Introduction and guest background

Welcome. Thank you all for joining us. Another edition of Mycotoxins and Chronic Illnesses, 2.0. And, today it's my pleasure to, interview and discuss, all things, irritable bowel and, otherwise and, Sibo with, doctor Mark Pimentel.

Doctor Pimentel is, currently, director of the Medical Associated, Science and Technologies program at, Cedars-Sinai. But I like to think of Doctor Pimentel as just a man who's really helped teach us, how to think about Sibo and now how to really, put irritable bowel in a, I think on a much more, functional, useful.

Forget about that. I don't like that word functional anymore. When it come, anytime I hear functional and gastroenterology, I have problems. And Doctor Pimentel will tell us all about why I might feel that way.

Okay, so, first of all, can you tell us a little bit about, I actually two minutes about how did you wind up as a gastroenterologist? Doing something which pardon me, but I, I, I love in doctors, but I find too rarely in specialists somebody who really knew that that people needed to be listened to and and that this was a big problem far bigger than, you know, a little poor digestion and neurotic patients.

I mean, it's not that long a story. I wanted to do medicine. And early on in medicine, I knew I wanted to do gastroenterology. So that part got squared away.

But remarkably, I wanted to do the function of the gut. But more people said, well, what do you want to do? And I said, well, I want to do esophagus, because esophagus seems interesting to me, the physiology of the esophagus.

But in hindsight. But, good decision. I didn't, the small little organ, a little bit boring. But I think, I think, the moment that it hit me, was when there was a, there was a patient, I think she was about 65 years old.

She came into the office and we had seen her. She had irritable bowel syndrome, and we treated her with antibiotics because we saw the breath was was abnormal.

And she came back and she had this brown paper bag she brought in and she literally had, I don't know, 10 or 15 pill bottles in there. And she dumped them on the table and she says, I can't believe how good I feel, and I don't need any more of this garbage anymore.

And the pill bottles were tricyclic and other, antidepressants that people were throwing at her or saying it was psychological or stress.

How IBS and SIBO science evolved

And I realized that, wow. I mean, we did something to her that made her 90% better. None of this stuff could. There's something here. And we need to do the science because you need the science to prove it.

I think that was a real big turning point for me. Yeah, but you but you and you did the science, which I think makes it. Lots of us think we need the science.

But you actually turned around and did it, so, Yeah. So, you know, so tell me, tell me about, you know, just, how you began to understand, the role of the bacterial overgrowth in IBS.

Well, think about 1999. I mean, I finished fellowship in 99. I was already starting the research on my third year fellowship, but 1999 people thought IBS was a psychological condition.

It was listed in the DSM book, which is a psychological, sort of catalog, psychiatric catalog. And and that's where IBS stood. Even the term irritable bowel syndrome is derogatory.

I mean, you're irritable and you're a syndrome because we don't know what the heck is going on. And and that's where it was. And that stress and anxiety were causing it.

And then I come out with a paper that says, well, it could be bacterial. Well, first of all, two things happened. The paper got a lot of attention in the media.

Second thing happened, the scientists said, are you kidding me? It's a psychological disease. And for about a decade, there was a sort of a would say it's a war or a battle.

It was more of a intellectual conversation in strong terms, of traditionalists versus the new microbiome, area of IBS. And and in the end, you know, as I, as I say, often, science is a regression to the truth.

So I may be wrong, somebody else may be right, but it's all about the patient. And at some point in the future, we'll have all the facts and know the truth.

And so, fortunately, the truth continues to move in the direction of the microbiome, in my case. But, I can I assure you, we'll get to this. We don't have all the answers yet, but we have a lot of them.

Yeah, yeah, it's it's been, you know, it's been so exciting, especially, you know, that you're bringing science to it because those of us in the, you know, alternative world or now we call it functional medicine, and integrative medicine, you know, we've always, you know, we learned from the natural paths, you know, a long time ago that the gut was at the heart of what was happening in the body for so many, so many illnesses.

But, you know, and we looked at a few bugs and, you know, we I don't know if you're familiar. I'm sure you are familiar with all the tech, but the testing companies that are out there that look at the microbiome now, but when what's now genome it first started, even before it became great Plains.

It was started by a guy in new Jersey who was just looking at stool tests and measuring a handful of bugs, and that's what we had, and we were playing with them.

But you've taken this to a whole, just a whole new level of of of, of sophistication and information. And what, are there but it with all that, do you have any families of bacteria that you think have more to do with it with, with developing of irritable bowel?

Well, you know, again, we continue to learn and you'll hear more about some of the new categories that we're, we're, we're seeing. But, but, at the current moment, we think Sibo breaks down into really three clusters.

Cluster one is the hydrogen producing Sibo. And now we're jumping to 2021 a little bit here. Right. But the hydrogen producing organisms we thought and we still think are E coli and Klebsiella.

Those are the those are the bad actors in the small bowel. And and we see that the higher E coli is in the small bowel, the more it inhibits all the organisms around it and creates this, you know, as we sometimes term a dysbiosis.

But dysbiosis can it is has many definitions. But what I, what I, what we're seeing is it's almost like they're a gang and people are leaving the community because the gang is taken over.

Yeah. It's a bad neighborhood now. Yep. It's a, it's a bad neighborhood. And, and E coli has forced people out of the neighborhood. And so the, the, the there's a disruption as we call the ecology disruptor.

There's a second cluster which is based on methanogens. So, when methane is elevated, it creates a different situation where it, it triggers constipation, methane gas triggers constipation.

And those bugs, which are not even bacteria, they're archaea. They produce methane. The new kid on the block is sulfate reducing bacteria or hydrogen sulfide producers.

And they are turning out to be the super interesting because they relate to the E coli and Klebsiella in the sense that they're getting hydrogen from there to make hydrogen sulfide.

And when hydrogen sulfide goes up, you get diarrhea.

Bacterial clusters, stool tests, and the microbiome

So now we've figured out how these, fiefdoms of bacteria, when you have one neighborhood, you get diarrhea, you have another neighborhood, you get constipation.

And that that's where we're at currently. But there's some really nifty new things coming out later this year that just expand that notion. It doesn't it's not going to be an apocalyptic finding, but it's it's a big sort of shift in understanding the complete picture of those three categories.

Wow. Okay. And that that's come a long way from yeah. Years ago we were just doing hydrogen breath testing and, you know, and, you know, that was normal.

So we you really had a functional growth. Well, I still have one of the old hydrogen machines from the 1980s. Some they will have a little, museum over here.

That has all these, all the instruments. But it wasn't even CO2. There wasn't methane, there was nothing. Just hydrogen related. So. Yeah. Yeah, yeah.

And it's just interesting like, because as an aside, the Klebsiella is there. Do you find, a significant relationship when you see, when you see elevated Klebsiella in the, in a stool test since that's, you know, quite a bit far away from your small bowel.

So what we know about stool microbiome, and I don't want to get too far in the weeds for your viewers. But when you, when you talk about this, this the color.

So about the colon first. Right. There's klebsiella in some people's colon. But that falls in the category of the phylum Proteobacteria. The Klebsiella, but the two phylum in the colon that are literally taking up 89% of the colon are from rickets and bacteria.

That's not Klebsiella, that's not E.coli. So while there's equal and klebsiella in the stool, they are by no means dominating anything. They are minor contributors.

And yes, you can see them on stool tests, but they're minor contributors. But now fast forward to the small intestine in bacterial overgrowth. When you add Klebsiella and E coli in a Sibo patients it's taking up 50% of all the bugs there.

That's how it's dominating everything. So can you imagine that two bacteria are encompassed? If you count on all the cells, 50% of them are those two bacteria.

It's remarkable what Sibo does. And you don't have an example of that in the colon. Now, some people use stool tests to say, well, there's ecola klebsiella there.

Maybe that's an abnormal gene. Maybe that's where your question was going. There is some spillover effect. So you will see some of the Sivo, E.coli and Klebsiella spill over to higher levels in the colon.

But nobody's said this is the level that Sibo. That would be a surprise, right? Yeah. That would be the reason that line has not been drawn correctly.

So, I don't know what I'm saying is stool testing. I'm not saying it's bad. I'm saying I don't know yet. Yeah. I think I think that's a fair statement.

I mean, just to reiterate, I mean, to our listeners is that I said, I've been doing stool tests since now, since about 1992. I can tell you that there, they'll give you an idea of a neighborhood vaguely like, don't, don't, don't hang your hat on them.

Because even now that they've gotten much more exact, we still don't know what it means. The thing, I mean, look, 50, so I'm sort of cutting across you.

But 15 years ago, the Human Microbiome Project was created. And at that time, they thought, oh, we know everything about the colon and therefore the whole that we're now 15 years past that I can tell you there's besides the methanogens, which we found in the colon, Klebsiella, which we found there are no one bug, one diseases that have ever been found from stool, except for death.

Right. But that was found in the 80s using old school microbiology. So despite all our technology, we haven't been able to say, this bug causes colon cancer.

This bug causes Crohn's or this bug causes also flies. That was the pie in the sky in 2006. Everybody thought here we go. We're going to unlock the mysteries of human health.

And it's way more complicated than that. Yeah. Well I mean, just once again, I said this, I think I know almost every, for every, episode is that chronic disease is an illness of the patient, not of the pathogen.

So you're going to find multiple packages, you're going to wind up with, similar looking diseases. And if we eat because it's our body's response that's causing this chronic inflammatory state, whether it be in your intestines or in your brain or anywhere in your body, it's your body that's running this show.

And so the it we're we're just going to get hints, we're going to get hints. And this is where I, the thank God took him into all because, you know, this is a far cry from, you know, the total pin, the tail on the donkey work we were doing 20 years ago.

Yeah. I mean, and this is a lot of improvement, but. Right, we're not going to probably find, you know, the one. But we got the neighborhood, so this is in, you know, just for our, our, our our, our listeners again.

So when you went through this, the, the, the, the methanogens, as you call them, the and the the are the archaea, the archaea, these are really primitive bacteria.

Is that what's the, you I mean, from a lay perspective, you could say that, but they're not even bacteria. So they're more primitive single celled organisms than bacteria are.

And they don't share a lot.

Methane, hydrogen sulfide, and breath testing

So. So they're really their own kingdom, you know? So you've got the, the different kingdoms of of, characterizing organisms and their, their own kingdom and bacteria is its own kingdom.

So they're really completely separate. But remarkably, they've been around a lot longer. And they're survivors because they've been here since the primordial soup in some way, shape or form, and, they're in us just to a greater or lesser extent. So.

And that they, they, they like our small intestine, they like our small intestine. And the methanogens also like our colon, which is why we can't use the term Sibo for methanogens.

We've changed it to IMO intestinal mismanaging overgrowth. To us it could be colon or it could be small bile. And that came up in the new Sibo guidelines we published just just over a year ago. Oh, okay.

So so yeah, these guys have been around, I guess literally since the dawn of, of, of of, biological time on this planet. Okay. And, and so and these seem to be to be more tied with constipation patterns.

Yeah, absolutely. I mean, so the more methane you produce, the more constipated you are. And that that is a direct correlation, which is really very few direct correlations like that in medicine.

But we see it absolutely that way with methanogens. It also again, I may be getting a little off topic, but please, and it also correlates with heart rate.

Interestingly, we just published that of just three months ago that the higher methane is, the slower your heart is, which is really fascinating. So methane has properties that could be vagal, properties that could affect muscle function in the gut.

And so there's a number of downstream effects of methane. Oh, that is fascinating. And while we're on gases, let's talk a little bit about hydrogen sulfide, because that that's, especially interesting because, I mean that all I'm not sure before we get to that, you know, many of these gases, like, you know, we know carbon dioxide, carbon monoxide, even, you know, these are, you know, they function as neurotransmitters.

They function is as in communication molecules in the body. Is the same thing possible? Is that happening for methane that we know than any, any other level other than in the gut?

Well, methane was recently sort of characterized as what we call a gas or transmitter. So it's a gas that actually has a physiologic neuromuscular effect.

In the case of constipation slowing the gut down, it's not slowing the gut down in the way you think. It's not paralyzing the colon. It's actually causing the colon to squeeze on both sides to hold things back.

So it's an active, slowing of the gut that methane does. Hydrogen sulfide. That's the new kid on the block. That one does all sorts of creative things to the wall of the intestine, including changes in secretion, changes in your the nerves of the gut in terms of their, sensation to pain.

And it also has consequences on blood vasculature. And in terms of, arterial tone. And these are things that have been known effects of hydrogen sulfide for a while.

Right? Yeah. No, because I mean, we've always I'm not always but we've known that it was a it was a gaseous, communication molecule. I'll say, but, yeah, I, I just didn't, realize that it also up until recently that that it had its, relationship to, to causing loose stools, and, and this the pain, the increased pain of irritable bowel.

Yeah. That's that that is one of the things, one of the things that, you know, was frustrating to me is we were seeing all these Sibo patients. And then there were patients with this flatline breath test.

And what was that? Because there's nobody with no bacteria in their intestine that use such that you should have no hydrogen at all, because there's so many hydrogen producers in the gut.

And it always, you know, perplexed me. And then there were patients where you would treat them and their hydrogen would go up and you're like, well, what is that?

You mean I just gave them antibiotics? I would have expected. There's no way it goes up. So what what was happening is, first of all, the Flatliners. Many of them turn out they're hydrogen sulfide producers.

Secondly, when the hydrogen goes up, it means we got rid of the hydrogen produced hydrogen sulfide. Producers know all this hydrogen is they're nowhere to be eaten.

So, you know, it's all those mysteries that we're trying to solve. But I can tell you, doing a three gas breath test was a challenge, and I was waiting for somebody to do it.

They didn't. So we we went ahead and helped to develop this new test that can do all three plus CO2 stably. Because hydrogen sulfide is difficult to transport.

Yeah. I would imagine these. Well, it's just it decays it back into reactive compounds. So yeah. So, you know, now that you have these, when you start seeing the patterns, I mean, what about the one, the you see some patients who who start off with very high levels or moderately high levels?

Right from the first breath. I mean, you, I mean, and they really haven't been eating, you know, what do you think about those? So, Doctor Rizzo, my partner, he actually, we both felt that the patients know.

If you're just talking about hydrogen now. Methane, if it's positive, it's positive right out the gate. 09. methane is high. Hydrogen sulfide has the same property.

If it's positive, it's positive right out of the gate. Almost always. Hydrogen is can be usually it's low at the beginning because you're fasted and then goes up with time.

But we do have an occasional patient, as you point out, that they start off as high hydrogen. And we thought, maybe that's poor prep. They ate breakfast.

They didn't tell us, snuck in a little bagel. But they assure us they hadn't. And we do see that it is associated with some symptoms and can respond to therapy. So.

So I think some people aren't telling us the truth about their snack for breakfast, but there are truly some people where it's high at baseline for hydrogen and it's real.

So, I think it's up to the clinician to sort of figure it out in their case by case. Right, right, right. And so for the for the patient, I mean, people always want to know, how did this happen to me?

I mean, you know, any other any, you know, stories that you have found that, that fit the good proportions of these of these folks? Yeah. I mean, I think that's where the violin weaves in because, we have now animal models that actually do exactly this.

Food poisoning, antibodies, and gut motility

We give them campylobacter food poisoning, and then three months later, they have Sibo, they have IBS, they have everything that humans have, just like IBS.

And and the seagull, as I mentioned. So it starts with food poisoning. We've actually identified the toxin Kttv, which is the culprit. In fact, now we don't give rats food poisoning.

We just give them CDB injections in the arm and they develop IBS. So Sibo, it's pretty remarkable that we found the toxin that's causing this. But the toxin CDB makes you form antibodies to yourself.

And that's to a protein called healing. And the specific subtype of insulin that it reacts to is present on the nerves in the muscles of the gut, particularly the nerves.

And so sequence is food poisoning exposure to the toxin. You develop antibodies to the toxin that cross react with you. And when that happens, the gut slows down.

And in the patterns of the gut change and the E.coli and Klebsiella are allowed to bloom because they for some reason, that part. We don't understand that because we don't have these cleaning waves of the gut and other muscular functions.

E coli loves it like that, and they become the bully or the the make the neighborhood all bad. Yeah, yeah, yeah. No. It's interesting you you I've used that same, and, I guess metaphor many, many times to explain, yeah.

The gut that, you know, we just got to change the neighborhood. It's, urban renewal, hopefully in a more positive vein than usually practiced. But the what what's interesting is how, you know, the the no vascular system because we see, you know, so many times when people have had this for a long time, and I always wonder which direction the information is going.

We see a lot of people, with, you know, they just pour stomach empty, you know, gastroparesis, as we say, you know, and also, their necks are usually a mess, you know, and we think that there's some there's some vagal, you know, there's some vagal irritation going on.

But, obviously most of the people you see, it's probably starting in the gut and feeding back to the central nervous system. Well, I mean, because in the animals, this is what we create.

So we can create the exact scenario that we see in humans with animals just by giving Ktvb. So my, my feeling is it starts in the gut, because the animal models support that.

But but you know, we do know there's a lot of neurochemicals that are produced by these bacteria in the gut. Serotonin, for example, can be produced by bacteria.

So there's, histamines, which is a whole separate topic. Probably another hour of conversation, that bacteria can produce. Klebsiella can produce histamine.

So what does that do? You know, some patients complain of sinus problems when they have over there. Some people complain of brain fog fatigue. Some people have more anxiety.

Some people have neck pain, as you describe. So there it could be that there particular subset of bacteria in there are different and leads to this nuances.

So there's the general theme bloating diarrhea constipation. And then there's the nuanced, subsets that are, what you describe and what I think what you're describing there are created by, by the individual, the person who has irritable mast cells because they probably been chronically infected with something else for a long time.

Then you introduce a little bit extra in their gut with with an overgrowth of Klebsiella. Maybe those people are the ones who are going to start having the mast cell type reactions.

I mean, that that that's I mean, you know, a. The, the, the joy of being of, of being a physician is being able to like, get people better and what really but the intellectual curiosity of it is finding the different ways that these threads interact.

Right? Okay. Because that that's, that's the thing is that it's, you know, like said, when you when you, when you have an acute illness, you know, you have to recognize it.

But exactly. And when you have a chronic illness, you have to figure it out that that's exactly right. One of the things that sort of bothers me and has bothered me about the irritable bowel syndrome old story is, you know, morphine is not a treatment for cancer.

Morphine makes the pain of cancer go away. But you got to treat the cancer. And so tricyclic antidepressants, while constipation is not a treatment for IBS, it's covering up symptoms and a lot of things of what we do in medicine when we don't understand a condition is simply trying to, you know, sugarcoat or cover up the symptoms of the patients.

And that's fine when you don't understand what's going on. But you sure as hell better try to understand what's going on and try to get to the root cause and the and the pathophysiology.

And I think that's where this story is really interesting, because it's not done by no means. At the end of the road. But but we've come a long way and and think about this.

I know the food poisoning causes IBS. I sort of know the mechanism of how this happens. There has been a quarter of $1 billion given by the NIH to Crohn's and ulcerative colitis research over the last decade, and they don't know those pieces.

Still, they don't know what triggers Crohn's or all sort of colitis. They don't know the first. You know, this is what starts it. We do with IBS. We're we're way better off in Crohn's and colitis now.

You know, 20 years ago we would have said no way. But now we can. So the targets for drug development, for therapy, for trying to understand this further are the map is there now.

And now we just need to keep going. Yeah. Yeah. And what the as I'm going I'm realizing you I believe you have a very you see Sibo as very much a subset of or a secondary effect from a lot of IBS is that do I have that correctly or am I making an assumption here.

So remember Sibo or IBS is a way. Yeah. No. Totally different. So, so anything that meets these four criteria get thrown in that wastebasket. So it was never possible to find something that caused 100% of that wastebasket.

And that that that's the problem. But I sort of look at it like H. Pylori and ulcers. Right? 100 people with a ulcers. Well, 20 or 30 are caused by aspirin, Advil, whatever you were taking.

About 60 of them are caused by each pylori. Well, we still call it peptic ulcer disease. We don't call it H. Pylori disease. And a whole bunch of people have H following that don't have ulcers.

So it's sort of following that path where, look, it's IBS for now and 60% of IBS is Sibo. And that's good because we can treat that. So it's not so much about changing the name of IBS is as much as it is.

Okay. You need to do a breath test, find out if possible is causing your IBS, treat that and it goes away. Or at least it gets better. And and I think that's how we have to work.

But remember, there's still a lot of people out there who don't still subscribe to the old school of IBS and patients out there are still frustrated by some of their practitioners who say, I don't think Steve was real.

I just did a debate. I did a debate, and this was with all academicians, which is really interesting and sort of an academic debate on Saturday. And they did a pretest and they said, what, you know, do you feel Sibo is the cause of IBS?

And I bet you wouldn't guess what percentage of these doctors feel see what's part of IBS, 10%, 83%. Oh, so you've okay. That's that's really good, right?

I simply I that's the way I was thinking. They were still in the Stone age. Okay. I was shocked and and, so the point is, yeah, there's still 17% of doctors who are out there frustrating patients with all, you know.

But my point is, it's really good. My job is not to be an evangelist. My job is is to keep putting papers out until the proof is so, convincing that the At 17% are there to.

Yeah. Okay. But I'm, I'm just really that's overwhelmingly exciting. Good news. Because I, you know, I, I always compare medicine to, to 1 or 2 aircraft carriers, you know, when you have the academics in the other, when you have like the, the FDA and they're both designed to be very slow moving, you know, and probably for good reason, because we don't want to flip on a dime, but it's it's impressive when you move one of them quite you.

That's a big turn I so I just one thing I realized that we should give your definition or the Rome definition of irritable bowel syndrome, because I always get confused.

I forget part of it so well. The definition changes with every iteration of Rome. Right? But, but, but so.

Treatment approaches: antibiotics, diet, and prokinetics

And this is I can tell you this is frustrating probably to the FDA as well because each definition creates a different cohort of patients. And so if you approve a drug with Rome three, is it even approved for for, IBS patients?

Because the cohort is different, but generally speaking, you have to have abdominal pain. They refuse to put bloating in the Rome criteria, which is really quite a shock since 90% of IBS patients can complain about looking.

Yeah, but this is a Rome bug that we can't get out of the ointment. And, and and then they have to have alterations in stool pattern and then there's other minor criteria such as incomplete evacuation urgency.

You know, those types of things. So that's it. I mean, the Rome criteria are so vague that if you took a Crohn's patient, 70% of Crohn's patients meet the Rome criteria.

So it's not helpful, you know? Okay. No, no, no, no, no. You know, but, you know, I mean, this is I don't think people I don't want to waste a lot of time here, but this is something that, again, for patients to understand is that, nose ology or the way we organize diseases is such a mismatched mishmash.

Okay. And, the idea that there is definitive diagnosis, is largely a fantasy. I mean, there are things, you know, pneumonia, we can, you know, get, especially now the CT scan.

We can see it. And am I we kind of agree on the EKG changes, you know, but, you know, a broken bone. We're cool. But when it comes to, you know, again, chronic illnesses, it's very vague.

On on on what? On what you want to name it, you know. You know, in all fairness to Rome, at the time, it started in late in the 1980s. You know, you have to have an anchor in, in the anchor is for the FDA to say, okay, we buy it.

This is some nebulous thing called irritable bowel syndrome. And if you take those patients and you put them on a placebo or a drug, we can track that.

And then you get drugs approved without an anchor or at least at being able to identify patients, you know. But we've moved on a lot since then. And, and now there are sort of new targets.

And so it creates a little bit of chaos when we're trying to do new drugs based on true physiology. Because we're stuck with antiquated anchors. Right.

And so where are you with, with treating these gases? I mean, like the what what's the I mean, a what are you doing? And B, how are you how is the FDA and, and the, and the farmers, not so much as the pharmaceutical industry, but actually the insurance industry, which has to we have to get to pay for these things.

How is that working out? So, well, I'll tell you what I do first. So Rifaximin is FDA approved for IBS with diarrhea on the basis that IBS is a microbiome condition.

Fantastic. FDA acknowledges IBS is in part a microbiome condition, which is a huge victory. And it works. And it's been terrifically successful. We use that for the hydrogen overgrowth part of IBS.

And and the breath tests for hydrogen predicts response to rifaximin. So that's been published on the methane side with the method in overgrowth we use rifaximin plus neomycin on the basis of one small randomized controlled trial that we've done.

So that's where we hang our hat. There in in the context of hydrogen sulfide. That's the new kid. So we don't know what works best there yet. But I can share with you that we've already completed one randomized controlled trial, which is not publicly available yet, on something completely new, but in the clinic, we're not using that because we don't have it.

And what we're doing is we're Flaxman with bismuth. Only. Yeah. 1990s bismuth inhibits hydrogen sulfide production, so weakens those organisms. And maybe the antibiotic slugged them across the head with, you know, and it would do these things, but but we're still using a sledgehammer for a small nail using antibiotics.

So hopefully over time, we'll have better, more boutique laser like the ability to get rid of these things. Yeah. What I love to talk about is, again, getting back the the nervous system, the structure, the the structural, musculoskeletal system and the nervous system have always intrigued me.

Because I think they're the stepchild of medicine since, you know, we, we really have been trained to do this unless broken. But anyway, but so I think the gut motility, you know, and since, you know, and I know you've done some work with the, with, with improving gut motility, other.

Can you give us a little more information about how you look at that and how you think about it. Yeah. Well, sort of there's sort of three arms to treating overgrowth.

There's the arm of the antibiotics, which I've just described. There's the arm of diet, which, you know, we may or may not have time to get into. And then there's the arm of motility, which is you know, we basically, know that the motility is slow.

We know that the majority of that problem is a lack of cleaning waves in the small intestine, or otherwise, we call them phase three. And we know drugs that trigger that phase three, like low dose or retro mycin, from kallikrein, which is another pro kinetic.

So in patients where the Siebel recurs, we want to try to make the cleaning wave go as best as we can possibly do it. But going even further back to the root, if we could get rid of the anti insulin antibodies from the bloodstream, we might be able to get everything cured.

And that's where, you know, our head is at for, let's say, the 5 to 10 year plan on this. Now, I know that may disappoint some listeners because damn, I got to wait 5 to 10 more years.

But that's the I mean, I've been doing 5 or 10 year plans for a long time, and, it's it's a 5 or 10 year plan. Okay. You you can see it. Well, I have a few things.

One thing I just love you to tell the story. They describe the difference between normal peristalsis and the cleaning waves, because I think people confuse that.

They often wonder. I have diarrhea. What do I need more of a cleaning wave? Yeah. So peristalsis is just a really simple generic term for the gut is moving forward.

Forward meaning from mouth to anus. But, but in fact, the small bowel is way more complex than that simple, you know, notion. So the cleaning waves or the phase three only occur when you're not eating.

So here's the analogy. You're sitting, you went to work, you didn't have time for breakfast, you got up late, didn't even have coffee, and you're sitting in the meeting room and your stomach is grumbling.

That's a cleaning way. That's a good thing. You may be embarrassing to you because it's very loud and obnoxious, but it lasts about ten minutes and then it disappears and you won't hear it for another hour and a half.

That's the cleaning wave. So you eat your dinner last night, you have some lettuce and pieces of things you can't digest. That small bowel is like your dinner plate.

It needs to go in the dishwasher. It needs to be washed before you use it for breakfast. So every 90 minutes the cleaning waves come through and strip everything out to the colon.

And if you don't do that, it gets dirty in the small bowel. And that dirtiness means E.coli, Klebsiella and those

characters. Wow. Okay. And and the important thing is if you're eating all the time, it's harder for that to happen.

If you're eating all day, you never have cleaning waves. So you know, when back and thousands of years ago, we killed the buffalo. We ate the buffalo.

We didn't eat it today. It was rotting tomorrow. And you couldn't. No refrigerator, no taco chips. From the, you know, from the cupboard. You didn't have bagels.

You didn't have Grubhub. You know, you ate and you didn't eat for 2 or 3 days. And that's the way the human body was designed. I mean, it evolved that way.

So people who are constantly eating, it's not the right way. It's not what the body physiologically is meant to do. Yes. Yeah. That, that that, that that's a whole other, wonderful discussion.

I to go outside one day is just especially how that affects when we take in, you know, sugars and fructose all the time and why we wind up with that. And diabetic and gouty and, you know, just because the, the very things that were designed to keep us alive in times of no food really do us in when there's too much to eat.

Yeah. And it's getting back to the anti, the cytotoxic whatever. But I can never remember because I want to make the last thing in eight and it's a b the CD, ptb CD, PTB okay.

Cytotoxic. Okay. Anyway, are these antibodies I mean, have you looked into the idea in people with severe cases of, using things like plasmapheresis or is that B to.

Well, we've done it, but we don't want to perpetuate the notion of doing it. So we're because it's, you know, plasmapheresis. We've done it in about five patients.

But these are the extreme. Yeah. That's why I'm talking about this is not garden variety. Yeah. These are not patients. These are patients who were in and out of the hospital are so distended in their vehicle.

An antibody is as high as we've ever seen it. And it's a mess. And that when you put a catheter in the neck, you got to filter the blood like dialysis three times a week, and then a month later, all the antibodies come back, so the disease comes back up.

But but we also you can't do it in a run of the mill IBS patient. Well, actually, but it doesn't sound a good idea if they're back. You know, it's not like some illnesses you remove them and this system kind of resets.

Yeah. And this one I know my back goes back and we've seen it in the patients but it does go away. So there's the optimism is that if we get rid of these antibodies I think I think we have a we have a shot at shoring this.

It's complicated to get rid of anybody. Right. Okay. But that's the exciting news that when you did get rid of the antibodies, the symptoms went away during that time.

Correct. That's that's very exciting because it's a proof of concept. At least you know that that this is doing it. Yeah. Exactly. Yeah. No, I like that, I like that.

That's that's that's very exciting. I, I've, I've, I've, I'm just interested because you know in, in our, in our field we have found, IVIg to be one of those surprising last ditch treatments.

Cleaning waves, fasting, and the future of therapy

You know, that that work often when we're not even sure why it's. Oh, we're never sure why it's working. Because it's another thing that we don't really understand.

Why it why it helps, at least with the plasmapheresis. It's a little cleaner. Just a little bit. Yeah. Okay. But, and so

you're just talk a little bit about diet, because I know that that's, my own experience has been that it's been so individual and what's going to work for the people, but do you have some broad strokes that you found with these, with, with these different subgroups that you feel comfortable about people starting?

Yeah. I mean, I think the, the, the what we term the diet now that we use is called the low fermentation eating diet. LFI so it's basically, and we came up with this long before low Fodmap.

We just didn't, you know, do the low Fodmap approach where we, you know, commercialize it, at least not a bad time. It's basically the premise that you don't eat between meals.

What we talked about with the cleaning wave. So it's not just what you eat, it's how you eat. And then what you eat is my goal at that time was I want patients with IBS to live a normal life so they could show up with friends to a restaurant and almost be guaranteed there's something on the menu that they could tolerate.

So it's not as restrictive as the low Fodmap diet and not as, you know, it doesn't have the risk of malnutrition or other things that the low Fodmap diet has, because that that's been demonstrated.

But and it allows you to be more liberal, like onions and garlic, or now you take onions and garlic off the list, which is the low Fodmap. And suddenly almost every Italian restaurant in the country, you can't eat that because they're using it.

So it really limits you immediately. But but there's many other things that are restricted in the low Fodmap that we allow. But basically, no, no, none of those were bad sugars.

You know, the artificial sweeteners. What always makes me laugh is they call it, sugar free, sugar free sucralose is a sugar. It's just not for you. The bacteria get 100% of it.

You get 0% of it. It's not sugar free. That's a that's not a correct term. So there's certain things that are absolutely no screaming like most, most of those alcohol, sugar things are all just food for your bacteria for you.

So it's like a I don't like the word prebiotic either, because I think prebiotic suggests that it's good. It is feeding the bacteria, that's for sure.

Okay. Okay. So that explains a lot of people's problem. And just going back to the onions and garlic, you do find that you just have that a good number of your patients, do you do fine with with with small amounts or is it, is it how much any in are you going to actually eat in the meal.

Truly. Right. No, that's I mean not very much or not like you're eating an apple. So, I think it's minuscule. The problem with onions and garlic, in terms of concentration, I think if you have a packet of Splenda, that's a really bad thing to serve with sucralose, I should say.

You're not going to pick on a brand sucralose. And and those sweeteners are fine if you don't have Sibo. It's just you have Sibo. You can't be eating. That's right.

Right, right. And any other really no go foods. Yeah. Beans genus beans are awful I mean so so those are really almost blacklisted for these patients.

And hummus which is of beans, peas, chickpeas, rebels. Yeah. Yeah. And and those are frequently put in things, I mean, even in Indian restaurants. And I love Indian food.

Often they use chickpea flour as a thickener for gravies and for for sauces. So you it says no dairy. It says this or not that, but the thick sauce that's on the chicken is actually with a chickpea base instead of a flour base, like, whole wheat or white.

Yeah. So that's a problem. And then, you know, miserable. Yeah. And just and what, what where do you see gluten

in, in this world? I mean, how much do you.

Because I mean, when my world, they tend to blend together because most of our patients, because of chronically inflamed gut, have wound up with some kind of wheat sensitivity in America.

But whereas your world, you know, I mean, you know, we're not always right. I was a very, I was not a believer of gluten free for the longest time. Unless you have celiac disease. Right? Right.

And I'm generally not prescribing gluten free to my Sibo patients, but we just recently did a study, and we found that if you compare people who are gluten free to all the other diets, including veganism, vegetarian, you know, lacto ovo, etc., the only group that had a low TNF tumor necrosis factor, a lower inflammatory score was people on local, which I was scratching my head.

I said, look, I got to I got to eat this one because I was a naysayer. And now the science tells me I'm wrong. And again, it's about the patients, not about me.

Yeah, yeah. There's something there's something there. I mean, we still have it in there. We don't want to make a religion, but it'd be really interesting to to do that with a group from Italy.

You know what? What many of us who who have trouble with, with gluten or wheat products, can get away. You know, we don't have celiac, but we just, you know, we eat a lot of things.

For myself, I eat a lot of gluten. I'll get that heavy fatigue. Like, I feel like I have to slap myself to stay awake and watch me. Real food allergy kind of response. Yeah.

And yeah, in Italy I can eat the stuff and it doesn't happen. I keep, I keep always afraid, and then I keep doing it because it tastes good. And I've heard this from many, many, many, many, many that, you know, you don't have to convince me and my IBS patients when they go to places like Italy or Greece or, you know, the food is coming from a farm just down the road, maybe no GMOs.

I don't know, I don't know what's going on. But they go to Italy. They have no problems. Yeah. And then yet here, the the same pasta. What I've been telling patients is, you know, Italy.

I know a now I'm telling you a brand. But there are other places, Italian markets that actually source flour from Italy and make your own pasta and you won't have as much trouble.

And a lot of patients do well that way. But yeah. So these are the mysteries that would be nice to be solved. But you know, I mean, like I said, as you said that that the NIH budget is, is is aimed and targeted at ways to make more money for the people who I mean, unfortunately, it doesn't didn't you know, I always tell people medicine is generally manned by a man and woman and by by people with good intentions.

There are very few evil people out there in this field. It's just that, you know, just habit patterns. And like you, the funding does seem to depend on funding and so on.

And yeah, absolutely. And that's, that's been our biggest challenge over these 25 years. It's it's better now. But we had to be scrappy. Because there is no funding for ideas.

And, we got scrappy, and did big things with little dollars. I mean, the first neomycin study we did, which was, you know, now we're sort of wrapping up with this little comment because it's so it's cute, you know, a randomized controlled trial, like a target trial for Rifaximin, which is about, you know, a couple hundred patients or 600 patients.

It was actually like $30 million trial if you combine both of them. We did the neomycin and placebo trial for 2000 bucks. We paid for the neomycin, we paid for the placebo.

The pharmacy blinded it, and that was it. The whole trial was $2,000. And that was the start of this whole story.

Wow. Wow. So but but it's but it took, you know, how many hours of your time and your staff's time that, you know, they, you didn't assign dollar value to, you know, that's true.

Blood, sweat and tears. A lot of sweat and tears. But but it was worth it because patients benefit and I think that's. Oh, yeah. No, no, I mean, you're our work has, you know, has transformed this world.

I mean, you know, we we were we were throwing stones at this, you know, like I said, you know, we we threw some of the right stones, you know, we, we kind of knew in the 90s we would treat people, but we would, you know, I said a lot of what I do, I would say is like, pin the tail on the donkey, we're blindfolded.

And with your help, we're not blindfolded anymore when we're treating this, you know, we we really have some good some, ability to, you know, have a pretty good idea what the target that we want is rather than just.

We're going to kill something and see what happens. Exactly. Exactly. Yeah. So I just want to thank you so much. This is, great. I hope you hope people didn't mind our meandering.

That is my style. So they're used to it. If they're watching this, they're they're used to it. I'd like to explore ideas. And you've given us a bunch.

Just the thing I can do is I don't know about you, but I'm allowed, trail smart if people are looking, you know, for the breath test, that's the place to go.

Yeah. And and we've been, you know, we've been very impressed. I mean, the results are helpful. I mean, clinically, we really like them. And also, I've been using the IBS smart, which is the one that looks at the antibody making with antibodies, you know, and, again, I think is going to, give us insight and hopefully be able to help us direct therapy over time.

Yep. One step closer. Moving step by step. Yeah. So again, thank you so much. Look forward to chatting with you again. And, stay healthy. Don't give up. Nope. Not giving up yet.

Thank you so much for.