

The IBS SIBO Autoimmune Connection

Irritable Bowel Syndrome (IBS) and Small Intestine Bacterial Overgrowth (SIBO)

Dr. Mark Pimentel, MD, is currently the head of the Pimentel Laboratory and executive director of the Medically Associated Science and Technology (MAST) Program at Cedars-Sinai. This program focuses on the development of drugs, diagnostic tests and devices related to conditions of the microbiome. The Pimentel Lab researches irritable bowel syndrome (IBS), one of the most prevalent gastrointestinal (GI) conditions effecting about 10 percent of the population worldwide. Professor of Medicine, Geffen School of Medicine and Associate Professor at Cedars-Sinai Medical Center, principal investigator or co-investigator for numerous basic science, transitional, and clinical studies in such areas as IBS, and the relationship between gut flora composition and human disease.

Dr. Pimentel: I think the whole microbiome space has been incredible. If you look at the last 10 years since the Human Microbiome Project was published, we are now starting to understand how the microbiome links to human disease. The chemicals they produce can manipulate us, influence us, help us. So, some things are good; some things are bad. We don't have all the answers clearly.

But I think what's exciting to me is that we realized that the microbiome is important. Done! The stool microbiome is leading to some dead-ends. And I think that's where we're having trouble because there's too much in there that may not be related to disease.

I think that what we're now seeing is the small bowel microbiome may be where all the action is or maybe where a lot of the action is. And that's what we're really excited about because we're now mapping the entire small intestine and finding smoking guns potentially. So that's very exciting. We're unveiling the first real deep sequencing of the small bowel. So you could say we're ahead of the game. But it's not a game. It's not a race. It's whoever get something to help humans and their disease. It's great! I just love where the field is going now.

SLIDE: How do SIBO and IBS overlap and why is it important to get a diagnosis?

Dr. Pimentel:

So, this is always a question that people ask. Is it SIBO or is it IBS? And the answer is it's both.

So, let me go back and explain peptic ulcer disease. Back in the 1980s, ulcers of the stomach were all the problem. Everybody was having ulcers. They were bleeding. And we didn't know what was causing it.

And so, a gentleman by the name of Dr. Barry Marshall discovered *H. pylori*. And *H. pylori* was suddenly the cause of ulcers.

Now, *H. pylori* only caused 70% of ulcers. It didn't cause all of ulcers. It only caused 70%. But of course, it's a big discovery. The irony is that the disease, peptic ulcer disease, didn't change. The name was still peptic ulcer disease. It didn't change to *H. pylori disease* because there were other causes of peptic ulcers.

The same thing here. That's what I'm getting at, is that IBS is an umbrella. And if we can explain 70% of IBS based on a microbiome shift, it's still IBS, but SIBO or bacterial overgrowth is the cause of the symptom in 70% of patients—which is, again, similar to what we saw in *H. pylori*.

SLIDE: What is the migrating motor complex?

Dr. Pimentel:

Yeah. So the migrating motor complex is one of the first things to go when you have neuropathy. A lot of diabetic patients, when they start to get gut neuropathy, you can sacrifice the migrating motor complex without sacrificing too much in terms of nutrition. But because the other things need to move, more importantly.

But when it comes to the microbiome, the migrating motor complex is critical. It keeps the gut clean.

So again, as I've said in many of my educational program, the migrating motor complex can be looked at like a dishwasher. So you've eaten dinner, you've eaten lunch, you've put everything in the dishwasher. And then, at night time, you turn the dishwasher on. And overnight, it washes the dishes. Then you take the plate out and you eat your breakfast. You don't take the plate out dirty. You take it out after it's been cleaned.

And so, another term for this migrating motor complex is the *cleaning wave* or the *housekeeper wave* as scientists used to call it. It cleans out the debris—so the lettuce, the stuff that humans can't digest that's just lying in the small bowel. It needs to be stripped out, so the small bowel is beautiful, clean and ready for food.

But if it doesn't happen, then of course, the material, the junk stays in there longer. And bacteria love that, so they're going to start growing. And once they figure out it's a better place to be because they're getting fresh food, not the junk, the trash that goes into the colon, they love it there, they do everything they can to stay.

And that's sort of the way we think bacterial overgrowth might form.

SLIDE: How do you know if your migrating motor complex is functioning properly?

Dr. Pimentel: It's tricky. There is a way to find out. It's a very invasive test. You have to put a tube in the nose, pass it away all the way down into the small intestine, and sit there for six hours with no food looking for this migrating motor complex which occurs once every 90 minutes.

So, if you imagine, if it only happens once every 90 minutes, you have to wait five hours to say it's not there because it doesn't happen all that often to really know that it's abnormal.

[05:11]

Dr. Pimentel: So it's a long test and invasive which is why we've been looking for other biome markers because we think there's something that's making the migrating motor complex not work.

SLIDE: Can you tell us what the IBS-SMART Test is and how a positive result on that test could impact the migrating motor complex?

Dr. Pimentel: So, the term IBS-SMART refers to a commercial product that is really representing the second generation blood testing of anti-CdtB and anti-vinculin antibodies. We now believe that food poisoning is the starting event that leads to a series of events leading to bacterial build-up in that subset of IBS that is SIBO.

And so, the blood test looks for a marker of food poisoning which is the anti-CdtB toxin, and then an auto-antibody that forms in a lot of these patients that attacks the nerves of the gut.

And in the studies that we've already published and done, we've shown that the antibodies actually bind to that one particular cell... among others. But in particular, it binds to the cell that we think is responsible for the cleaning wave.

And so, we think these antibodies is impairing the nerves of the gut and impairing the cleaning wave. And that's the hypothesis.

SLIDE: Let's talk about breath testing for SIBO. What is breath testing for and why is it important?

Dr. Pimentel: So recently, we were able to validate breath testing completely. I mean there's been controversy about breath testing. People say, "Well, it's not as accurate as culture" or "We don't know if it means that..."

Let me start from the beginning.

When you do a breath test, you drink a sugar. And the sugar we prefer to use is lactulose. It's a non-absorbed sugar. So it stays in the gut and gets all the way to the colon. So you can get a good flavor of what's going on in the entire gut.

When the sugar sees bacteria, they ferment it. When they ferment it, they produce gases. And we look for the gases that humans don't produce. And the ones we've been looking for are hydrogen and methane. Until recently, just those two.

So, when we see those rise early, meaning within 90 minutes, we know that it's likely that those gases came from the small intestine. The argument has been: "Well, but what if things go too fast to the colon? Then all the sugar gets dumped in the colon. And then, maybe you're going to get hydrogen from there. Maybe that makes the test inaccurate."

But recently, we've shown now that using deep sequencing of the small bowel, we show that SIBO can be proven by deep sequencing—greater than 1000 bacteria per milliliter in the gut is SIBO—and that both of those

correlate directly with 90-minute breath tests, meaning the breath test is valid. Culture greater than 10^3 , not 10^5 is the correct number. And we can identify all of these with sequencing.

And the most important thing, they all interdigitate with symptoms. So, we can correlate with diarrhea, urgency and bloating with these markers.

So, the point is, for the first time, we've internally validated the breath test. So breath tests are valid. And they predict response to antibiotics. That's another paper that we presented at a previous meeting.

SLIDE: What is hydrogen sulfide?

Dr. Pimentel: Hydrogen sulfide is the missing gas. So we haven't been able to measure hydrogen sulfide until recently.

So, look at it like this. Hydrogen is the fuel. So the main bugs that produce gas, the main gas is hydrogen. But hydrogen is also a fuel for other bugs. For example, methane, we've known for a long time, so we have a better understanding of it. Methanogens or methane-producing organisms take the hydrogen and make methane.

So then your hydrogen goes down, but your methane goes up.

And there are patients where they have no hydrogen, no methane. It literally looks like a flat line. And we couldn't understand it. But we did know there was a third gas that we haven't measured before which was hydrogen sulfide.

The bugs that make hydrogen sulfide take hydrogen, make hydrogen sulfide with it, and we now know that hydrogen sulfide means diarrhea. And we've known for a long time that methane makes constipation.

So, without that third gas, we're missing a whole element of SIBO or understanding the breath test... until now. And so that's coming very soon.

SLIDE: Why is it so hard to distinguish between IBS and SIBO? - from Jackie in Sydney

Dr. Pimentel:

So, it's well-known in medicine that from the time a patient comes to the clinic to the time a diagnosis is made, it's the best you can do to save cost. So the longer that relationship goes before you have a diagnosis, the more burden it is on the patient—meaning test after test after test, days off work to do this scan or that ultrasound or this colonoscopy.

[10:12]

Dr. Pimentel:

But it's also a burden to the healthcare system with the cost of these invasive tests.

And the third burden—because there's lots of burdens here—the third burden is the burden to the patient financially because they have to do the co-pays. And the final burden is really not a burden, but a burn. And the burn is that, at the end of the day, all those tests are negative!

So, they paid all this money, taken days off work to do it, and all they find out at the end of the day is they don't have anything, and therefore it's IBS or SIBO or what-not.

So, it's quite a frustrating series of events that these patients have to go through. It's been sort of tragic—hence, the reason we're trying to get to the SIBO diagnosis or develop blood tests that can identify the patient right now because the sooner you get to a diagnosis, the more money patients save, the less the burn, the burden and all of that.

SLIDE: How long does it really take for somebody to get an IBS diagnosis?

Dr. Pimentel:

So, the average in the United States—there's been studies published on this—it takes about 6.6 years.

You say, “Well, that doesn't make sense. You saw the doctor. The doctor makes the diagnosis of IBS. They've done the colonoscopy. All of that can be done maybe within two or three months, all that testing. So how can you say six years?”

Well, the reality is you go to a doctor, the doctor says, “Let's do a colonoscopy, let's do a scan, let's do some blood work, some stool tests.” Fifteen to twenty thousand dollars of testing later, it's all negative. You say to the doctor, “So what do you think, doc?” The doc says, “I think it's

IBS.” And you say, “Well, how do you know?” And the doctor says, “Well, all the tests are negative, and I’m a doctor.”

And the patient walks away, gets some treatment, doesn’t work, loses confidence: “Maybe this doctor doesn’t know the answer. Maybe I’ll go to another doctor.”

And then, you start over, and you start doing other things.

And then, eventually, you get frustrated. You leave the healthcare system for a while because you say, “Nobody is giving me an answer that makes me satisfied” and on and on and on.

So, the six years really represents the time where the patient sort of just throws their hands up and say, “Well, everybody says it’s IBS, I guess it’s IBS.” And that’s not a way to make a diagnosis. At least, traditionally, medicine, you will want to be definitive.

SLIDE: When it comes to IBS and women, it seems like—do more women have IBS? - from Hannah in California

Dr. Pimentel: That’s a complicated answer because the answer globally is yes. So if you took all IBS across the entire spectrum, more women have IBS than men by about a factor of 1.4. So it’s not that much different.

But if you look in the spectrum, if you look at the extreme constipation, so the patients who are constipation all the time, it’s actually 8:1 women-to-men. So men don’t have a lot of the constipation phenotype. We don’t understand why.

But if you go to the far right end of the spectrum which is the diarrhea and almost no constipation, it’s actually almost 2:1 men-to-women.

So, it depends on where you look on the IBS spectrum as to which gender is dominating the other in terms of prevalence of the disease.

SLIDE: What about the idea that gut issues like IBS are “all in your head?” - from John in Arizona

Dr. Pimentel:

It's tricky to answer this question because, respectfully, we have to understand that people have tragic life events, people have experienced abuse of various kinds, people suffer from anxiety, depression, addiction. There's many different psychological sufferings that go on. And as physicians, it's our obligation, our job, to identify all these aspects that influence a patient's care. So, those things are true.

What's not true or has been shown to not be the case is that the notion that IBS was caused by that is apparently not very clearly true.

So, we should address all those problems. We should enforce or at least encourage psychological help for patients who suffer from these conditions. But that is not going to make IBS better. And it's not the cause of IBS.

And let me tell you why I know this now. It's because the US military has tracked the deployments to various warzones. And they come back with IBS, these troupes. After one deployment, there's a very high rate of irritable bowel syndrome. And they looked at whether you discharge your weapon, were you were in active combat or sitting at basecamp on a computer, whether you witnessed or observed psychological traumatic events—human death, human suffering. And none of those predicted the development of IBS. The main predictor of the development of IBS was did you get food poisoning when you were deployed.

[15:08]

Dr. Pimentel:

So, they can be cofactors, but they are not primarily or principally the trigger.

I would say, as we move forward, we now know for at least the last couple of years, that food poisoning is a trigger for IBS—which I've already stated. But I want to state it even more clearly. I think now, in IBS, we know more about the trigger event than we do for Crohn's or ulcerative colitis which is a major thing for this disease because Crohn's and ulcerative colitis has received almost all of the funding from federally-funded grants. IBS generally doesn't get much funding.

So it's a huge leap for this field, a huge leap for 45 million Americans, one billion people worldwide who have IBS.

SLIDE: Tell us about food spacing, meal spacing and the migrating motor complex. - from Sarah in Ohio

Dr. Pimentel:

So diets are really important for IBS. And they have been shown to be important clinically and scientifically. There's the low FODMAP diet, which probably many of you have heard of; there's our low fermentation diet which is often used; and many others.

But they talk about what you eat. They don't talk about *how* you eat.

Now, think about the migrating motor complex for a minute. We've really discussed this a little, the cleaning wave of the gut.

So, let me start again and say it in a different way.

The intestine of the gut has two computer programs like a switch. You're either in eating mode or you're in cleaning mode. So when you eat (or the moment you put food in your mouth really), you switch to eating mode. And that means you've switched off the cleaning mode.

So, let's say five minutes from now, you were supposed to have a cleaning wave, but you just decided to have two bites of a bagel. Done! That cleaning wave isn't coming because you're now in eating mode and those mechanisms shut down completely.

So, if you put a bite of a bagel in your mouth every half hour all day, you'll never get a cleaning wave because you're always shutting off the cleaning waves. You're keeping yourself in fed state or eating mode.

It's only when you leave spaces of no calories, no food between meals that you allow the cleaning waves to happen.

Now, in people who are perfectly normal who don't have IBS, you get plenty of cleaning waves at night—maybe four or five because you're sleeping, and you're not eating. And maybe that's good enough for people

who don't have disturbed cleaning waves. And maybe you can gnash or nibble all day, and it won't really impact you as much.

But in people who have a dysfunction of the cleaning wave, you want every cleaning wave you get because that will help you keep the remission or keep the disease in check.

So, we recommend spacing meals, meaning eat breakfast, then four or five hours, zero calories. You eat lunch, and four or five hours, zero calories. Let whatever cleaning waves happen in you happen naturally and that you're not blocking them from happening.

We sit at our desks and offices, and we've got candy there. We've got bagels in the break room. We've got so much snack stuff around us that we're always tempted. And that just disturbs the cleaning wave.

SLIDE: What do you think about intermittent fasting? - from Barb in New Jersey

Dr. Pimentel:

Yeah, intermittent fasting is taking off. The challenge—and I'm going to say this in a crass way, and then I'm going to sort of jump into reality. If you never eat, your bacterial overgrowth will go away. But that's not life. You have to get food and nutrition. So the more extreme your diet, the more likely the bacteria are to go down. But the more extreme your diet, the more likely you are to create disturbances in the microbiota in your nutrition.

So, we now know that the low FODMAP diet which has been proven to be beneficial in IBS, and even reduce hydrogen on breath testing, it's not nutritionally balanced in the long run. And even the people, the proponents and the scientists from Australia who work on the low FODMAP diet, they're very careful to encourage people to liberate the diet after three months so you're not all fully restricted on it.

It also reduces microbial diversity. That's been shown recently. If you reduce microbial diversity, that's believed to be associated with risks for diseases.

So, we don't know what we don't know. That's a term I use quite often. And we don't know what the long-term effects of restricting calories in that way.

But I would say that intermittent fasting has some benefit potentially. So if you can fast for 12 hours a couple of times a week, that may allow your cleaning waves to occur more often and may be beneficial.

It hasn't been studied. Hypothetically, it sounds like a good idea and possibly could work. But again, it hasn't been studied.

SLIDE: How can we use the Elemental Diet? - from Greg in New York

Dr. Pimentel: So, the elemental diet is very good at getting rid of bacterial overgrowth. And how the elemental diet works is that you take food fully balanced. Most of the diets that are used for this are 100% RDA (recommended daily allowance) of vitamins, minerals and all the things that humans need. But they're in their simplest form so the human can absorb and digest it immediately.

[20:22]

Dr. Pimentel: And so, it's sort of like you're getting all the calories, and the bacteria is not getting anything.

Now, when I say that, patients are like, "I'm getting all the calories. That means I'm going to gain weight." That's not what I'm saying. You're getting all the calories you've just taken—which is your daily requirement for nutrition and health. You're not taking more calories than you normally would. It's just you're getting them all instead of sharing with the bacteria.

And so, by restricting calories to the bacteria, the bacteria basically die of starvation. And like anything else, it takes time to starve to death. And the number that seems to be ideal is 14 days.

SLIDE: What's your take on eating fiber if you have SIBO? What about eating fiber to avoid colon cancer? - from Jane in Florida

Dr. Pimentel: So, the answer to that is tricky because the fiber people will be frustrated with something I say. But it puzzles me that we've eaten fiber in excessive

quantities. I mean we're putting it in cereal as additives now to say, "Okay, more fiber. It's great for the market. It's great for helping prevent colon cancer" or whatever the thought is.

But now, we're at a point where we're screening for colon cancer not at age 50 anymore, we're proposing 45 because we're seeing colon cancer creeping into lower age groups. And so now, the guideline is, 45 years old, you need to start getting colon cancer screening.

So, all these fiber for 20 years, what have we got? We're screening at a lower age.

I'm not sure. I mean, to me, that raises a debate about what we're doing with fiber and everything else to be honest.

SLIDE: If somebody is on one of these diets and they "cheat," does that set back your SIBO condition? - from Carol in New Hampshire

Dr. Pimentel:

So, if you're on an elemental diet and you cheat, that's a problem. I have patients who say to me, "Well, but coffee is neutral. It doesn't have any calories in it." And I said: "Look, I have 3000+ patients with the elemental diet. I have not studied 3000+ patients with elemental diet with coffee added." So what I would hate for a patient to do is go through the elemental diet for two weeks and drink coffee every morning and it didn't work. And then we're scratching our heads wondering whether that coffee screwed it up.

So, with these diets, either you're in or you're not. Can you imagine being on a liquid diet for two weeks, and because you just couldn't do it, it didn't work? It's miserable for two weeks. So you've got to either commit or not.

And I know that sounds very radical or very cold, but I'd rather you not suffer for two weeks if you can't make it. And it's expensive as well, so that's harsh.

SLIDE: People have lots and lots of questions about digestive enzymes—can you take too many, when should you take them? And what's the difference between a digestive enzyme and a pancreatic enzyme, for example?

Dr. Pimentel: So, it's sort of the same, but sort of not. So there are natural enzyme products that are able to digest certain products in food.

Look, for example, lactase is a digestive enzyme. It digests lactose sugar for milk. And then, there's Bean-o which is a commercial blend. It digests some of the carbohydrates that are in beans. So those are all digestive "enzymes" that help break down food.

And then, there's papaya enzymes. And then there's pancreatic enzymes that you get as a prescription. Pancreatic enzymes basically are meant to represent the entire complement of enzymes produced by your pancreas to help digest food. The pancreatic enzymes, the full brand, the full amount, can really digest food a little bit better. But it's not going to digest it to an elemental diet level.

So, you can't say, "Well, instead of the elemental diet, I'll just take pancreatic enzymes." It's not going to get rid of overgrowth. It might make you 20% better or 30% better, but it's not like an elemental diet unfortunately.

SLIDE: Can enzymes or HCL help with symptoms?

Dr. Pimentel: So when I give enzymes, generally, I give prescription. And we do see in patients where nothing else is working some benefit. There's no doubt it works a little bit.

Dr. Pimentel: So, HCl is complicated because—well, I'll tell you a couple of things about HCl.

Number one, it's believed that proton pump inhibitors cause bacterial overgrowth, but we're showing that that's not true in deep sequencing. Yes, there's a couple of changes in the microbiome that occur. But in terms of triggering overgrowth, no acid, not true. Sorry, it's not causing overgrowth, at least not by sequencing, with the most modern technology. And we've shown in breath testing that it doesn't make the breath test go up either.

[25:10]

Dr. Pimentel:

So, I'm not sure HCl does a lot. What HCl is meant to do or believed to do is to kill bacteria as it's passing through the stomach. And maybe that's more important for pathogens or food poisoning-type bugs, and not really all that important for the colonizers of the small bowel because once you have your warriors, the warriors that you like, in your small bowel, it's hard for others to sort of invade and start taking over.

So, I'm not sure HCl is all that great.

But it's not wrong. It may not be bad for you unless you're methane. So we do see that when you reduce—

Methane can use hydrogen as gas or it can use hydrogen as acid. And what we see is that people who take a proton pump inhibitor have less methane. So you say, “Well, can we treat methane with proton pump inhibitors?” And the answer is we haven't done that study, but what we have seen is that if you're on a proton pump inhibitor, less people are methane-positive.

So theoretically, if you're on HCl, you could fuel methane production which could fuel the constipation side of IBS.

SLIDE: What treatments work for methane-dominant SIBO? - from Nancy in California

Dr. Pimentel:

So methane SIBO is different. And the terminology of SIBO may not be exactly a fit for methane because part of the methane bugs are in the colon, part of them are in the small bowel. So, the term “small intestinal bacterial overgrowth” may not be a perfect fit for methane.

But let's look at it this way.

When the methane overgrow, we're sort of calling it a *bloom* or a *blossom* of methane. And when there's too much of them—you should be here—when you're here, it causes constipation.

The way we treat it is because methane producers are not bacteria, we haven't really created antibiotics for archaea or these ancient bacteria that are the methanogens, but some of the antibiotics do work. But what we

found is that a combination of antibiotics such as rifaximin + neomycin or rifaximin + metronidazole appear to work.

We have one double blind study that was published comparing neomycin alone with placebo to neomycin and rifaximin. And the two antibiotics together were far superior.

Here's where the problem comes in. The methane comes back quite quickly.

And so, even with those courses, even with that good benefit that we see, it's short-lived. So we've been working really hard to develop—and we're in the middle of a clinical trial that we think will finish some time—

If you block methane production with a statin, particularly lovastatin in a form that's delivered specifically to the bugs and doesn't get absorbed, we can stop methane production.

Now, the question is, if we stop methane production, does it mean you have to be on this forever? The answer is we don't know. We have to do the trial. But we have seen some patients where when they get rid of the methane for long enough, a new world order occurs, and the methane doesn't want to come back so easily.

So, I think let's put the jury on hold for that until we get the trial done, so we know exactly if what I'm saying is true or not. But it's very promising, at least hypothetically.

SLIDE: Can Rifaximin hurt the microbiome? What about long term use or periodic use over time? - from Matt in Alberta

Dr. Pimentel:

We've studied that. I mean, the whole target 3 trial—which the FDA required a microbiome element of study—found that the microbiome, 98% of the bugs that were there at the beginning, aren't there in the end... in stool. We don't know what's going on in the small bowel.

In one small animal study, we do see that the microbiome of the small bowel changes which is exactly what we want in SIBO; but not the colon bacteria which is exactly what we want. We don't want to hurt the colon

bacteria, but we do want to reduce the bacteria where they don't belong. And so we're optimistic that it's not really damaging the microbiome.

Dr. Pimentel:

So, again, it points back to studies that we've done. We did a study where we looked at one treatment plus up to five re-treatments. And it looks like once rifaximin works once in a patient, it almost always works in the same way.

Yes, maybe treatment three, not as effective. But then you do it again, treatment 4, and all of a sudden, it's effective again.

It doesn't make sense. Maybe the diet you were on when you were taking the one treatment where it didn't work. Maybe there was some kind of conflict with other things you were doing. But in general, if it works, it will work again and again. That's what we showed in that trial.

But the question is does it affect the microbiome long-term, long-term, long-term. The drug has been available for 30+ years globally. And despite all that information and all the information about bacterial resistance, we don't see it.

[30:07]

Dr. Pimentel:

In the target 3 trial, the FDA also required bacterial resistance panels be done. And so thousands of cultures from various parts of the body were done to be sure that rifaximin wasn't creating superbugs on the body, in the colon, et cetera. And it was basically clean.

Any resistance that did develop went right away after the drug was stopped.

And most particularly, which is important for women with vaginal yeast infections, yeast did not accumulate. There was no more growing yeast—meaning after three courses of rifaximin, you don't have more yeasts in your stool—which is a good thing.

SLIDE: There's also a lot of talk about SIFO, small intestine fungal overgrowth, speaking of yeast. How do you see that as being interrelated to SIBO? Are they on their own lanes? They seem to have the same symptoms.

Dr. Pimentel: Yeah. I mean, fungus produces gases. They ferment as well. So it's hard to know how they relate to each other.

What we do know is rifaximin does not generally kill fungus. So if you respond to rifaximin, it doesn't make sense that it's SIFO. Rifaximin generally doesn't cultivate the fungus, meaning because you're reducing bacteria, it doesn't mean that fungus is overgrowing.

But the question is if you've eliminated SIBO, can some of the people in the remaining group be SIFO? And we don't have an answer to that.

Although Dr. Satish Rao is studying it. And he does have some data on that. You have to talk to him to get the exact quotes on what he's finding in his population. What I can tell you is that in our deep sequencing study, we have all the aspirates. And one of the targets we intend to go after eventually is to look at fungal elements and to see if they're related to disease as well.

SLIDE: If somebody has not responded to SIBO treatment, has similar symptoms to SIBO, they may very well have SIFO?

Dr. Pimentel: Again, the answer is a little complicated to that. Everything is always complicated... because we don't have hydrogen sulfide yet.

So, one element that's missing is the hydrogen sulfide piece. The other element that might be missing is the SIFO piece.

Now, hopefully, the H²S problem is solved. The SIFO problem, there's no good indirect test that you could just do in an office. You'd have to scope and gather the material from the small bowel and test it that way. And that's how Dr. Rao is doing it I think.

SLIDE: Any tips for getting that rifaximin prescription approved by insurance? - from Tina

Dr. Pimentel: Well, that's tricky although I think—so what we're seeing in study again that we published, we're seeing a 30%+ reduction in the number of patients being sent to offices like me who have diarrhea-IBS. Don't get it in your mind that I'm seeing less patients because I'll tell you what's happening.

So, diarrhea IBS Is going down in terms of coming to the tertiary care medical center. That, in and of itself, means we're saving money in IBS for the first time. And patients are getting treated at lower levels of care appropriately, and potentially, their disease is going away temporarily. So that's great.

On the constipation side on the other hand, we're seeing a 30% to 40% increase. And that's why my clinics are not changing, and there are still a lot of patients there.

But hopefully, all of that means that insurance companies get it. If you're treating at lower levels of care, and you don't need to come all the way to see me in our offices and Dr. Che in Michigan and Dr. Rao in Georgia, that you're saving money because you're not getting all those testings and all that expensive stuff that we do at tertiary care medical centers. And the insurance companies will say, "Okay. Well, this makes sense because it's saving money in the long run."

SLIDE: Do you recommend probiotics for SIBO? - from Mary Ann in Vancouver

Dr. Pimentel:

So, the challenge with probiotics is that if you smooch all the studies together, you can say, "Okay, look, there's an effect with probiotics." And that is true. There are meta-analyses of probiotics in IBS, for example. There's even one meta-analyses in SIBO.

The problem is you're smooching studies of 20 patients, 40 patients... small trials. And in general, small trials that are positive get accepted at journals. Small trials that are negative, people say, "Well, it's a small trial. That's why it didn't show a result."

So, you have to be careful with how you assemble trials. There's a lot of what we call *publication bias for positive trials*. Journals don't want to publish trials that are negative as much. And so that skews the number of trials that are out there that are negative.

[35:01]

Dr. Pimentel:

Either way, my point is when you add more bacteria, you're adding it when you already have too much bacteria. So are you simply adding more gas-producing organisms or are you making a benefit? And the jury is out!

I personally think there is a probiotic out there, there will be a probiotic out there that, when studied carefully and correctly, might be beneficial. But what we do know is that fecal transplant, and we've even looked at some of these data in systematic reviews, fecal transplant, five trials, and two of the trials show placebo works better than fecal transplant. That tells you that it's not about fecal transplant. It's not that placebo is better than fecal transplant. It's that, potentially, fecal transplant makes people worse.

So, be careful! And I advise my patients no fecal transplants for IBS or SIBO right now because we really don't know.

SLIDE: What are prokinetics and why are they useful?

Dr. Pimentel:

So, if a patient responds to treatment for SIBO, and it's gone for a year, I don't need to do anything. You can do diet. We usually recommend the low fermentation diet that we've adopted.

Again, the low fermentation diet is more than just what food it is, but how to eat timing-wise.

But if they don't relapse for a year, I don't want people on anything else. Just go about your business and live your life!

Obviously, we counsel them to stay away from any risky behaviors, food poisoning. I don't say, "Don't eat off food trucks." But in California, if there's a C on the food truck, maybe don't choose that one. And be careful with travel so that you don't get food poisoning.

But if your SIBO relapses, which unfortunately is probably about 70% of SIBO (so it's the bulk), then we have to do something. And generally, we start with erythromycin because it's cheap.

Now erythromycin by name is an antibiotic; but by dose, it can either be an antibiotic or a prokinetic. So, at a high dose, 2000 mg. a day, it's an antibiotic. But at very low dose, 15 mg., it's prokinetic.

And so, generally, we use it at nighttime to trigger cleaning waves. And it's been well-known—we do this with the manometry test, six hours of manometry. During the test, we get a shot in the arm in the IV of 15 mg. of erythromycin. Five minutes later, cleaning wave. So erythromycin instantly triggers cleaning waves.

And its bioavailability is exactly the same by mouth as it is by IV. So you don't need to take an IV to get that boost. And it works quite well.

Now, it doesn't last long. So we do have other prokinetics that are more powerful. And we're excited that a drug, Prucalopride, was recently approved by the FDA which also has a potent effect on cleaning waves and other motility events of the gut.

SLIDE: Do you have to take a prokinetic every time you want a cleaning wave? - from Thomas

Dr. Pimentel: No, I mean it will last for a few hours. But ideally, if it could last for eight to ten throughout the entire night, you get a whole bunch of cleaning waves, that will be great.

I will say that, when you get a lot of cleaning waves, and you haven't had them for a while, you could feel them. And I don't mean cramping. I just mean the gurgling.

This is what I tell my patients. If you hear gurgling for 10 minutes, and you're embarrassed, be very happy. That's the cleaning wave coming through.

So people, when they haven't eaten breakfast, they come down for a meeting, and their stomach is making that sound, and they're embarrassed, that is what you want. You want those. Those are your cleaning waves. And count blessings. Don't be embarrassed.

SLIDE: How are fertility and SIBO related? - from Katie in New Mexico

Dr. Pimentel: We don't think SIBO causes infertility... at least there's no data as yet. There's really no tips for getting pregnant; I mean besides the obvious ones. But if you're having trouble with fertility, you need to see a fertility specialist because they have a lot of tricks and answers on what could be

happening and how things could be challenging for that individual patient. I think that pretty much...

We are preparing a review article on this topic to try to review the literature because there's really not a lot there. And so you could stay tuned for more information on that.

SLIDE: How are diabetes and SIBO related? - from Karen in Texas

Dr. Pimentel: I think there's a growing list of what SIBO can cause. So when we talk principally about IBS and 60% to 70% of IBS is SIBO, there's also a whole bunch of SIBO that's not IBS-related.

[40:09]

Dr. Pimentel: So, if you have an obstruction of your bowel or an adhesion, that can cause SIBO. Diabetes, a chronic diabetic, gets impairment from neuropathy, and that can cause SIBO. Scleroderma which is a really tragic disease, an autoimmune disease that impairs muscular function of the gut, that causes SIBO. And EDS, Ehlers-Danlos... there's many on the list that can cause SIBO.

The question is cause-and-effect. So if you have an adhesion, the SIBO didn't cause the adhesion, the adhesion caused the SIBO. If you have other diseases like, for example, rosacea, there's some association that when the SIBO is there, it's triggering some immune response that's creating rosacea. It's incompletely understood how that works. But there are physicians who treat SIBO on the basis of making rosacea better. And dermatologists are doing this routinely.

So, what I say is I'd like to know what's going on before I get too down a particular channel. If you think of the thousands of bugs in the gut, they can produce a lot of what you can produce. And they can produce inflammation. And they can produce chemicals that can make you do things you're not supposed to do or don't want to do. And so, we're starting to unfold. And when we do, then we'll be able to more clearly associate bug or pattern of bugs with disease and tackle it in that way.

And to be honest, that may be where the probiotics start to fit in. If we can actually see one bug missing or one bug too many, then you can either

take a probiotic to replace or some kind of laser-focused antibiotic, if you want to call it, something to reduce the one that's too high without touching anything else. I think that's the future.



“I Know What It's Like To Live With SIBO And Gut Issues. And exactly how confusing, overwhelming, & painful it can be. Sometimes living with the symptoms feels easier than trying to get help. I don't want you to suffer anymore. SIBO SOS™ has the tools you need to make getting a healthy gut simple.”

~ Shivan - SIBO Patient & Founder of SIBO SOS®

My name is Shivan Sarna, and I've suffered just like you. And while I could have let my pain rule my life... I decided instead to find its root causes - so I in turn could help others. It's been a harrowing journey. I've seen it all and done it all - from acupuncture and Ayurveda, to colonoscopies and emergency room trips. I've always been 100% committed to revealing the truth about what really works in addressing our gut issues and what doesn't... the latest research and innovations... and who are the “best of the best” when it comes to gastroenterologists, naturopaths, functional medicine practitioners, scientists, nutritionists and more. As a TV personality for the last 20+ years, I gather all of this information and make it easier for patients and practitioners to understand.

And remember, there is always hope in healing.

XOXO,
Shivan

36 VIDEO LESSONS • RECIPES & COOKING GUIDES • Q&A VAULT • HANDOUTS & TRANSCRIPTS

SIBO
Recovery Roadmap™

YOUR START-TO-FINISH
HEALING PLAN. [Join the course >>](#)