Dear Functional Medicine Discussion Group Members:

Once again, we had an awesome Functional Medicine Discussion Group meeting in January on Small **Intestinal Bacterial Overgrowth** as the cause of **Irritable Bowel Syndrome** with the brilliant **Dr. Mark Pimentel,** who very graciously spent several hours of his very valuable time with us. We thank **Metagenics,** once again, for sponsoring the food and the venue, and for having supported our group since we started. Thanks to all our members who participated in the meeting. Our next meeting will be **Thursday, March 30** at 6:30 at the Santa Monica Library at 601 Santa Monica Blvd. and **Dr. Melanie Gisler** will join us for a discussion on **Lyme Disease** and how to treat it. Please email me if you will be able to attend and place **Lyme RSVP** in the subject line. I will send out another email with some papers to read in a week or so. If you are not already a member, please join **our closed Facebook page, Functional Medicine Discussion Group of Santa Monica**. Also, please check out my new weekly podcast, **Rational Wellness**, on Itunes or Youtube: http://www.drweitz.com/2017/03/rational-wellness-episode-006-with-dr-arland-hill/ or https://youtu.be/r7SEHrdY_FQ

I introduced the topic, **Irritable Bowel Syndrome** (IBS), which occurs in up to 20% of the population in the US. IBS is a condition marked by abdominal pain, diarrhea, constipation, or both, gas, bloating, and/or urgency. IBS patients have a negative colonoscopy, unlike patients with Inflammatory Bowel Disease. **For many years, IBS was seen as a condition arising from psychological stress until Dr. Pimentel discovered that an overgrowth of bacteria from the colon into the small intestine was the causative agent in an overwhelming majority of cases of IBS (84%).** However, this has not been easily accepted by the medical profession and many MDs have still not fully accepted this way of understanding IBS. The Mayo Clinic web site describes IBS as a functional disorder whose cause is not understood and that it is a condition that can't be cured. They say that lab tests are only rarely needed and that treatment is only to control symptoms. As you may already know, on average, it takes 17 years for a new idea in medicine to be accepted into common practice.

I then introduced **Dr. Mark Pimentel**, the world's leading expert on Small Intestinal Bacterial Overgrowth and its link as the cause of IBS. Check out some of Dr. Pimentel's papers and his book, *A New IBS Solution: Bacteria—The Missing Link in Treating Irritable Bowel Syndrome*. Dr. Pimentel has achieved so much with his research, including discovering and proving that IBS often follows food poisoning (acute gastroenteritis) through an autoimmune mechanism—**Cytolethal Distending Toxin B** (CDTB) sets off an immune response and antibodies are produced both to this toxin and to **Vinculin** and this autoimmune reaction often damages the MMC, thus affecting intestinal motility. Dr. Pimentel also developed a blood test for CDTB and Vinculin antibodies, known as the **IBS Check test**. Dr. Pimentel is the Director of the GI Motility Clinic at Cedar Sinai.

I asked Dr. Pimentel how he got started with a clinical focus on IBS. Dr. Pimentel explained that when he started looking at Irritable Bowel Syndrome, everybody was just focused on putting band aids on the symptoms. If you have diarrhea, let's give Imodium. If you have constipation, let's give a laxative. And that is still the way it is treated in some clinics today. Dr. Pimentel joked that it's kind of like if you have cancer and your doctor gives you morphine so you don't feel it. Dr. Pimentel believes that you should try to find the cause (like Functional Doctors) and treat the cause and not just subject your patients to

medications that don't cure them and may have significant side effects. He was finding that his patients were not happy with the approach of just treating symptoms and they were complaining about the bloating, which nobody was doing anything about. And gas is the source of bloating and bacteria is the source of bloating. He said that he started to figure this out in 1996 and he published his first paper in 1999.

I asked Dr. Pimentel, how do you define SIBO? Dr. Pimentel said that Small Intestinal Bacterial Overgrowth is when you have too many bacteria where they are not supposed to be—in the small intestine. On the methane story, that is changing a little. When methanogens are too much, they are too much everywhere and we are calling that a bloom. They are overabundant, even in places where they do belong. He explained that methanogens are primitive species known as archea and when they get out of balance, you have to prune them back.

I asked how many in the audience treat SIBO and use the lactulose hydrogen/methane breath test and approximately a third of the audience raised their hand. I would have guessed that nearly all of us were.

I then mentioned that Dr. Pimentel in his papers tells the story of how food poisoning leads to SIBO through an autoimmune mechanism, so IBS is now essentially an autoimmune disease. Dr. Pimentel explained that it took a decade to figure out this story of how SIBO starts and how it causes IBS. He explained that he was trying to figure out how bacterial overgrowth could occur. He knew that if you have a blockage of your bowel, if you have previous surgery and you have scar tissue, you can get a kink or a bend in the bowel, then the bowel will not drain and you can get overgrowth from that. He explained that it is like when a river is stagnant and you get bacteria buildup. But these patients with IBS did not have actual stagnation, but they had a motility problem. And a group of researchers in England at the same time were saying that food poisoning was causing IBS and they too were dismissed. In the US, the prevailing view was that IBS was caused by stress, that it was psychological. Dr. Pimentel then explained that we understand the stress response as being something that has allowed us to survive as a species. When you are on the African savannah 10,000 years ago and you are being chased by a saber toothed tiger, the stress response shunts blood away from digestion, so that your muscles can contract and allows you to run away. But this would obviously be no time for a bowel movement. So, IBS does not fit with our understanding of the stress response.

Dr. Pimentel was trying to figure out how food poisoning could fit with his understanding of bacterial overgrowth, so he ordered a huge book on toxins in 2003. In the front of the book was a letter from the Department of Homeland Security letter saying that we see that you have bought a big book on toxins and you are Canadian, and this was around the time that there had been some anthrax attacks on politicians. He noticed that one toxin was common to the bacteria that cause food poisoning, which was the Cytolethal Distending Toxin B (CDTB), which he and his colleagues discovered produces an immune response. And CDTB resembles Vinculin, a protein that plays a role in smooth muscle movement and how nerves reach out to each other and grab onto each other. These CDTB antibodies cross react or attack the Vinculin in the intestine via molecular mimicry, thus damaging intestinal motility.

I asked Dr. Pimentel to explain what the Migrating Motor Complex (MMC) is. He said that if you wake up in the morning without eating and you hear that gurgling sound in your stomach. That gurgling sound is the cleansing action of the MMC that goes on for about 10 minutes every 90 minutes when you haven't eaten in several hours that cleans out the small intestine and reduces the likelihood that bacteria will take root.

Dr. Pimentel told us how when he started treating IBS/SIBO patients with antibiotics and how it would frequently recur in 3 or 6 months. Then they started studying this cleaning wave and they realized that it was not happening in a majority of IBS patients. He explained that they can make it happen with pro-kinetic drugs. Such drugs when given during the day around meals will increase the speed that the food will move through the digestive tract, while when given at night apart from meals will stimulate these cleansing waves. Even though the nerves are damaged and not properly connected, a prokinetic drug can ramp up the amount of electricity and stimulate these cleaning waves to delay the return of the overgrowth. He also said that he instructs patients being treated to not eat for 5 hours between meals without snacking to encourage these cleansing waves to occur.

Dr. Dahlstrom asked what is the upstream neurological control for this stimulation of the intestinal motility? Dr. Pimentel said that it is the vagus nerve that is responsible for turning the toggle switch to "fed" and then turning the "fed" switch off. You don't turn "fasting" on. It's just when fed is on, it's on, and when fed is off, you are in fasting. So the natural state of the gut is to have the cleaning wave function, except for when the switch is flipped to "fed".

I asked Dr. Pimentel if performing certain activities like the gag reflex, gargling, and coffee enemas, which are recommended by Dr. Kharrazian to stimulate the MMC via the vagal nerve and to promote GI motility in SIBO patients is a strategy that can be effective. Dr. Pimentel said that caffeine can stimulate GI motility, such as through coffee enemas, and this could be beneficial. Dr. Pimentel explained that when you stimulate the vagal nerve by chewing some food and spitting it out or chewing gum, which is similar to gargling, or anything that stimulates the oral cavity as if eating a meal, the toggle switch goes to fed. It doesn't go to not fed/cleaning. So this type of strategy will not accomplish what you need with SIBO, which is to stimulate these cleaning waves. Dr. Pimentel said that humans are built to not eat for long periods of time, to fast, and not to have chips and candies on the desk all day long like we do now. This is why going 5 hrs without eating between meals for SIBO patients is a good thing.

Somebody asked if intermittent fasting is helpful with SIBO? Dr. Pimentel said that they discovered that the **Elemental Diet** using a product called Vivanex, which was being promoted as something to take prior to colon surgery to reduce infections, was helpful in reducing bacterial overgrowth. They found that about 14 days of this elemental diet works the best.

I asked how you can make sure that a medication that can improve GI motility will stimulate the cleaning waves rather than posprandial motility? Dr. Pimentel said that as long as you give the medication at night when there is no food in the stomach, it will stimulate the MMC to make cleaning waves during the night. I asked isn't it the case that serotonin promotes gut motility? Dr. Pimentel said that Zelnorm was a serotonin receptor agonist that was approved as a prokinetic but then pulled from

the market in 2007. I asked couldn't we use 5-HTP at night to stimulate serotonin which might help with motility as well as with sleep? Dr. Pimentel said that it makes sense, but he hasn't studied it.

Somebody asked about using CBT oil. Dr. Pimentel said that there are cannabinoid receptors in the gut and they have effects on motility. This practitioner mentioned that CBT oil stimulates the vagal nerve. Dr. Pimentel explained that it tends to completely turn motility off, depending upon which cannabinoid receptor it grabs on to. CBT oil definitely helps with nausea, though.

Dr. Miles asked what about patients who might have yeast (SIFO) who would respond poorly to a simple carbohydrate diet? Dr. Pimentel said he has always been concerned that some patients with IBS could have overgrowth of fungus but that he does not think that it occurs in more than about 10% of the cases. He also said that Rifaximin works 70% of the time and it would not work if it were fungus. Dr. Pimentel also mentioned that his colleague, Dr. Satish Rao, is doing a lot of research on SIFO. Here is a link to a podcast interview with Dr. Rao conducted by Dr. Michael Ruscio: https://drruscio.com/sifo-small-intestinal-fungal-overgrowth/ Dr. Pimentel also mentioned that when he uses the elemental diet which includes simple sugar it tends to result in yeast on the tongue

I mentioned to Dr. Pimentel that I have heard him explain that when he treats a patient with SIBO he does not have them restrict their diet while they are being treated with antibiotics, since he wants the bacteria to be well fed so that they are easier to kill off. But Functional Medicine doctors like myself and Dr. Siebecker and many of the doctors in this room treat SIBO with natural anti-microbials along with a restricted carbohydrate diet like the low FODMAP diet and we get good results. So why do we get good results while starving the bacteria? Dr. Pimentel said that it depends on what you are doing as a treatment. Antibiotics work on the replicating bacteria and antibiotics can't penetrate if bacteria are in hibernation. The reason why you give antibiotics every 8 hrs is because you kill off the bacteria that are replicating and because you have killed off those bacteria, there is now more room and the ones who were hibernating start to replicate and then these can be killed off with the next dosage of antibiotics. But natural antimicrobials may not work by attacking the replicating cell walls of the bacteria, which could be why they can work in a low or restricted carb environment.

Dr. Pimentel also explained that Rifaximin, the antibiotic that he usually uses is 99.6% non-absorbed and that it does not adversely affect the bacteria in the colon. Dr. Pimentel also explained that he is developing a new breath test that will be able to measure hydrogen, methane, hydrogen sulfide, and carbon dioxide, which will be able to detect more bacterial and perhaps fungus as well. He also said that their group has scientifically validated the breath test offered by Commonwealth Labs. This doesn't mean that the breath test offered by Genova is not accurate, only that they have not validated it.

I remarked that some of the things that keep the small intestine relatively asceptic are pancreatic enzymes, hydrochloric acid, and bile and I asked Dr. Pimentel if he had looked into using these types of products. He admitted that each of these can work to kill bacteria, but he explained that if there are methanogens, they can use the HCL as a source of hydrogen, which they consume. Taking HCL will tend to increase methane, so if the patient is constipated, it is not a good idea to take Betaine HCL.

Dr. Pimentel mentioned that high methane gas is correlated with obesity and also high cholesterol levels.

Dr. Niles asked about syndromes that may mimic SIBO, such as C-Diff. Dr. Pimentel explained that C-Diff has CBTD toxin, so it can cause IBS. What about using probiotics for IBS? Dr. Pimentel mentioned that certain strains of bifido bacteria can trigger the MMCs. While some earlier studies showed some benefit for SIBO with taking probiotics, more recent studies have not shown any benefit in overgrowth. He thinks that probiotics got ahead of the science. In fact, the PLACIDE study in Lancet found that taking probiotics not only did not reduce diarrhea, but it caused increased bloating, though the patients in this study were suffering from antibiotic associated diarrhea while in the hospital rather than SIBO, they were elderly, and they were suffering with quite a number of other conditions. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)61218-0/fulltext

Dr. Pimentel also explained that in his lab, he is working on a way to treat IBS patients by ridding the body of the CDTB antibody and reversing the autoimmune disease. They have cured one patient so far by removing the antibody from the blood stream using plasmapheresis.

We discussed the idea of adding fiber back into the diet, such as with prebiotics, and there are no clear guidelines when this should be done. Staying on a low FODMAP diet cannot be healthy long term, since it rules out so many healthy foods, such as broccoli. Dr. Pimentel also noted that bacterial fermentation in the colon is a good thing and colonic distension stimulates GI motility. Somebody asked about fermented foods and Dr. Pimentel noted that they have been shown to increase the risk of stomach cancer.

Dr. Pimentel also mentioned that some of his colleagues are using Low Dose Naltroxen as a prokinetic. He also spoke about a timed release version of lovastatin that he is developing to use as a prokinetic. He explained that the aspergillus that produces the lovastatin did not make it to reduce cholesterol, but to help it compete in the swamp by reducing bacteria. Also, Lovastatin binds with the enzyme that produces methane.

Dr. Pimentel mentioned that he thinks that calling the condition Irritable Bowel Syndrome is bad because it is demeaning for patients to be labelled as “irritable” and to be told that they have an irritable syndrome. He said that it would be better to call it an autoimmune enteropathy.

Check out the video of this meeting on Youtube at https://youtu.be/ARaEnKQIPTo