day. Some people are still wary of the idea of being on an antibiotic long-term,

even at a low dose. CYP3A4 interactions should be considered that can prolong QT waves when co-administered with other CYP3A4-metabolized medications. It is contraindicated in people with pre-existing heart conditions. And a reminder that this is really the concern as to the co-administration of other medications here that you have to take caution with these other metabolized medications.

Dosing is a little bit higher for gastroparesis, typically 250 milligrams three times daily, 30 minutes before meals. [Taken] for symptom relief, it's about 50 to 62.5 milligrams to 100 milligrams, 30 minutes before meals or in between meals. And as I mentioned, there are some studies that show potential for the tachyphylaxis or tolerance when used at that multiple time[s] per day dosing. In my practice, I'm mostly using this for SIBO relapse prevention or with the positive ibs-smart test with recalcitrant or persistent SIBO. The dosing for SIBO prevention is 50 milligrams or 62.5 milligrams, which is technically a 250 milligram tablet cut into quarters at night. And the 50 milligram dose would be through a compounding pharmacy. And I have found the cost to be pretty reasonable.

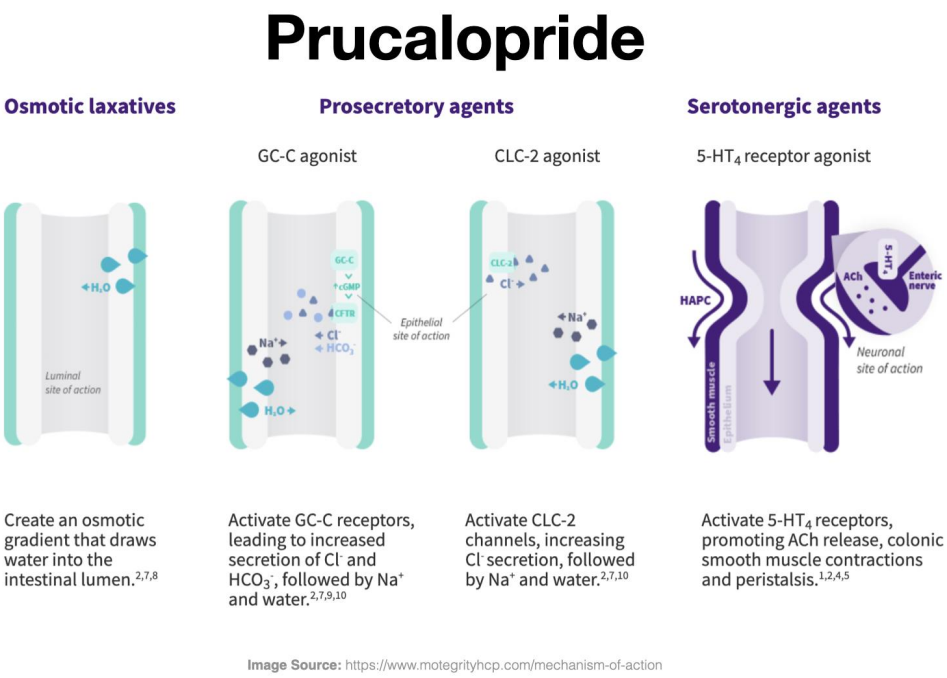


Image Source: https://www.motegrityhcp.com/mechanism-of-action

Prucalopride or Motegrity is "the newer kid on the block." It's a highly selective 5-HT4 receptor agonist. I would consider it a safer option because of its high selectivity to the receptor. It does impact the entire GI tract in addition to stimulating the [MMC]. It's well-studied and very effective for a wide array of GI disorders and symptoms, safer than a lot of other prescription prokinetics

on the market, i.e., with the QT prolongation or CYP450 concerns. There's a low side effect profile and maybe even some neuroprotective healing of the MMC nerve damage over time. Some considerations, though, are that it can be expensive. It can also take several weeks to get in the mail, and it's not FDA approved yet. There have been very rare reports of increased suicidal thoughts and behavior during [the] initial onset of therapy or after stopping therapy. I will say that these studies were usually using higher doses for constipation at 2 milligrams or more daily. Again, [it's] pretty rare in the literature, and I've never seen it happen in practice, but I do always let my patients know, and some of them have avoided this medication, those who have a pretty severe history of depression or are really uncomfortable with that rare side effect. Dosing varies depending on the disorder being targeted.

For constipation, dosing [ranges] from 0.5 to 4 milligrams daily, with an average of 2 milligrams at night. For SIBO relapse prevention, the range is 0.25 to 1 milligram nightly, with 0.5 milligrams often being the most common dosing in my experience. I have been able to get coverage for some patients with the constipation diagnosis and proof that they have tried other first-line modalities for constipation, but coverage can be pretty tricky.

2006 **Study**

Low-dose naltrexone is the other pharmaceutical prokinetic that I use in practice. You may be familiar with this medication and its use in a variety of illnesses but most famously for its use in autoimmune conditions. It has proven prokinetic effects via its opioid receptor antagonist action

binding to the opioid receptors in the body, temporarily blocking them and then stimulating the body to release its own opioids. Endorphins reduce pain, but they also are very important in modulating the immune system. It also binds and blocks toll-like receptors, which release inflammatory cytokines, therefore reducing inflammation. So it's used for pain. It's used for inflammation, especially central nervous system, glial cell inflammation. We use it regularly for immune regulation, and honestly, the list goes on and on as the potential for low-dose naltrexone use. It's safe in kids and, in my clinical experience, is safe during pregnancy and lactation. But it's really important to be transparent with that patient population that studies are limited depending on what you're using [low-dose naltrexone] for. You may consider stopping at 37 weeks' [gestation] or sooner just in case they need pain medication during labor. Again, this is difficult to find in the studies, but there is some use of this during pregnancy.

As far as prokinetic effects go, it does affect the whole GI tract, not just the upper GI, but I find it to be a tad more gentle when it comes to impacting bowel movements. It showed a 76 percent improvement in IBS, so I think that's pretty good. And for SIBO, it has also [been] studied for relapse prevention, and it had a 68 percent success rate. So I've used this quite extensively in my patient population for autoimmune disease but have started using it more often for my patients [with] motility disorders or post-infectious IBS and SIBO.

[There are] lots of variations of dosing for [low-dose naltrexone]. For mild IBS, [the dosage is] 0.5 milligrams once a day and higher for IBD, or the more standard therapeutic dose of 4.5 milligrams daily when you have a GI autoimmune condition. Using this as a prokinetic for SIBO relapse prevention, the dosing can look like a dose of 2.5 milligrams at night for diarrhea and then maybe a little higher, like 2.5 milligrams BID or 4.5 at night for constipation. I'll often start with 0.5 milligrams and titrate up every 6- to 12-week period, depending on how well they tolerate it. And this is mostly to lessen any potential side effects. I use this in my pediatric patients at 0.01 milligrams per kilogram dosing. They have liquid and transdermal options. This is all from a compounded pharmacy. We usually get most of ours from Skip's Pharmacy in Florida or Koshland [Pharm] in California, but you can likely find it at most compounding pharmacies.