

**Shivan Sarna:** Hi, I'm Shivan Sarna, founder of <u>SIBO SOS®</u>. What a pleasure to have you all here with our very special guest, Dr. Mark Pimentel. He's currently the head of Pimentel Labs and executive director of the Medically Associated Science & Technology (MAST) Program at Cedar–Sinai. This program focuses on the development of drugs, diagnostic tests, and devices related to the conditions of the microbiome.

He is in the process of what I think and I like to say "finding the cure for SIBO." The lab, Pimentel Lab researches irritable bowel syndrome, one of the most prevalent GI conditions affecting about 10% of the population worldwide and about 10% to 15% of the population in the US.

In the past, there was no definitive test to diagnose IBS. And for the first time now, there is called <u>ibs-smart</u>. There are also three different types of gases that make you "have SIBO" (small intestine bacterial overgrowth). And he has also created a test for that called <u>trio-smart</u>.

And with that, I'm going to hand things over to him and have him explain to us all of these so we can figure out what is going on with our gut.

Hi! Thank you for being here again. I'm so thrilled.

**Dr. Mark Pimentel:** Thank you for having me. It's a great pleasure to see you. And congratulations on the book again. That's perfect!

So, what I plan to do today is just to take you through some slides. But really, it's not about the slides. It's about how the slides sort of guide the conversation or at least the education about SIBO. And so I'll try and walk you through these slides carefully.

So, shall I share my screen?

**Shivan Sarna:** Please do, yup! I'm just checking to make sure that all of our streams are working. Yup! And they are. Okay, great!

And by the way if someone is listening to this on the podcast versus seeing it in the Facebook Live or the Zoom session, we'll give you a link so you can actually see the slides as well.

**Dr. Mark Pimentel:** Well, here they are. So, I think you can probably understand just from my conversation part of this... the slides are a very good guide for those who are able to see them live. But I'm going to talk about irritable bowel syndrome and the microbiome because, really, things have dramatically shifted in 2020. We now know more about the microbiome and IBS. And there's more and more evidence that the microbiome is important in IBS. And I'll share some of those new things with you.

One thing I like to start with is... with IBS, you are *irritable*. So the terminology we use for IBS, that you're irritable and you're a bowel and you're a syndrome are really sort of derogatory terms. They're not really embracing of the patient experience. And the fact that you're called a "syndrome" implies that you're not a real disease – you're just a syndrome and that there really is no understanding of IBS. And that's the part I really don't like. And I think the terminology needs to change.

I recently did a Twitter poll on this concept, whether they're the public or doctors, whoever would respond in Twitter. Would they consider this derogatory to consider it a syndrome rather than a disease? And it was overwhelming that both patients and physicians alike felt that this terminology really did not represent what was going on for patients.

And it also implied a diagnosis of exclusion.

Now, what that means, a "diagnosis of exclusion" for those of you who may not be familiar with this term, it means that this disease is the waste basket. After you ruled everything else out, after you've done all your tests, you're left with this.

You have changes in your bowel function. You have bloating. But we don't know what causes it. We can't see anything. You're IBS.

And that also drives a problem because you end up getting a lot of investigations. You never feel comfortable with your diagnosis. You're never sort of settled and you say, "Okay, I know I have IBS." No, you don't because there's no test for it or there hadn't been. And so that's the term, "diagnosis of exclusion."

Well, where does that end up for you as the patient? It means you're going to run around and see doctors and spend more money. And doctors are going to be doing more tests, all of which are negative. And then, you're still going to end up in the same place.

So, we'd like to put an end to that. And that's part of the story of the microbiome here.

Here's another ridiculous concept. But this was something that was quite common especially in the 1990s and before. And I'm quoting here. This is not my quote. This is somebody else's quote: "IBS is the disease of hysterical women!"

So, IBS was, quote, attributed to women. We're all, it seems, blaming women for this condition that nobody understood or that it was due to some previous traumatic event or

psychological event or it's due to depression or it's due to anxiety or it's due to all these different things for lack of a better understanding of the condition. And this is certainly not an appropriate way to refer to irritable bowel syndrome, one would think.

And so, I want to leave you—well, not leave you with that thought. But I want to *start* you with that thought.

Not to mention, there's no shortage of patients to study. If you wanted to do research on IBS, you just need to walk down the street, and you pass a bunch of people as you're walking. So it's not a rare disease—40 million people in the US, one billion people worldwide. Research could've easily been done for decades. But you were left with that previous comment I mentioned.

It is the most expensive disorder in gastroenterology because of the diagnosis of exclusion term—that you do all these tests, they're all negative, you waste all these money, the patient pays the co-pay in the US and so on and so forth. I've had patients come to me and say that, out of pocket, they have paid over \$20,000 before they finally got to the diagnosis.

But it's expensive not because of the testing. It's expensive because of this notion of the Rome Criteria which are the previous criteria for diagnosing IBS stating that part of their mantra was that it was a diagnosis of exclusion. "It's up to you, doc! If you feel comfortable, and you've done everything you need to do, and it's negative, you can call it IBS." And that doesn't serve the patient well. It's expensive.

Well, we're now in 2021. So let's fast-forward to 2021 and this concept here that we now know food poisoning causes IBS. I'm going to show you that evidence. We now know a toxin in food poisoning is important to the development of IBS and that *that* creates autoimmunity to a protein in your body called **vinculin**.

And then, you get a change in the nerve structure or nerve function of the gut—meaning the gut is slower or it changes its flow patterns. And when it changes its flow patterns, you get build up bacteria, and that's bacterial overgrowth. And therefore IBS is SIBO, and SIBO is IBS, in a sense. And I'll walk you through what I mean by that.

We're going to start with the bacterial part of this, the bacterial overgrowth part of IBS, and specifically talk about SIBO, small intestinal bacterial overgrowth.

Now, I want you to focus on those three letters: *small intestine* which is the small intestine, which is the part in the middle here. About 15 to 20 ft. of the bowel is small intestine, about 3 to 5 ft. is colon or large intestine. But the small intestine is where you do all your absorption. You can take the whole human colon out, and the human will survive just fine. It will be runny, but you would survive just fine because the small intestine is where you absorb things. That's your most important part of the gut.

And that part of the gut is meant to be cleaner—less bacteria eating your food, and you get most of it. And the number we now refer to as "normal" is less than 10<sup>12</sup> bacteria/ml of fluid in the small bowel. That's the normal range.

Now, when we're diagnosing small intestine bacterial overgrowth, it requires a breath test.

Now, you could culture the small bowel, but then you have to have a scope. The scope would have to be placed in there, suck some juice out and send it to the lab... of which is expensive and invasive. And you have to be put to sleep or at least given some form of sedation. So what's easier is a breath test.

You simply ingest a sugar. And then, the sugar gets into your stomach and into the small intestine. And then, you expel the gases that are produced by the bacteria in the gut through your lungs, and then out your breath. And that's how a breath test is done.

Now, SIBO has been a problem in the sense that there had been no guidelines or consensus on how to interpret a breath test. And for those who've had a breath test, there are doctors who say, "Well, it's got to rise by 10 or 12," or "It's got to rise by 20 ppm," or "It's got to rise by 60 minutes or 90 minutes on the breath test." And so we set out in two papers. The first paper, which I don't have listed here, was the North American Consensus which set the standards for how you should be doing breath testing and how you should be doing breath testing.

But because of the tremendous interest—and I mean this sincerely, tremendous interest in the gastroenterology community about SIBO, the American College of Gastroenterology commissioned a guideline (which is presented on this slide). And we confirmed a lot of the things in the North American Consensus.

But a very important part of the guideline said—for those of you who know about methanogens or methane, methane is another form of overgrowth. There's a hydrogen form, a methane form, and a third form of hydrogen sulfide—and I promise, I will get to that. But the methane part, those bugs aren't bacteria. So when you look at small intestine *bacterial* overgrowth, that doesn't fit.

So, we created a new term called IMO, intestinal methanogen overgrowth. And that's the new term.

So, SIBO is now being broken down into maybe three parts. And you'll see those parts momentarily.

But we also said you should consider breath testing in the diagnosis of SIBO and IBS because the evidence is now quite overwhelming. And I'll show you what that evidence is.

So, using this Venn diagram, we now think SIBO accounts for 60% of the diarrhea and mixed IBS. So in other words, 60% of people with diarrhea/mixed would have a hydrogen-positive breath test. That doesn't mean that all of IBS is caused by SIBO. A part of IBS is caused by SIBO,

but not all of IBS. And so we now think it's 60%. And I'll show you the data that substantiates that.

But SIBO Is caused by IBS in the bulk of cases. But anything that slows the intestine down—so if the intestine is slower, whether it's because you have scar tissue or adhesions, whether it's because you're on narcotics that slow the gut down, you have long-standing diabetes with nerve problems from the diabetes, many things can cause SIBO and not just IBS. But IBS is such a huge disease base, 40 to 60 million in the US. That probably encompasses the vast majority of SIBO.

But there are three types of IBS. So going back to IBS, there's the diarrhea IBS, there's the mixed—which is the middle (mixed means you're going back and forth between diarrhea and constipation)—and then there's the constipation side of IBS. But essentially, what we're seeing is two conditions because of the microbiome findings we're having, that methane on the breath test or methane or methanogens in the intestine is associated with constipation, and then the diarrhea & mixed is associated more on the hydrogen and now hydrogen sulfide side.

There's two Shah's in the literature in gastroenterology. And everybody mixes them up. So I call this "the other Shah" paper. This is the Shah from Australia. This is a very prominent group. Nick Talley, previously from the Mayo Clinic, he's now the Chancellor of New Castle University. I think that's where he's at. He's a very prominent figure in Australia and a very prolific researcher.

But basically, this was a pivotal moment in 2020 because, essentially, this paper says for the first time: "IBS, full stop, is associated with SIBO based on breath testing." And there's 25 papers summarized in this document. And it's clear. Done. Full stop.

Now, that may surprise you that we're saying "done" now when we knew this two decades ago. But look, you have to continue to march forward. And then, as people summarize the data, they start to see the pattern.

Now, the challenge we had with trying to understand SIBO and its relationship with IBS, or just SIBO in general, is the challenge with the breath test.

So, the breath test emerge probably in the 1980s. And the original breath test only measured hydrogen. And then, later, methane was added. But there was no real understanding of what methane was related to. But the understanding of the gas dynamics just wasn't complete with the breath test, hence the challenges with breath testing.

But let me show you graphically that you've got the hydrogen bacteria which are producing hydrogen (they're flooding the environment with hydrogen, that's what they do), but that hydrogen is like a fuel for other organisms. So the methane organisms, the methanogens, use four hydrogens to make one methane.

So, if you have methane on your breath test—which we can now measure with regular instruments—you can't rely on the number for hydrogen because four of the hydrogens are going to one methane. So the more methane you make, the less hydrogen you're going to have on the breath test. So the hydrogen becomes unreliable on that test.

But there were also patients where the breath hydrogen and methane were zero across the board. And we always suspected that there was a third gas. And that third gas is hydrogen sulfide produced by hydrogen sulfide-producers, otherwise known as sulfate-reducing bacteria. And they use five hydrogens to make one hydrogen sulfide.

So, the point of this slide is simple. If you don't measure all three gases—and these are the only three gases that they produce—you don't get the complete picture. If you don't measure H2S, you can't rely on hydrogen because you don't know how much is making H2S. if you don't

measure methane, you can't understand that methane is causing constipation, which I'll get to also. And we now know hydrogen sulfide is associated with diarrhea.

So, without measuring all three gases, you can't understand the full patient profile. As a consequence, breath testing can be confusing without understanding these three gases.

Okay, now we've got to take a step backwards and say, "Okay! Well, what about culturing the bowel? Do we have proof of SIBO based on culture?" In IBS, we do all the way back to 2007.

And you can see this study from Sweden. Clearly, the orange bar is IBS, the gray bar is healthy controls, and the orange bar is much higher which means that there's a lot more patients with SIBO in IBS than in controls.

Taking that one step further, this study took people who are coming in for scope. So these were sick people, all of them. So the control group in the gray, they're sick people. They're not healthy controls. But the diarrhea IBS patients, the orange, 60% had SIBO. So that's where we get our 60% number from, from this study.

Now, we know more about SIBO, and we continue to know more. And I'll show you some really interesting stuff here in a moment that's new. But when we took these duodenal aspirates, this juice from the small bowel, these two characters came out of the mix–klebsiella and E. coli.

Now, it doesn't look like klebsiella was a lot of higher than the gray (healthy). But each number on this y-axis is 10 times higher. So this is a log<sup>10</sup> scale. So when you go from four to five, it means there's 10 times more bacteria. So E. coli and klebsiella are bad actors.

Now, what we were saying in 2015 is that E. coli and klebsiella were like weeds in the garden, that they were choking other things out. Now, that was just us hypothesizing as to why these two characters are so problematic in SIBO and what was happening. But I have proof now that that is true.

And we get this proof from what's called the Relmagined Study. The Relmagined Study at Cedars is anybody who's coming in for an upper scope, we offer them the opportunity to be part of this study. We collect their information. There'd be questionnaires. We get blood. We get genetics. We get juice from the small bowel and a couple of biopsies from the duodenum, from the small bowel there. And then, we're able to archive that and study the microbiome. And we've gotten almost to 500 patients. So we have a very, very good understanding of the small bowel microbiome. And that's never been done before.

The first provocative finding from our study, the Relmagined Study, was presented and published this past July in Digestive Disease Sciences. This actually made the cover of the journal. The reason this is important is this is the first across-the-gut snapshot of what the microbiome looks like.

I want to point a couple of things out to you. There are many people out there doing stool testing for the microbiome. Yes, stool testing for the microbiome tells you the microbiome in stool. But you can see the colors represent families of bacteria. And you can see the colors here.

But look at the small intestine. You cannot get any understanding of the small intestine from stool because the small intestine is completely different than the stool. And that's my point here. We now can see.

But here's another point. As you go further down the gut—and these are patients who were getting double balloon endoscopies. So we were able to get almost to the end of the small bowel with these patients—the number of bacteria does not go up. We thought it did. The profile of the bacteria doesn't slowly become closer to like colon. No, it just basically drops off a cliff. Everything in the small bowel looks very similar. And it's until you cross the ileocecal valve that everything goes into this format... or this, what looks like stool.

So, it's pretty remarkable to describe this for the first time.

Okay! So now we could use sequencing of the bowel which is the most latest greatest technology for understanding the microbiome. And we can do this in the small intestine. And what we show here is SIBO. These were patients not with a positive breath test, but these patients had literally SIBO by culture which is considered the gold standard. The other is no SIBO. But immediately—I'll only just describe this. It gets a little tricky to understand.

The first ring is the kingdom of life which is bacteria. That's why it's called *bact*. And same on this side. The next level is the phylum. Phylum is the next breaking down of what type of bacteria is present. And you can see immediately even at this super high level look that proteobacteria—which you'll understand what proteobacteria is in a minute—is so much more in SIBO than in non-SIBO.

As we get further out to the rings—and the second last ring is the genus, the last ring is the species, klebsiella and E. coli is this other gray ring—is all-encompassing in SIBO. And we see that here again.

So, the point is we keep seeing the same thing over and over again—E. coli and klebsiella, E. coli and klebsiella. Those are the SIBO bad actors.

The other amazing thing in this study is we were, for the first time, able to validate the breath test with lactulose. We didn't validate it with glucose. We don't do glucose. We validated it with lactulose.

So, if your breath test at 90 minutes rises to more than 20 on hydrogen, a few things are noted. It's the most specific. For SIBO by culture, it's more specific for all of the factors along this line, meaning that even though some of the other factors had greater p-values, this lined up the best. So that's my first point.

The second point is I want to show you this last two columns. It also lined up that the bacteria of the small bowel when you had SIBO had increased metabolic function for hydrogen production seen on their metabolic pathway analysis. What does that mean? That means that the hydrogen in SIBO is coming from the small bowel, not the colon.

This is the argument that's been forever. Well, the lactulose gets to the colon and the hydrogen is coming from the colon because lactulose doesn't get absorbed. Non-sense! This study proves that there's up-regulation of hydrogen in the small intestine in these patients.

So, a lot to dissect on this slide. I'm not going to get too far into the weeds. But very, very interesting...

So, this was presented at the American College of Gastroenterology. It's an abstract that was presented. It's a paper that's emerging. But what's important here?

Okay! So this is called a community analysis or a network analysis. So when you look at the microbiome, it's like a community. You have doctors, plumbers, lawyers and others. And in some communities, the more lawyers you have, the more jails you have. The more plumbers you have, the more buildings that need plumbing you have. And so, you can see relationships between things.

And each circle represents a genus of bacteria. The larger the circle, the larger that particular organisms is in popularity or number.

But I've put red circles around two—E. coli at 33 and klebsiella at 45. And there are small, little circles in this beautiful community. And you can see, it looks like a community. Very nice! Lots of connections, lots of diversity.

But look what happens when you have SIBO. In SIBO, E. coli is this circle... huge! Forty-five. This klebsiella, also much larger. And look what it does to the network. The network is broken down.

There's less circles. It's not cohesive anymore. So not only is SIBO an overgrowth of E. coli and klebsiella. Their overgrowth continues to destroy the networks that are network. And the bacterial community starts to collapse. And that's what you see very vividly here on this picture.

And there's more details to this that are very complicated to explain. But these two pictures I think are pretty self-explanatory on what's happening when SIBO occurs.

Okay! But there's the hydrogen SIBO. And then there's the IMO which is methane. And we knew early on that methane seem to be associated with constipation. Actually, it was the final figure in a paper from 2001 that I wrote. You never look at the last figure of a paper because the meat is figures 1, 2 and 3. Figure 4 is sort of like, "Oh, it's an afterthought," or it's a back-up story.

But it was really important because we continue to show that methane was associated with constipation as this shows.

Not only that, methane is the cause of the constipation. It's not the bugs. It's the methane itself because if you infuse methane in this animal model, you get 60% to 70% slowing of intestinal transit.

So, what do we do about SIBO? What's the best way to treat SIBO? Well, you can treat it with antibiotics. Rifaximin is one of the ones that we use quite commonly. And that works very well for IBS. It's not approved for SIBO. It's approved for irritable bowel syndrome with diarrhea. But I think it's due to the fact that they have SIBO. And it works for up to three months.

And then, the amazing thing about rifaximin is that 36% of people who got rifaximin, they stayed better after the treatment for an indefinite period of time... which is quite remarkable.

Interestingly, the meta-analysis of antibiotics and IBS show that there are no unsuccessful

trials. Every antibiotic trial in IBS shows that it works—and again, pointing to this being a

microbiome condition.

As you continue to use rifaximin, as rifaximin use went up, so did the referral to tertiary care

centers for diarrhea and mixed IBS. And that was very interesting as well.

But this is where I wanted to get to...

Shivan Sarna: What does that mean? Can you just re-state what that means?

Dr. Mark Pimentel: So, as you continue over a decade—this was a decade-long period of

time—as the use of rifaximin for IBS continued to increase, our hospitals were seeing less and

less referrals for mixed diarrhea IBS.

Shivan Sarna: Got it!

Dr. Mark Pimentel: But that means things were happening in the community. Doctors were

giving it and we were seeing less.

Now, in one of the trials, we saw that breath testing was associated with the response to

rifaximin. So in other words, even though rifaximin is approved for IBS, not SIBO specifically, if

your breath test-

First of all, all patients, 44% responded. But if the breath test was positive before they started

rifaximin, 56% responded to rifaximin. And the breath test retained negative. You had a

positive breath test, rifaximin made the breath test negative, you're the best outcome. You

had 76% chance that you met that crazy, very difficult FDA end point.

For methane, it's also interesting. You give neomycin + rifaximin, and you get the best

response. This is a double-blind study! Everybody gets antibiotics in this study. This groups

get neomycin with placebo. But this group gets the combination of neo & rifaximin. You can see the constipation score after treatment is much lower when you take these two antibiotics.

And this is why, in our practice, we use neomycin & rifaximin for methane, and rifaximin alone for the hydrogen side.

Bloating got better with this cocktail. But forget about the antibiotic! The most important thing in the patients with methane who have constipation is getting their methane less than 3 because that was clearly what made it most effective.

Okay! Now, the new kid on the block. This is a new device that measures hydrogen, methane and hydrogen sulfide. And the challenge for hydrogen sulfide is this. The hydrogen sulfide gas is highly volatile and toxic. Even hydrogen and methane are not easy to transport over long distances. So we needed to change all the sensors and array them in a particular fashion in the instrument. You had to have a transport system to be able to transport the gas without any of the gases deteriorating—which is not easy, especially with hydrogen sulfide. And then, do the clinical trials to prove what the cut-off is that's ideal.

But just to show you... these sensors in this instrument are sensitive to 0.2 ppm—not 2ppm, 0.2ppm (2ppm are the older instruments). And it correlates perfectly with older instruments. That's not the question. That, we know already, for hydrogen and methane. But hydrogen sulfide is new.

So, for the first time—and you mentioned <u>trio-smart™</u>, that's the test—we can measure all three gases, do it at home, it transports perfectly without any deterioration in any of the gases. And you get your result.

Remember, hydrogen sulfide correlates with diarrhea; methane correlates with constipation.

And by not knowing all three, you really have an incomplete understanding of your SIBO.

Now, I know I'm talking about the IBS story. And I know it feels like I'm drifting back and forth between IBS and SIBO. But it's all the same thing because of this pattern that I showed you earlier. But I'm now going to talk about how food poisoning causes IBS and SIBO. We had a big paper last year.

This paper came out in 2017. So, I should say, if in 2017, you don't realize that food poisoning causes IBS, then you need to read this paper because this is from the Mayo Clinic. It summarizes more than 40 papers. But the point is, if you had a case of food poisoning, you develop IBS 11% of the time. So 1 in 9 people who experience food poisoning gets IBS.

There's no argument here anymore. Food poisoning causes IBS. It's not all of IBS though. Remember, there's a hundred people with IBS coming in your office who have diarrhea because their colonoscopies are negative, there are many things that could cause that patient. But in that group, sixty percent, it's food poisoning.

But I get this question all the time, "I don't remember ever having food poisoning." You're having diarrhea now. So you obviously have diarrhea from day one. You don't know if that was food poisoning or not. And now, you still have diarrhea which is your IBS.

So you don't have to remember food poisoning for this to be true. And that's why the ibs-smart™ blood test becomes super important.

But the risk factors for food poisoning, the top three are the top three: the severity of the food poisoning. If you had seven days of diarrhea, if you had fever, if you had to get admitted to the hospital, you're way more likely to get IBS.

But look at number two... this is not a disease of "hysterical women." This is women are more susceptible to developing IBS from food poisoning. And as you'll see, it's an auto-antibody that occurs, and women tend to get more autoimmune diseases in general (i.e. rheumatoid arthritis, Lupus and so forth).

So, we're starting to understand why more women have IBS because of this mechanism of action.

This is animal work. I don't want to get too deep in this. But basically, we created the first animal model where we gave campylobacter food poisoning to a group of rats. And the other rats just got nothing. They just continued on their way. And then, we were able to see after three months, after they've recovered from the food poisoning, what they had. And the rats got SIBO.

Twenty-seven of the rats who got campylobacter now have SIBO... but they had food poisoning! So food poisoning causes IBS, but food poisoning causes SIBO. So could it be the same mechanism for IBS in terms of its relationship with SIBO.

Not only that, if the rats got campylobacter, and they developed SIBO, more than 80% of them had weird bowel patterns, weird wet weights of their stool... meaning they developed IBS in general. We don't have a criteria for IBS in rats, but that's what happened. And they got what's called increased rectal lymphocytes. So these are white cells, a small increase in number, in the rectum of these animals. And this is the one thing that's found in humans with post-infectious IBS.

So, one toxin in common with all food poisoning is called CdtB. And we don't think C. diff has this toxin very often. But I put it here because it occasionally can. C. diff can precipitate IBS.

So, cytolethal-distending toxin, this is the toxin that we think is super important for the development of IBS and SIBO in general. So, we did another study where we created a campylobacter food poisoning that was missing this toxin.

**Shivan Sarna:** Dr. Pimentel, when you're moving your mouse around—no pun intended because there's a mouse on the screen, I get that—it's just kind of messing around with the microphone. It's coming across as really static-y.

**Dr. Mark Pimentel:** Okay, alright. I'll try not to move too quickly.

Shivan Sarna: Okay, thanks!

Dr. Mark Pimentel: Alright! So I won't move my mouse around anymore because I don't want

to create static.

So, campylobacter in the middle is missing the toxin. Campylobacter on the left has the toxin.

And then, on the right, let's say you're going someplace where the chances of getting

campylobacter are very high. If you took rifaximin with every meal, could you prevent IBS?

And the answer is rifaximin works great. Not having the toxin works great as well.

So, we knew the toxin was important. But this is the study that was published just in the last six

months and is very important. What we did is we said, "Okay! Maybe you don't need

campylobacter. Maybe all you need is the toxin." And so we injected the toxin into the back

leg of the rat to see if they would develop IBS. And they developed anti-CdtB antibodies

because we gave them CdtB toxin. And they developed autoimmunity to themselves to

vinculin.

And so, vinculin is an important protein on the nerves of the gut that help the nerve stay

together, stuck together.

Not only that, these animals developed SIBO. And they developed a change in the wet weight

of their stool because they were developing IBS. So, we could make an animal have IBS just by

giving the CdtB toxin.

It works like this. You have the cytolethal-distending toxin. You get exposed to food poisoning.

You see this toxin, your body reacts to it and produces antibodies. But one part of CdtB looks

like vinculin. And then, you form antibodies to yourself. And that was supposed to go on to the

vinculin... and it didn't. It flew past. But yes, that is what happened.

So, we took that idea, and we said, "We need to develop a test. Could we diagnose IBS that you got it from food poisoning, you don't need a colonoscopy, you don't need to waste all that resources? And within 48 hours to a week, you know if you have IBS using anti-CdtB and anti-vinculin?" And the answer is... absolutely! And we see that here. The red bar is anti-CdtB, and the red bar here is anti-vinculin. And this is Crohn's and ulcerative colitis patients. And it's head and shoulders above.

So, we could actually diagnose this. And the post-test probability—which is really important—if you have the test, and the test is positive, it's about 90% likely you have IBS.

The specificity is also high, over 90%.

So, I was graced with the opportunity to be part of the Irritable Bowel Syndrome Guidelines for the American College of Gastroenterology. And one of the mandates that was set by this guideline is we need to have a positive diagnostic strategy. IBS should not be a diagnosis of exclusion. That is dismissive to patients. It is suggesting that IBS is not a real disease. And it's a step in the right direct to maybe changing that syndrome word to something else because it really is a disease. And these patients suffer immensely.

And they suffer often at an age when they should be more productive because this can affect people in their 20's all the way up to their 80's.

So this is a sequence. I tried to show you as much of the evidence as much as I could.

Obviously, we need a SIBO Symposium a couple of years back. And it was eight hours of broadcast. So I'm covering a lot of background in a short period of time. But I hope I was able to at least express to you a lot of the most important parts, and some of the more interesting parts that have happened more recently.

But people ask me, "What do you do in clinic?" What do I do in clinic? And so I actually created this in terms of how SIBO and the IBS blood testing fits into my clinic—not in the whole spectrum of what I do because we see very complicated patients.

But in the case of chronic diarrhea patients where they've had some degree of work-up by the time they see me, you could just flat out give rifaximin. If they respond to rifaximin, it can't be Crohn's disease. And it probably can't be Celiac disease because you'd have to be off gluten for Celiac to improve. And Crohn's disease doesn't get better in like 10 days or 14 days of an antibiotic.

But I prefer to go down the middle path which is I get the anti-CdtB and the anti-vinculin. And the second generation test, the ibs-smart<sup>™</sup> test, is much more specific. There was a study that piggybacked to our CdtB inoculation studies. This is from Mexico. And of course, Max Wilson noted that the new second generation test is much more specific for his patients. And we see that as well. It's much more accurate.

And I also do the 3-gas breath test because if they have diarrhea, I want to know if they have hydrogen sulfide because I can use that as a guide to treatment.

Now, if the anti-CdtB antibody is positive, then I know they have post-infectious IBS with 90%+ specificity. I've got to counsel them about traveling, how to eat, what not to eat, what to be careful with because, if they get food poisoning again—and we've seen this in our clinic—the antibodies get higher and they're harder to treat.

And when I put extreme measures, I'm talking about patients who are quite sick. If you're traveling, you should consider prophylactic antibiotics. That's what I do. Of course, it's not FDA-approved. This is just the pattern of practice that I practice because I can't let them get higher on the antibodies.

Of course, if they're negative, that's the patient that should have a colonoscopy. And I have

lots of examples of where the test was negative, and we found something. And so, the test

helps a lot.

The 3-gas breath test, of course, if it's negative, again, consider further work-up. But if you're

negative on the blood test, and you're negative on the 3-gas test, you got to move on.

Something else is going on. And that can be all determined within a week or 10 days. So it's

very fast to get to this point. And then, consider other things, maybe a colonoscopy and other

things.

If you're hydrogen positive or you're hydrogen sulfide-positive, I use rifaximin for hydrogen. I

use rifaximin with bismuth. But there are a lot of emerging cocktails for hydrogen sulfide. So

I'm not sort of married to this cocktail yet because I think we don't understand everything

about hydrogen sulfide. So don't take this as gospel. But this is what I do currently.

Shivan Sarna: Can you explain what bismuth you're using? Is it bismuth subnitrate? Is it

PeptoBismol?

Dr. Mark Pimentel: Yeah, it's PeptoBismol right now. It's just the easiest for patients to

understand and get. There are people who get compounded bismuth and bismuth

subnitrated and other forms. I don't think it matters. I think it's the bismuth itself more than it is

the formulation.

**Shivan Sarna:** And is it three swigs a day?

Dr. Mark Pimentel: Yeah! So, rifaximin three times a day, bismuth three times a day. That's

what we do.

And then, chronic constipation, we do the 3-gas. You could do the 2-gas because, if it's

methane, you don't need three gases for that. But it's just convenient. And if

methane-positive, I give rifaximin and neomycin. If it's methane-negative, I consider further

work-up because something else is going on. I might do anal-rectal testing and other things.

I do consider a prokinetic for all of these situations after treatment because I want to prevent

the need for antibiotics again as much as possible. And that's why a prokinetic can be

beneficial.

So, the conclusion of my presentation part of this is that IBS is, in part, a microbiome disease.

SIBO is an important contributor to IBS. That's clear from 2020. The meta-analyses from Shah

and Nick Talley from Australia really capstoned this. They even had a paper which I didn't

present that is again showing elevated bacteria in the small bowel of IBS. I mean, the data

are pretty substantial and overwhelming.

The most important organisms for SIBO... E. coli, klebsiella, E. coli, klebsiella. I showed you lots

of data on that.

Methane is associated with constipation. Hydrogen sulfide is the key to understanding SIBO

more completely. If you don't have hydrogen sulfide, it's an incomplete picture.

Rifaximin is the first treatment for causative agent in IBS because we think that the bacteria

are deranged as we went through. And you can give it repeatedly.

Autoimmunity produced by CdtB to vinculin is an impo

rtant pathogenesis of IBS.

And so this is really sort of the capstone of what's going on. It's 20 years of work to get to this

very brief lecture. But you can see that we understand this more completely. I would say that

we understand the starting point of IBS more than we do Crohn's and ulcerative colitis now

with this work.

I will say one last thing, and then I will open it up to questions or comments. But that quote I put at the beginning of the lecture where it says, "IBS is a disease of hysterical women," we talked about in the 1980s and '90s where stress and psychology were the mainstay of IBS pathophysiological understanding... but that quote was from 2018. And that's the sad part because, in 2018, we knew post-infectious IBS, we knew SIBO. We knew all these things, and yet there are still practitioners out there who haven't evolved into these new concepts and still reside in the '90s and '80s. And that's unfortunate for patients who might see these practitioners.

Shivan Sarna: Well, thank you so much, Dr. Pimentel. That was very illuminating and really comprehensive. If anyone has any questions about the <u>trio-smart™ breath test</u>, email Paige at support@triosmartbreath.com. And for the <u>ibs-smart™ test</u>, please email patientcare@ibssmart.com

A lot of the questions we've been receiving could be answered through those emails. And because we have a limited amount of time, I wanted to give you another resource. So it's support@triosmartbreath.com, and then ibs-smart™ questions is patientcare@ibssmart.com.

Also, because if you're part of the SIBO SOS® Community, we have a special on the ibs-smart™ test... which is 25% off. You don't need a doctor's script. You can use their in-house physician, filling out the questionnaire at no extra charge. And make sure to look for your email that we will send to you because we'll put a link there. You can also find that at sibosos.com in the shop area.

Dr. Pimentel, here's the big question. So, just to clarify, does hydrogen SIBO exists? You've been talking about it, but there's this question about how the hydrogen feeds the methane. So is hydrogen SIBO is a thing?

Dr. Mark Pimentel: Every two years, I think I understand what's going on. And then, I think

about it some more, and I understand it better.

So, I showed you that figure. That hydrogen predicts that you're going to respond to rifaximin.

So that throws a little wrench in the fact that hydrogen is important because you can't make

hydrogen sulfide if you don't have hydrogen.

So, I think the starting point for SIBO or IMO is you have to have elevated hydrogen because

you need the gas to make the other two cars go. But the analogy I use is you need a lot of

rabbits so that the wolf population or the coyote population is satisfied. And the wolves are

methanogens and the coyotes are sulfate-reducing bacteria that produce hydrogen sulfide.

Interestingly, they don't like to exist together. So if the wolves are there, they're eating all the

hydrogen, and they don't want the other guys there. If the sulfate-reducing bacteria are there,

they tend to not want the wolves there. So usually, the two don't go together.

But as with anything in medicine, there are examples of where that doesn't work. And some

patients have hydrogen sulfide, methane and hydrogen. So it's complicated.

**Shivan Sarna:** It is complicated, okay.

This is from Ramona, one of our long-time participants. If you do get antibodies being positive

from the ibs-smart test™ showing that the food poisoning episode has impacted your

migrating motor complex, you have these antibodies, and therefore you have post-infectious

IBS/SIBO. What do you do for treatment to impact the antibodies? Is there anything you do to

help people with those antibody levels?

Shivan Sarna: So, we had extreme examples of things we've done. But I don't recommend

these for the general practitioner or even the regular gastroenterologist. IV Ig is something

that we have use. And IV Ig seems to bring the antibodies down, and some people get better.

Again, it's not an FDA-approved use. But it has worked.

We've done plasmapheresis in some of the most extreme cases of distension and

bloating—five cases, and their IBS completely disappears for a month. The point of that is

don't do plasmapheresis please, none of you. What I'm saying is that we know that if you get

rid of these antibodies, it looks like IBS goes away. That's a super important finding. We're not

going to publish that because we don't want people doing that because that's like dialysis.

You can't put IBS patients or SIBO patients on dialysis to get their antibodies up. Plus, they

don't form antibodies if you do that. But it just goes to show you that we're really, really, really

close to what could be the end story of how to make this better. And that's what we're

working on. So stay tuned because there's always more to come.

Shivan Sarna: And in June of 2021, we already have our time booked for a 2-hour

conversation—thank you—after Digestive Disease Week where, hopefully, you'll be making

some exciting announcements.

**Dr. Mark Pimentel:** I'm exhausted already.

Shivan Sarna: I'm sure you are. I'm sure you are. Well, we're all very excited.

Okay! If someone needs help with their doctor interpreting the results of the trio-smart™

breath test, how can we help them? Get to support? I gave the email address a few minutes

ago? I mean, I guess some people are getting their doctors to give them the test, and then

the doctors aren't totally being clear about the interpretation...? That's coming soon.

Dr. Mark Pimentel: Yeah, I think the support of the company will give guidance to the doctor

or the patient as necessary. But there's a lot of things that can guide that clinician. There are

review articles and other things that I think the company can provide as guidance. So that's

not a problem.

Shivan Sarna: Okay! I'm just going to ask this in a different way. I do the trio-smart™ breath test, it shows high hydrogen. I have hydrogen SIBO... true? It shows high hydrogen sulfide, I have hydrogen sulfide. It shows high methane, I have methane. So once again, I'm still getting a barrage of these questions. So do I have hydrogen SIBO and should I treat it that way versus treating hydrogen sulfide SIBO?

I know I keep asking you the same question. Just keep coming at me with an answer.

**Dr. Mark Pimentel:** So hydrogen sulfide predicts diarrhea, methane predicts constipation. Hydrogen predicts just the general concept of SIBO.

However, if you think about it, there's going to be a different treatment. Rifaximin, we know works well for hydrogen. Neomycin and rifaximin (you can substitute metronidazole if you wish for the neomycin), it works well for methane.

For the hydrogen sulfide, we're still working that out. And we're doing a randomized control trial right now to see if this new thing works great for hydrogen sulfide or various forms of SIBO. So we're coming to some conclusions on what will work best for hydrogen sulfide.

But just to think it another way because I'm sure this question comes up... think about diet. We think there might be actually three diets for SIBO—one for hydrogen, one for methane, and one for hydrogen sulfide (because if you go on a low sulfur diet, maybe that helps hydrogen sulfide).

So, there are a lot of things coming down the pipeline that we think will help you understand better, help you treat your patients better. But it starts with knowing you have it, and then exploring ways to make it better. And that's where we're at now.

**Shivan Sarna:** From one of your colleagues, Dr. Steven Sandberg-Lewis: "If a patient has IBS/IBD, say Crohn's and SIBO, how does ibs-smart™ distinguish that? They have both."

Dr. Mark Pimentel: So, let me explain the sensitivity and specificity for the blood test. People

say, "Well, it's a low sensitivity, 43% to 56% sensitive." Well yeah, it can't be more than 56%

sensitive because, I've already told you, out of a hundred people who show up at your office,

maybe only 60%, it was due to food poisoning.

So if you knew who had food poisoning, it would be 100% sensitive. So I'm not worried about

that.

The specificity is more important. If you're positive, it started from food poisoning with more

than 90% certainty. So that's part of the test.

Now on the other side of the equation, which is the point of the question, in the IBD group, the

reason our specificity is 90% and not 100% is because 10% of people with IBD have a positive

test. But 10% of all populations have IBS. Makes sense?

Shivan Sarna: Yeah.

Dr. Mark Pimentel: Because 10% of the entire planet has IBS, including 10% of IBD. So you're

always going to have a few patients who have IBS and IBD together. And that's why we can

never get more than 90% specific with the test.

So, if you understand the statistics of things, you understand that the test is quite impressive

given those discussion points.

But I think Dr. Sandberg-Lewis' point is, if you have both, how do you treat both? Well, you have

to treat both in order to get the patient better. There are many patients, for example, with

Crohn's or ulcerative colitis, the primary treatment that's been used in the past is steroids. So,

the patient goes to the doctor, they have IBD, they have Crohn's or ulcerative colitis, they get

whacked with steroids... a lot of side effects. Part of it gets better. But they still have bloating

and a little bit of diarrhea. So the doctor says, "Well, let's go more steroids... and more steroids." And then, they do a scope, and they see nothing... the Crohn's is gone.

So, they were jacking up the steroids treating IBS on top of IBD instead of the Crohn's that was gone.

So, my point is knowing that they have both is really important so you don't jack up all these drugs that are harmful while you can just so easily treat both there.

**Shivan Sarna:** If someone has a breath test, and only has hydrogen show up on that breath test, how show we interpret that?

**Dr. Mark Pimentel:** I still call it SIBO because it's E. coli and klebsiella. And maybe the rabbits are all by themselves... that's okay. I'll treat it.

**Shivan Sarna:** Okay. When it comes to the future... okay, that's going to be revealed, you guys, in June hopefully with high impact information. So hang in there.

Go to the SIBO SOS® Facebook Community because a lot of the questions that you guys are asking are answered there. Dr. Allison Siebecker and I created a course called <a href="https://doi.org/10.21/20.21/

Your questions are amazing. We have covered a lot of them. This is sort of Dr. Pimentel's breaking news and comprehensive overview right now.

How often do you see people have negative SIBO breath tests and it's actually parasites or it's actually SIFO, small intestine *fungal* overgrowth. Please... the percentages?

**Dr. Mark Pimentel:** So what I understand from Satish Rao who does a lot of getting juice from patients where antibiotics have failed... generally, if you're taking an antibiotic and it's not

working, or you have a negative breath test and it's not SIBO, but everything else is negative, then you really ought to consider these other options or possibilities.

Obviously, with parasites, you should look for it. And people do parasite testing. I do it at Cedars as well. But it's not my first thought because, if you look at the data, and if you had a hundred consecutive patients coming in with IBS, most of them would not have a parasite (except for blastocystis which is somewhat common. Even in my population, we pick it up quite infrequently). So, my point is parasites are not as common as SIBO itself. So to treat it that way first is probably your best bet.

Again, it depends. If the breath test is negative, then you can go at it and look for other things like that.

**Shivan Sarna:** Because we do get people with negative SIBO breath tests, and they're confused about "well, what else could it be?" So you do suggest the scoping, a parasite test... and then, you can't really easily test for SIFO, for fungal overgrowth. But Dr. Satish Rao for all of that information.

**Dr. Mark Pimentel:** Probably about 10% of his population—I'd have to ask him what his latest numbers are—could have SIFO. And the 10% of the patients he sees is different than the 10% of the general population because he's seeing patients that have been around the block a few times.

**Shivan Sarna:** When it comes to adhesions—that is such a big proportion of people with adhesions who have SIBO. In case someone's new... welcome! But could you explain what adhesions are and how do you treat adhesions.

**Dr. Mark Pimentel:** So adhesions are you've had surgery. Sometimes, you didn't have surgery. Maybe you had an appendix that got inflamed and healed on its own. You didn't even know. I've had cases like that.

But you have scar tissue in the cavity, but on the outer side of the bowel. And it basically creates a kink in the hose, like your garden hose, where the water doesn't flow through it that well. And then, you get this filled up.

There are therapeutic ways where massage and other abdominal massage can break adhesions down. It's hard to quantify that because you can't quantify adhesions to begin with. It's very hard to know. We've seen CT scans, everything looks like normal, you go on inside and there's adhesions everywhere. So you can't, with regular radiology, quantify adhesions. But that works! Or surgery unfortunately is sometimes the option we have to go down.

**Shivan Sarna:** In case someone's also fairly new, like they've been playing around with this whole hydrogen and methane dominance, and they're like, "Hydrogen sulfide? Wait a minute! I didn't know about that!", what are some of the symptoms to suspect hydrogen sulfide?

**Dr. Mark Pimentel:** Yeah, the two main symptoms that the hydrogen sulfide patients have that the others don't have as much of is diarrhea and abdominal pain, those two. Hydrogen sulfide is pretty toxic. So it causes pain fibers to be amplified, and then also, the diarrhea, which we've shown already.

Shivan Sarna: And what about SIBO causing GERD, breaking news there!

**Dr. Mark Pimentel:** Long ago, when we did what's called a factor analysis—so we broke SIBO down to two buckets (we didn't have the third, we didn't have hydrogen sulfide. It was only two buckets at the time), methane, it turns out, was associated with constipation. We know it slows the gut down. But we showed that, because it's slowing the gut down, it was associated with more reflux than hydrogen SIBO.

But anything that causes the abdomen to distend and create pressure means the pressure to back up into your esophagus is higher. Esophageal reflux is pressure below the diaphragm

relative to pressure above the diaphragm to make the acid come up. And if you increase that pressure below the diaphragm, that's when you get reflux.

**Shivan Sarna:** One minute to go... you know I like to keep you on your schedule because I so appreciate you giving us so much time. There's a big virus running around right now. And a lot of people are very interested in getting vaccinated. And I'm just wondering if you've seen in your practice any correlation with people with SIBO and IBS having an adverse reaction? Any advice you have for us on our gut patient population and the vaccine.

**Dr. Mark Pimentel:** So, what we're seeing with the virus itself is a lot of patients are getting digestive symptoms. It ranges from 10% to 30%. The biggest question I get is: "Is CoVID causing IBS?" And we haven't seen that data yet.

There are people who they call "long haulers." They don't get better over time, or they take a long period of time to get better. That's usually not the digestive part. It's more body aches, weakness and these types of symptoms.

But the virus can be in the gut.

**Shivan Sarna:** Can you say that again because it just bleeped. That was like a cliffhanger. The internet just went out. Say it again?

**Dr. Mark Pimentel:** The virus is in the gut. It can be in the gut. And it can bind to ace receptors in the gut. So yes, the virus can be transmitted through stool, it's believed. All of that is true during acute CoVID or when you have CoVID.

But in terms of the vaccine, we haven't seen any GI consequences of the vaccine that we know of... just fatigue, fever, all of those sorts of things in the early days. So, so far, so good with the vaccine.

Shivan Sarna: That's great. Thank you so much, Dr. Pimentel. We'll look forward to speaking to

you again after Digestive Disease Week. Keep up the fantastic work. Let's talk to you in June.

And in the meantime, let me do my best to get this information out to as many millions of

people as possible. So thank you so much.

**Dr. Mark Pimentel:** Thank you.

Shivan Sarna: I'm going to have Dr. Pimentel sign off. And I want to say thank you to everyone

who has been here for this presentation from SIBO SOS®. And if you have not gotten into our

Facebook Group, for those of you in the zoom call and not on the Facebook Live feed right

now, I think it's SIBO SOS® Community.

A lot of the questions that you all have been asking are fantastic of course. And SSL, I think

you're going to have to ask him some of those questions directly. Water, making you bloat...

Dr. Pimentel has explained that before where it's like a balloon from a kids' birthday party with

a clown just tying them up into different knots. It just has to do with the plumbing and the

tube. So yes, even drinking water can cause bloating if you have issues.

What I want to also let you know is that we have a whole library of Dr. Pimentel's previous

presentations where a lot of these questions are ultimately answered. We call it The Pimentel

Chronicles. And it is on SIBOSOS.com. You can go to the Resources area, you can see our

on-demand learning library... and there are tons of fantastic resources there.

That is something I have not done a fabulous job of getting out to the world. It's a little bit

hidden. And I'm working on getting that more out there. A lot of times, they're part of our

summits, the SIBO SOS® Masterclass Summit and then the Next Steps for Treating Tough SIBO

Masterclass Summit which we've just wrapped. You can find it all in SIBOSOS.com.

Also, there are tons of free resources at SIBOinfo.com, Dr. Allison Siebecker's website.

The book, #HealingSIBO, is going to be the best \$20 you've spent on figuring out what to do next. It's based on everything Dr. Pimentel was talking about. On page 111 is the algorithm that so many people have followed that he started and that Dr. Allison Siebecker and Dr. Steven Sandberg-Lewis added to. It's right here. That's also a free download on SIBOSOS.com.

Okay, I'm going to wrap it up! We are very appreciative of you. Thank you so much for being here everybody. I really, really treasure you. And I want to wish you the best. Do not give up. There are tons and tons of hope. Dr. Pimentel and his team are working basically 24/7 to figure this out. I do think, in June, there are going to be some revelations that we're going to feel really good about it. But that hydrogen sulfide treatment he just talked about with PeptoBismol is terrific.

Also, Dr. Siebecker, another world-renowned SIBO specialist like Dr. Lisa Shaver who's joined us today, and Dr. Steven Sandberg-Lewis and so many more—thank you guys for being here—if you go to the SIBO SOS® Facebook Group, and you look under "Files," tons of information there... including Dr. Siebecker's perspective on Hydrogen Sulfide Treatment.

Remember that if you sign up—I don't get a kickback or anything on this. If you want to <u>do the</u>
<a href="mailto:ibs-smart™ test">ibs-smart™ test</a>, use the coupon, sibosos2021, when you order it, and you get 25% off which is huge, HUGE! Thank you so much to Gemelli Labs for that.

And if you have any questions about the ibs-smart test™, which is the anti-vinculin, the test and all of that for the food poisoning leading to SIBO, email patientcare@ibssmart.com and Paige will help you.

And the coupon is case sensitive. Ooh, that's complicated. Okay, it's SiboSOS2021. That's complicated, sorry! Well, look for it on SIBOSOS.com because I think we have it typed up there really nicely.

And then, I just wanted to find the email address again for anybody who wants to get their questions answered about the <u>trio-smart™ breath test</u>, like directly from the lab itself.

And international, they're working on it. I know that it's not as prevalently available as they want it to be. So they're constantly working on it. Paige, are you with me? Can you type that in the email address again? Here you go... yeah, support@triosmartbreath.com.

It's support@triosmartbreath.com for the breath test, and then patientcare@ibssmart.com.

Love you guys! Thank you so much for being here. If anybody is interested in the lymphatic system—my mom passed away in the '90s from lymphoma. And so, with all of my gut work, at the back of my mind, I had another summit brewing, and it's called the Lymphatic Rescue Summit. And if you're interested in that, please email us at info@sibosos.com. Make sure you're on our email list. I'll send you out the opportunity to sign up for that for free. That's happening in April.

And so, it's a tribute to her. I didn't know what was going on with SIBO. What's the lymphatic system?! In the '90s, no one knew! And I wanted to make sure no one went through what we went through. So that's a new summit that I'm doing.

Also, in September, I'm doing a summit on Biological Dentistry, the connection from the mouth to the rest of your body, and your amalgams... we're the only country that separates the mouth from the rest of the body! So it has been incredibly illuminating. I can't wait to share that with you. That's in September.

And the next year, I'm doing the Liver & Gallbladder Summit.

So, be sure to stay on the email list. And we will keep you posted. Okay, I'm going to wrap up. Clarissa, who's in the background... would you do me a favor and gather all the questions? Throw it into a spreadsheet and let's see what we could do with those.

Yes, you will have a replay sent to you on Friday. That's our goal. And yes, if you go into the Facebook group, you will find this recording. And yes, I'm going to have this transcribed, so everyone can read what Dr. Pimentel was saying.

If you're listening to the podcast, you obviously won't be able to right now see the slides. But we'll give you a link so you can go watch the video too! Peace everyone. Thank you.

Yes, we'll send all the URL's and website info. Sure! Absolutely! I'm going to send you everything and make your life easier... all kinds of stuff. So I'll send you all the links that I was just trying to read... and the coupon. But you can find that at SIBOSOS.com if you're really enthusiastic and you want to find it sooner.

Okay! Bye!