Kiran Krishnan:

... who are supposed to. Function of medicine doctors, their mandate is to look at root cause issues have inadvertently taken an allopathic approach to this with natural ingredients. That is the part that maybe we feel like, "Okay, we're doing something better." But we're still taking a very allopathic approach. And allopathic doctors, of course, are treating SIBO, but they're treating it and there's only one treatment so far, and that is they're using off-label Rifaximin. Rifaximin started off as a super, and this is one of the parts of the pharmaceutical industry that does irk me is that Rifaximin has been around for a long time. It's an antibiotic, stays in the small bowel for much longer than any other antibiotic. And for that reason, it was very successful as a treatment for gut infections, for travelers' diarrhea.

It used to be a product you could buy at a pharmacy in Mexico, if you have Montezuma's Revenge for $3, it's nothing. It's super cheap antibiotic, been around for a long time because it stays in the small gut for a while, the thought is it can help with SIBO because of the overgrowth in the small gut. But then once they start using a placebo, now they're charging about $600 a prescription. If you go to your gastroenterologist with bloating, he or she's going to write you a script for Rifaximin typically 10 day treatment and it's off label so most people's insurance aren't going to cover it. And you're going to pay out of pocket somewhere upwards of $600 for that. And of course, it's going to basically destroy your gut microbiome in many ways and not really help the root cause of the problem.

And then gastroenterologists are also starting to recommend a low FODMAP diet because of FODMAPs in these fiber rich foods that are actually really good for your gut, microbiome are very important for your gut, microbiome are the primary ones that cause a lot of the bloating symptoms in SIBO. You do the Rifaximin, you do the low FODMAP diet. It may bring down your bloating and then that seems to be a measure of success. But it comes right back the moment you stop the Rifaximin and you stop this super strict diet that doesn't allow you to eat dozens upon dozens of super healthy foods. The moment you do a little tweak on that, it comes right back. And then the-

Michael Roesslein:

People already commented in the chat that they took it and it stopped working after they stopped taking it.

Kiran Krishnan:

Yeah, exactly. It comes right back. The bacteria grow right back like that within six hours of the dose going away from your gut, the bacteria will come right back and then you just happen to take a second dose and then knocks it back down, third dose. But by the time the course is done at day 10, it's all coming right back. And why? It's because we're not looking at the root cause, where are these microbes coming from? Why are they overgrowing? All of those questions. Now, functional medicine does a very similar thing, but with different ingredients. The idea is that, yes, you need an antimicrobial to carpet bomb everything, but we don't use antibiotics because those are bad, but we will carpet bomb the shit out of your gut with antimicrobials, from natural sources.

But they do the same thing. They kill bacteria. I met so many people who are struggling with SIBO that have been on antimicrobials for six months, a year or longer. And their gut is just a wreck and are also on a low FODMAP diet. Which is also a thing that's recommended quite a bit from functional medicine. And the combination of those two things does nobody any good. You might get some temporary relief of bloating and so on, but it's not going after the root cause.

I Started digging into this whole SIBO idea and thinking, how is it that we're not taking a better and different approach to this? What really is the problem here? And then what I'm going to present today is really my scientific journey with you guys, going through and showing how I looked at this as a problem and what I think

needs to be addressed. We're not presenting like you do this, your SIBO's going to be gone, that's not the goal today. I want you guys to start really thinking about what all may be going wrong and what may be the important thing to focus on when you're thinking about your SIBO.

And if any of your practitioners, when you're thinking about your SIBO for your clients. And then there are some things you can do, as well. We'll cover that as well. We really just have to start stoking some thought in a different angle than just killing, killing, killing in the small bowel, because it doesn't work.

Michael Roesslein:

Okay. Sounds good. Yeah. I'm excited. There's so many people with so much frustration around this and I just want to say that, let's do this. All right. I am going to be manning the chat best I can. If you have questions, put them in the Q&A it's a lot easier that way, things can get lost in the chat. There's a Q&A thing on the bottom. We'll get to as many as we can. And I'm going to be taking notes because for this one, I'm going to be putting together a special little gift for everybody here. I know that people tend to frantically try to take tons of notes and try to remember everything and then try to memorize all this stuff.

I'm going to be putting together, as a little bonus for everybody who attends this webinar, a super simple PDF CliffsNotes guide to SIBO based on what I personally learned during this presentation, I'm going to send it out with the recording of this webinar later this week. I'm going to be taking notes. I'll be manning the chat. I'll ask questions. If I come up with some and I thought that'd be a nice little bonus for everybody. We're going to do that. And I'm going to be a student right along with you, because I learn by writing notes. It's a memorization thing. That's for me and the floor is yours and you can start whenever you would like.

Kiran Krishnan:

Awesome. I'll turn off my camera for the moment while I'm talking so I can minimize this little window here. Okay. You guys got the background explanation and I titled this talk Going Beyond the Bloat. And the reason I made that the title is because what I wanted for practitioners who I normally present this to, to think about is the bloat is not the mark of success in SIBO. What I hear over and over again, both from patients and the practitioners is that I tried this and I was still bloated. Well, the bloat is the last symptom that shows up. There's a whole lot of other physiology that's changing, which is actually more important and more scary for long term health, than the bloating part itself. But I understand why the bloat is at the forefront because that's a part that's very obvious that you see, that gives you insecurities that affects the quality of life and so on. I totally get that.

But the success of a SIBO treatment is not necessarily measured by how fast and how quickly the bloat goes away. That's one thing to keep thinking about, down the road the bloat will go away if you're doing the right things. But I hear often enough people say, "Oh, I tried that for two weeks and I was still bloated." But that doesn't mean it didn't work and that doesn't mean it's not working in a positive way. Let's keep that in mind as we think through this. I also want to compare a few things that are very common languaging in diagnosis in the GI world like IBS C and D and SIBO for example. They are distinguished as different conditions. And when you look at the statistics on this, you see things like this between four and 78% of irritable bowel syndrome is caused by SIBO. That's literally statistic that I pulled off a-

Michael Roesslein:

That's so ridiculous.

Kiran Krishnan:

Right?

Michael Roesslein:

The statistical relevance of that is whatever zero would be.

Kiran Krishnan:

Exactly. And when you see things like that you're, "So really they have no idea what they're talking about." And what is IBS to begin with. There's no definition for IBS other than your bowels are irritated and they throw the S the syndrome on there because that provides a medical excuse to be able to say that there's too many factors, we don't really know what's going on. And then when you look at the common symptoms of IBS C and B, which are abdominal pain, discomfort, irregular stool, form, passage, bloating, constipation, or diarrhea, and then the most common symptoms of SIBO are also abdominal pain or discomfort, bloating, flatulence, loose motion, constipation. So many overlapping symptoms, four to 78%. This is IBS C. This is IBS D. This is SIBO methane. This is SIBO a different kind.

It's just hydrogen SIBO, methane. They want so badly to create a diagnosis and a label that you slap some things on it, create some parameters around the condition and the symptoms and call it something. But the problem with that is, I think we're overlooking the most important aspect of this, which is the underlying mechanisms that are driving all of these things. There's no reason why we can't think of IBS, like symptoms, SIBO like symptoms and the dysfunctions that are occurring in the gut as one thing. It's all a dysfunctional gut that's driven by a specific root cause or multiple root causes. Just the fact that we compartmentalize and divide these and label them and all that in itself, is crazy to me. And it's not productive for trying to figure out how to resolve these issues.

SIBO is defined as an increase in bacterial equal to or greater than 10 to five colony forming unit per mL of upper gut aspirate. If you're not familiar with scientific notation, that's 10 to the power of five, basically, colony forming units, each colony forming unit represents one bacteria per milliliter of upper gut aspirate. The real way of diagnosing SIBO is not through the breath test and all that. Those have at least a 50% error rate, but you have to do an invasive aspirate test where you send in a tube, you pick up aspirate from the small bowel itself, and then you plate it out and you get the colony forming units. That's the only true way to diagnose SIBO based on how it is defined in terms of its disease characteristic.

Lots of people use these breath tests and all that, but studies are shown there 50% or less accurate. I was even talking to a doc this week at A4M and she was talking to me about SIBO. And she was saying how she has this patient that keeps taking this breath test. And the breath test keeps showing that she has SIBO, but she's done all kinds of good stuff. Some of the stuff that we're going to talk about today and the bloating and the symptoms and all that are gone for the most part, but the breath test still every once in a while, shows that it's positive. And Then the patient can't let that go. And when you ask the question, "How do you feel?" "Oh, I feel fine." "Can you eat this, that, and the other that you weren't able to eat before?" "Yeah. I've been able to enjoy these foods that I can't eat before, but my breath test still says I have SIBO."

And the patient's obsessed with it. And continuing to try to take things and all that, that may actually make things worse. We've branded this in such a way, we've created labels for it and all that when in actual fact, hopefully what you'll see by the end of this talk is as there're other explanations of why, to me, IBS and SIBO are not conditions in of themselves. IBS and SIBO to me are symptoms of a bigger problem that's occurring within the body. And that's my whole message that I came to in this journey that I'll take you through in an abbreviated form. That IBS and SIBO are not conditions. And I don't like that they have these labels because when they have a label, they themselves are a condition and they're distinguished from one another and they themselves have a definition and unless your treatment meets that definition, then you're not at resolving the condition.

Hopefully that makes sense. I want people to divorce themselves from these labels, and let's go through the big root causes that are driving lots of these symptomology. And I think you'll start to see that the bloat that you find in SIBO and the food intolerances and the loose bowels and all of the discomfort and all that are really symptoms of something else that's happening in the system. And it is also widely accepted that SIBO has this feature of stasis in it. The bowels not moving. And the bowels not moving is a big driver of why you get overgrowth. And dealing with that not moving bowel is another clue as to there being a bigger issue happening in the body.

The bowels are supposed to move. They're designed from day one to move. They have a number of mechanisms that trigger them to move. And there's very specific reasons why the bowels move and we'll cover a lot of that when we go through. But the fact that the bowel stops moving is a bigger issue than the resulting overgrowth from the bowel being stopped, in terms of its movement. And we're not necessarily addressing what is causing the bowel to stop moving. We're going, "Oh, what about the secondary effect of the overgrowth that is a result of the bowels not moving?" We're not dealing with why the movement is stopped. And so that in itself to me is an error in how we're looking at this problem.

When I started looking at SIBO, I had to ask a number of questions. To me, to really understand what may be driving this. You have to know what is overgrowing. When you have small intestinal bacterial overgrowth, we have to know what is actually overgrowing. And if we know what's overgrowing, we may be able to answer if these are dysbiotic bacteria or are these bacteria that are native to the region. And you ask most practitioners that, they don't know. Most practitioners who are treating SIBO, who will use antimicrobials and things to try to kill it all off. But when you ask the fundamental question, "Well, what is actually overgrowing?" And is it a dysbiotic bacteria that's coming from somewhere else? Or is it the native bacteria that naturally live there, that for some reason are now overgrowing, they don't actually know and that's because we're not thinking about the root cause and the mechanisms here enough.

And if they are dysbiotic bacteria, where are they coming from? How are they getting into the small bowel? Where are they coming from that they're inoculating the small bowel and then overgrowing? We need to know that as well to really understand this question. And then the last question is, why are they overgrowing? Why is it that people that don't have SIBO can somehow maintain a certain low level of bacteria, remember SIBO's 10 to the five colony forming units per mL of aspirate. That's actually a relatively low amount of bacteria, 10 to the five is pretty low. That's a one with five zeros or four zeros next to it. And so it's not that big of a number. And when you compare that to the large bowel, for example, the large bowel can have almost 10 to the 12 or 10 to the 13 CFU's per in the case of a large bowel, we always look at CFU's per stool, per gram of stool.

And each of those units of power, when you go from 10 to the five, to 10 to the six, to 10 to the seven, that's a factor of 10 that you're increasing. When you go from 10 to the five, to 10 to the 12 in the large bowel that's a factor of 10 times the six decimal points that you're moving up. It's a huge change in the concentration of bacteria. People who don't have SIBO have a very low amount of bacteria in the small bowel, despite that being a very ideal place for bacteria to grow. The small bowel, all 20 something feet of it, is a wonderful place for bacteria to grow because it's warm, it's moist, there's constantly food and drinks coming in. There's constantly calories and carbon sources for fermenting and so on.

The big question becomes, why are these vector overgrowing and why don't they overgrow in people without SIBO? What's controlling it. And then if the bowel movement is stopped in SIBO and that's a well known feature of SIBO, the big question is why have the bowels stopped? Why is there stasis? Why aren't the bowels moving any anymore? And then finally for me, what are our natural protections against these issues? Because clearly something is going wrong in the system, where the bowels stop moving, bacteria are overgrowing and these can be bacteria from a different source, not necessarily native to the small intestine. That question has to be answered. And then whatever mechanism is in place, under natural, healthy conditions that prevent

bacteria from growing in this seemingly ideal environment for bacteria to grow, those features and protections aren't working.

What are those natural features and protection? Why didn't the human race always suffer from this problem? Why didn't the human race always have SIBO if it's merely in overgrowth of bacteria? Clearly there are mechanisms in place to prevent this overgrowth from happening and what are those mechanisms that prevent the overgrowth from happening? And my conclusion is number one, because it's so common and because it affects so many different types of people and there's no specific trend, its not like it's affecting middle aged men only, or prepubescent women or menopausal women. It's not affecting one specific group where there're commonalities in lifestyle and time of life and hormone cycling or whatever it may be. It can affect a 12 year old girl, as much as it affects a 90 year old man.

It must be multifactorial, because it must be number of things driving this condition, because that's such a big diversity of individuals that suffer from it. And because there's also such a big diversity of individuals, there must be a very common source that's driving this. A source or an issue that can be experienced by a lot of people, it's not something exotic. It's not something that'll only people that have traveled to the Congo have picked up. It's something that is super common, super prevalent, it must be driven by common behavior. Those are two of the things that I started thinking about when you start looking at answers to these questions and features of this condition itself. Let's first look at answering the question, what is overgrowing and are they dysbiotic or native bacteria to the region?

And fortunately, there are a number of studies that have been done on SIBO and this is SIBO associated with liver dysfunction. This is SIBO as is it's established in non-alcoholic fatty liver disease, and Nonalcoholic steatohepatitis or hepatic steatosis. In these conditions SIBO is very common and prevalent. And they've done a lot of studies on the microbes that are found overgrowing in the small bowel in these conditions. And what they found is that the predominant microbes in a healthy, small intestine are gram positive bacteria, like Blautia, Rumminococcaceae and so on. These are good, healthy gram positive bacteria. And that's an important fact to remember gram positive are microbes that have a cell wall structure, and they call gram positive because in microbiology, one of the first things you learn is how to gram stain bacteria. Any bacteria you take, you put a stain on it, which is an indigo stain, it's called a gram stain.

And if the bacteria has a cell wall, it will absorb that stain and appear blue or purple under a microscope, that makes some gram positive. Gram negative bacteria do not have a cell wall, they only have a cell membrane and they do not pick up the stain and when you look at them under the microscope, they don't have that color appearance. Gram negative bacteria have LPS, Lipopolysaccharides. That's a very important thing to keep in mind. That's one of the things I call talk about a lot. And it's no coincidence when you looked at the overgrowth in SIBO, it is characterized by what we call a taxa shift from gram positive, to gram negative bacteria.

In a healthy small bowel you have predominantly gram positive bacteria. Now, when you have SIBO, you start to see a shift in the levels of gram negative bacteria. And then eventually you end up with a predominance of gram negative bacteria.

Some of those gram negative bacteria are Enterbacteriaceae, Ecoli, Klebsiella pneumonia, Proteus mirabilis and other gram negatives like Pseudomonas. Those are all the types of microbes that end up being present and prevalent in a SIBO large bowel. There are some gram positive that we found as well, but they're not the normal gram positives like Blautia, Rumminococcaceae. They are more opportunistic and problematic gram positive, like Staphylococcus, Enterococcus faecalis, Enterococcus faecium and so on. There are opportunistic/problematic bacteria.

What's absolutely clear from the studies that have been done in this space is that there is a taxa shift from gram positive to gram negative dominant, and the gram negative and the remaining gram positive bacteria are

all questionable, opportunistic, pathogenic like organisms. They are not the native bacteria to the small intestine.

We've answered the first couple of questions. Number one, what is overgrowing? You're getting a taxa shift to gram negative bacteria, like Klebsiella pneumonia, Proteus mirabilis, Ecoli and so on. And then you're also getting some opportunistic type of gram positive, like Staphylococcus, Streptococcus species and Entrococcus. We also know that they are dysbiotic because those are not the native microbes to a healthy, small bowel microbiome. Those are important things to answer.

Now, if they're not native and they're dysbiotic where are they coming from? How are they getting to the small intestine? Now, when I first started looking into SIBO almost six, seven years ago, every time I'd ask a practitioner about it, they were convinced that the bacteria are moving up from the large bowel. That there is some dysfunction in the ileocaecal valve. And the ileocaecal valve is that valve in between the end of the small intestine and the beginning of the large intestine, that's supposed to keep things moving in that direction and not letting things come up. They would always say, "Oh, there's probably a dysfunction in the ileocaecal valve and microbes from the large bowl are moving up." And so...

Kiran Krishnan:

Microbes from the large bowel are moving up, right? And so that was kind of the theory that people hung onto for a while, and I think most still do. But in my view, it's actually not the primary source, right? Because that would be a very long movement for those microbes, in any large amount, to keep moving up from the large bowel, against gravity, moving up and moving up into the proximal part of the small intestine. They'd have to move up quite a bit and move up quite far, and fight their way through all of the microbes that are designed to live there. And also, lots of the large bowel microbes are anaerobic, meaning they actually do better in a non oxygen environment. Whereas once you start moving up to the middle or the beginning part of the small intestine, it's a mixed aerobic environment, where there is some oxygen in that area.

So some of those large bowel microbes don't do very well. So although some of the dysbiotic bacteria and SIBO do live in the large intestine, to me, that's a completely secondary route. I think there's a very, very clear and much more well rationalized source, and that is going to be the mouth, right? The mouth is a major source of all of these types of gram negative bacteria, right? The mouth has lots of E coli in it, has pseudomonas in it... Sorry, has Klebsiella in it, has Enterobacteriaceae, has Enterococcus in it. Enterococcus faecium, [inaudible 00:26:40] Of course, staph and strep are all found in the mouth, because they grow in sinus passages and all that. And these are all the microbes. Many of these microbes are the fecal oral contaminant microbes, right? Fecal oral contaminant microbes are the main microbes that we pass onto each other from the fecal oral route.

Meaning, somebody has fecal matter on their hands, they don't clean their hand. And I can't tell you how many times I go into a public restroom and you see a guy coming right out of the stall and walking right out, right? Or even the urinal, walking right out, not washing his hands. So people are filthy and they're touching things with their dirty poop filled hands, and then we touch the same thing. And then at some point, we're going to put our hands in our mouth, in our mouth or near our mouth. And that fecal oral transmission, these are the main bacteria that come through it. It also can come-

PART 1 OF 4 ENDS [00:25:04]

Michael Roesslein:

Who's ready for dinner?

Kiran Krishnan:

Yeah, exactly. I'm sure everyone's appetite is stoked. And these can also come through contaminated food, of course. We know E coli is a common in meat. Staphylococcus, Staphylococcus you can get from food sources. If you buy a burrito at a gas station, there's a good chance you're going to pick up a little staph from it. So these are very common dysbiotic bacteria that enter in through the oral route, and then also are present in our mouths all the time. They colonize our mouths, and guess what? We swallow spit by the gallon, every single day, right? So we have this major source of continuous inoculum moving from our mouth, into our small bowel, every single day, right?

So to me, that became the number one culprit here, but there's more we've got to examine, in order to really confirm that. Now, using that as an example. Tying in oral microbes with other dysfunctions that are occurring systemically, looking at patients, diabetic patients, for example. 60% of diabetic patients yielded oral Enterococcus Faecalis, and Enterococcus faecium, right? So when you look at the oral microbiome of people with diabetes, 60% of them have these two microbes in their mouth, right? For whatever reason, these are the predominant microbes in the mouth of diabetic patients, compared to 6.6% in controls, meaning age match, non-diabetics.

So diabetics have 10 times more frequently, have these two microbes in their mouth, than non-diabetics. And a recent study found that in SIBO, SIBO was present in 43% of diabetic patients with chronic diarrhea, and 75% had a significant improvement in symptoms after being treated with antibiotics. Meaning that, SIBO individuals also have a much higher prevalence of diabetes, right? 43% of SIBO individuals have diabetes. Compare that to the normal population that has diabetes, it's almost three or four times higher, right? So there's this connection between diabetes and SIBO. And then there's this connection between SIBO... Sorry, diabetes and Enterococcus faecium and Enterococcus Faecalis being present in the mouth. We also know that in SIBO, Enterococcus faecium, Enterococcus Faecalis and fecal, tend to be some of the dysbiotic bacteria that are growing in the gut.

So a lot of this can be tied together. And when they say that symptom improvement... Symptoms improved when you took antibiotics, it means that killing off something in this pathology, in the mouth, small gut pathology, killing off a microbe, improved symptoms. So it's driven by a dysbiotic microbe, right? So this is just a touch on a connection. I was looking through in the literature, and sure enough, you find it in the case of diabetes. But let's get a little bit more specific, as to why these microbes, if they're coming in... Let's take an example that they're coming in from the mouth, they're entering into the small intestine. Why are they overgrowing, right? That's the very important question, because we have all of these natural protective mechanisms against SIBO. Because remember, I told you in the beginning, that the small intestine is actually a great place for bacteria to grow, right?

There's all of the features for a great place for bacteria to grow, including moisture, warmth, continuous food, calories, sugars, all of that coming through, but there are a number of protective mechanisms. Number one, stomach acid, right? The gastric barrier. This gastric barrier really reduces the number of bacteria that can survive through the upper GI system, and then colonize and grow in the small bowel. Now, some of that acid also leaks into areas like the duodenum, and acidifies that area. That again, makes it hard for bacteria to overgrow in that region of the body. So stomach acid plays a really important role. The second thing, is bile secretion and the bile acid pool. So bile, as you know, is made by the liver. It is stored in the gallbladder and is secreted into the proximal, the upper part of a small intestine.

Bile does a number of things in the body. It, of course, helps you absorb fat-based nutrients because it does the surfactant reaction. But it also combines with long chain fatty acids, to create a surfactant that acts as an antimicrobial, right? So bile, in itself, as you're eating and you're digesting, bile is circulating. In a single meal, bile can circulate through your small bowel, upwards of 15 times, right? Where it's released in the duodenum, it coats through your small intestine, it gets reabsorbed at the end of the small intestine in the ileum, and then

it goes back to the liver where the liver will detoxify it. Meaning, removing all the toxins that bile picked up, because remember, bile also picks up... Is important for neutralizing and picking up toxins from the food and from the environment. And then it takes it to the liver, the liver cleans out the toxin, cleans up the bile and then resends the bile back to the gallbladder so it can be recycled again.

A single meal, you can go through 15 cycles of bile continuously coating the small intestine and acting as an antimicrobial blanket, if you will, to prevent bacteria from enjoying all of the food that's coming in and overgrowing, right? So it's there to protect the microbes, or it's there to protect the host from the microbes over indulging in all the food and beverage and liquid that's coming in, and preventing them from growing. Bile also does this other really interesting thing. Before it gets absorbed, at the end of the ileum, it activates something called the nuclear FXR receptor. That receptor at the end of the small intestine, will then turn on the intestinal epithelial cells, so the lining of the gut cells, to release antimicrobial compounds into the lumen and into the mucosa. So not only is bile acting as an antimicrobial itself, preventing bacteria from overgrowing when food is present, which is a time that bacteria would grow, it also triggers your intestinal lining cells to release antimicrobials, so that bacteria in that region are not allowed to grow, right? So bile does some really, really important things.

Peristalsis, the movement of the bowel, is a very important aspect in keeping the bowel... From keeping the bacteria in the small bowels from overgrowing. Because when food is allowed to stay and remain in one position, that gives more chance for bacteria to ferment and grow. Remember, bacteria have this lag phase in their growth, right? They don't grow immediately. So if you take back to... If you take, for example, a piece of meat or a fruit or something like that, and you set it out on the counter, there are microbes already on it, but it doesn't get spoiled in a matter of hours, right? It takes a few days for it to get spoiled, and why is that? That's because all bacteria have a lag phase and a log phase in their growth. The lag phase is a very slow growth movement in the beginning part of their life cycle. So it takes them hours, in fact, up to 12 to 24 hours, to come out of that lag phase and then start growing log rhythmically.

And when they start growing log rhythmically, because it is a log rhythmic growth, meaning they increase tenfold every cycle, then they grow very fast and then things start to escalate or things get spoiled very quickly, right? That's why food can sit outside for a couple of days, and then all of a sudden, it goes bad. And when it goes bad, it goes bad fast, right? So remember that log and lag phase growth. And the way, naturally, the small bowels designed, is to allow food to slowly move through there in a six to eight hour period, right? That good gastric emptying, that good peristaltic movement time, moves food through the system at that pace, where six to eight, maybe sometimes even 10 hours, it takes for the food to clear the system.

That's fine, because any bacteria there, that's not already inhibited by the bile or by the nuclear FXR receptor activation, is still not going to be able to grow log rhythmically and create a huge overgrowth problem. Because of food, its source of fermentation, its source of energy, is moving through at a pace that is faster than its ability to come out of the lag phase of growth. Does that make sense? And that's part of the reason why stasis is such a big issue, because when the food is allowed to sit there for 12, 13, 14 hours, then the microbes in that region are coming out of the lag phase growth and moving into the log phase growth, so then they can start overgrowing much faster. So that movement in the bowel, is so important as a protective mechanism.

And then we have this electrical sweeping mechanism as well, that sweeps through the empty bowel, called a migrating motor complex, that basically cleans out any debris and remaining food chunks and things like that, that may be in there, that may cause further overgrowth or problems, right? So these are the natural mechanisms that protect against SIBO. When you ask the question, why is it that some people do not have, or many people do not have this overgrowth in the small bowel? It's because they've got good stomach acid, they've got good bile secretion, and a high level of bile acid pool. They've got bio to activate the nuclear FXR receptor, they've got strong peristalsis and movement of the bowel, and they've got a strong migrating motor

complex. If you have these things in place, you're not going to overgrow bacteria in small intestine. And remember, these are dysbiotic bacteria. They're coming from another source, from the mouth, they're entering into the small bowel and they're entering into a place where if it's functioning the way it should, is really designed to hinder bacterial growth, right?

Michael Roesslein:

Got a quick question.

Kiran Krishnan:

Yeah.

Michael Roesslein:

The difference between peristalsis and migrating motor complex.

Kiran Krishnan:

Yeah. So peristalsis is the physical contraction of the bowel, right?

Michael Roesslein:

Yeah.

Kiran Krishnan:

So, it's kind of like squeezing toothpaste out of a tube.

Michael Roesslein:

Yeah, squeezing. The thing you feel when your belly goes [inaudible 00:38:27]

Kiran Krishnan:

Exactly. Yep. It's literally squeezing the food through the tube of your intestine.

Michael Roesslein:

Okay.

Kiran Krishnan:

And that's the emotion that occurs when there's food present in the gut, right? Migrating motor complex doesn't really work when there's food in the gut, and that's why it's only triggered by fasting. Yeah. And it's turned off the moment food shows up, so it's turned off the moment the stomach expands. Meaning, there's food coming in, the stomach expands, the migrating motor complex is turned off. Or when there's liquid that enters into the large... In the small intestine, or food enters the small intestine, the migrating motor complex is turned off. It turns back on after a certain number of hours of the bowel being cleared and empty. And it's a sweeping electrical motion. It's a tiny low level motion that basically sweeps through the lining and moves things down-

Michael Roesslein:

Much smaller scale, much more subtle. And it's more electric, you said, versus-

Kiran Krishnan:

Exactly.

Michael Roesslein:

Muscular.

Kiran Krishnan:

Exactly. Yeah. And you will feel that, to some degree. Part of the migrating motor complex is, after the hunger pains hit you or when you feel the hunger pains, after about two hours, is when the migrating motor complex starts running, right? So one is important to move food along and not allow food to stay in the stomach or the small bowel for too long. And the other is important to clean up and sweep through after the food's been there, right?

Michael Roesslein:

Gotcha.

Kiran Krishnan:

So, that's the thing. So now, if you have these five mechanisms functioning, you will not get SIBO, right? Even if dysbiotic bacteria make its way into your small bowel or into your upper GI tract, they're going to get knocked out by one of these things and they're not going to be allowed to overgrow, right? So then when you look at the things that are creating dysfunction in those five protective mechanisms, my big question is, if you disrupt those mechanisms, does that lead to SIBO, right? And if that's true, if we can show that when you disrupt those mechanisms, SIBO becomes a risk, then we know that those are the underlying mechanisms that are protecting us against SIBO, that are becoming dysfunctional, that is then leading to SIBO.

So the first one being, stomach acid, right? We talked about out how that's important. And when you think about the oral route as a main source of dysbiotic bacteria, then stomach acid becomes even more important, because stomach acid is known as a gastric barrier, right? Its job, in part, among other things, is to kill and neutralize unwanted bacteria that is entering in through the oral route, including all of the bacteria we constantly swallow almost every minute of every day from our mouths, right? Your oral bacteria are not supposed to be in your small bowel, in viable form. The stomach acid kills and neutralizes those bacteria before they can get into the small bowel, right?

So that's what the stomach acid is supposed to do. The stomach acid, is of course, magnesium dependent, in terms of its formation and excretion. And if you are, as simple as really deficient in a micronutrient like magnesium, you could have an issue with ACL production, right? And if you have an issue with ACL production, you have low stomach acid. When you have low stomach acid, more microbes from the oral route, including all of the ones you swallow every day with your spit, will actually survive through and enter the small intestine in a viable state. The other thing is, one of the main stimulus for the production of stomach acid, is histamine. So histamine acts as a signal, and binds something called the H2 histamine receptor, which is the most significant contributor to stimulating the release of stomach acid. And when you think about that, think about all of the antihistamine drugs that people take for allergies and all of that stuff, right? Could that be inhibiting the most significant activator or contributor to the production of stomach acid, right?

So deficiencies in magnesium, we know stress, we know H. pylori infection, maybe antihistamines, these things can all reduce your stomach acid production. And that in itself, could become a problem, because that's one of the five critical protective mechanisms against SIBO. Now the most prevalent form... Oh, sorry. The most prevalent form of inhibiting stomach acid, is through the use of PPIs, right? Proton pump inhibitors.

They've always been... Since they're released, they've always been one of the top two or three drugs being sold, and they are... Now they're OTC, so anyone can kind of walk into a store and buy them without a doctor's prescription. But they are one of the top selling categories of drugs in the United States, and they inhibit stomach acid production, right?

So if that's the case, if inhibition of stomach acid production is a risk factor for SIBO, then we should be able to see, that when you take a PPI, it actually induces SIBO, right? And we'll see that in a second. In the meantime, let me just mention bile again. And I talked about how important bile is. Again, it's made in the liver, stored in the gallbladder, released. And it can be recycled about upwards of 15 times, through the digestive process. And bile acids are so important, because of course, they also enhance the absorption of fat soluble nutrients. They detoxify the body from fat soluble toxins, and then of course, they upregulate the nuclear FXR receptor at the end of the small intestine in the ileum, which then promotes the release of antimicrobials from the intestinal epithelium. So the barrier cells themselves, are releasing antimicrobials into the lumen, to prevent bacteria from growing in that space.

Now also, some of the primary bile salts, which are found in bile acids, have been shown to promote the germination of C. difficle spores. And some of it, the secondary bile salts, will actually inhibit the germination. So what's so interesting about this process, is if you have C. Diff as an opportunistic organism sitting in the very beginning of your small... Of your large intestine, it can actually be promoted to grow, if primary bile acids enter into the large intestine at higher amounts, right? Because remember, primary bile acids are supposed to get reabsorbed at the end of the small intestine, and not enter into the large intestine. But about 5% of that primary bile acid is actually converted to secondary bile salts, by microbes in those small intestine. Those secondary bile salts will enter into the large intestine, and those will actually inhibit the germination of C. Diff spores, right?

So what's interesting about this, when you think about C. diff and how common that infection is and how it's associated with taking antibiotics, a big driver here could be, you take an antibiotic, it kills off the small intestinal bacteria whose job it is to convert primary bile acids to secondary bile acids at the very terminal end of the intestine. And if that vector is not there, or at lowest levels, you're going to get more and more primary bile acids moving into the large intestine, where it will actually promote the germination of C. Diff, hence you start getting an overgrowth and opportunistic infection with C. Diff. So it's so interesting to see, that if you disrupt one or two simple things, it can be a lifelong of medical conditions that you're dealing with, right?

So decreasing the level of bile acids in the gut, favor gram negative bacteria. So keep that in mind, right? Bile acids being an antimicrobial, it works really well in terms of inhibiting bacterial growth. It, in fact, even works better on gram negative bacteria. Because remember, gram negative bacteria only have a lipid bilayer. They don't have that firm cell wall structure around them. And the lipid layers are fatty acid layers, right? And so when you have bile, the bile will actually conjugate with the fatty acid layers that are in the cell membrane, and really disrupt the growth and functioning of gram negative bacteria. So if you see bile decreasing your bile flow or your bile acid pool, that gives more opportunity for gram negative bacteria, which are the dysbiotic types of bacteria, to grow in your small intestine.

And then when you look at peristalsis and the migrating motor complex and their role in SIBO, it becomes clear, because there's a couple of studies that have shown this. Because remember, this is number three, protective mechanism against SIBO. I mentioned both peristalsis and migrating motor complex. This is a really interesting study published in 2014, where they were looking at pediatric cases of small intestinal bacterial overgrowth in all of these low income countries, right? We've all seen those images and pictures of the starving kids in Africa, and they have these big bloated bellies, right, even though they're not eating any food. That's a quintessential example of a low income country, and kids having this crazy overgrowth of bacteria in the small bowel, and this constant bloat. This study was interesting, because they said it was their hypothesis,

that the mechanism of SIBO development in the setting of unsanitary living conditions, stems from repeated exposure to abnormal levels of lipo polysaccharide.

Remember, gram negative bacteria, we shift in SIBO from having predominantly gram positive to predominantly gram negative in the small bowel. And gram negative bacteria, all of them, contain LPS, Lipopolysaccharide, right? So what this study is showing, is that the development of SIBO in these low income countries, stem from continuous and repeated exposure to Lipopolysaccharide from gram negative bacteria. And in this case, they hypothesized, from contaminated soil and drinking water, which aggregates the migrating motor complex, leading to luminal stasis, right? So the presence of LPS, stops the migrating motor complex. And the presence of LPS, stops the peristalsis activity. And so it's no surprise that SIBO has a predominant feature of the bowels not moving, right? An arrested peristaltic function and an arrested migrating motor complex. And all of that is driven by high levels of LPS. High levels of LPS is another characteristic of SIBO dysbiosis. Because remember, you go from gram positive, which has no LPS, to gram negative, which has LPS. And you have this [inaudible 00:49:58] shift, right? So the pieces start coming together. You go, okay.

Kiran Krishnan:

...the pieces start coming together. You go, okay. So taxa shift to gram negative. That means lots of LPS. Oh. And the LPS is somehow connected to stopping the bowels from moving. Right? So the picture starts to become a little bit more clear. In other studies, like in this study, they showed that in animal models, E. coli derived LPS has been shown to decrease both the frequency and strength of the small intestinal contractions and that it can completely eliminate the migrating motor complex. That is super interesting to see. So this is... here's an example of that article where they showed that the induction of endogenous tumor necrosis factor, so this is TNF alpha, will suppress the centrally stimulated gastric motility. What they showed is that systemic LPS, so endotoxemia, what we've been talking about for years now, endotoxemia and having too much LPS will induce TNF alpha, which will stop gastric motility.

And this can occur within 60 minutes of injecting LPS. So they did this study on animals, of course. They took animals with completely normal bowel functions, fed them a meal and just before feeding them a meal, injects LPS into the circulation of the animals. That LPS causes inflammation not only systemically but in the gut. And that inflammation releases something called TNF alpha. TNF alpha then plays a role in stopping the migrating motor complex. And in this case, motility agents like gastrokinetics, they were not able to regenerate or reactivate the migrating motor complex. And what was so interesting about this is if you had the question of how does LPS, lipopolysaccaride, stop the migrating water complex and the peristaltic movement? It's because LPS that's derived from the gut will leak through the gut and make its way up the vagus nerve, where it'll stop at an area in your brain stem called a dorsal vagal complex.

In the dorsal vagal complex it can actually will bind two receptors that will drive it... it'll drive inflammation and then that'll cause binding to receptors that will actually stop the signals from the brain to the bowel. So it's LPS that's generating this issue.

Here's another study following up on that, where they show LPS induced suppression of gastric motility. It can be relieved if they use a compound that counteracts the inflammatory response of TNF alpha. So the stopping of the migrating motor complex and peristaltic activity in the gut is driven by this taxa shift towards gram negative bacteria. Gram negative bacteria now contain a lot more LPS in the gut than previously. And that LPS is going to cause inflammation and was going to end up leaking through. And when it leaks through, it can make it's way up to the dorsal vagal complex in the bottom of the brain stem where it will bind and actually stop the signals from the brain for the bowels to move and for the peristaltic activity.

So this is when the bowels undergo stasis. And because the bowels have undergone stasis, then the food that you eat, move through the small intestine quick enough, that means you feel full for longer, and it may be

remaining there long enough for the bacteria to exit out of lag phase growth and actually go into log phase growth. And then when it's in log phase growth, the bacteria can really take advantage of the food that's present in the system, and really grow rapidly and create lots of gas and bloating and so on. So this follow up study is really important because the author, again, induced inhibition of gastric motility with systemic LPS administration. So they injected the LPS into peripheral circulation, and it still had this effect on stopping the movement of the bowels by increasing the expression of TNF alpha through the inflammatory system.

And then when they used an anti TNF compound in these animals, they were able to show a restoration of the central thyrotropin-releasing hormone, which increases motility. So hopefully that makes sense. So the simple progression. Taxa shift to gram negative, gram negative provides more LPS, LPS causes leaky gut, and then that LPS leaks through. Once that LPS leaks through you get the stopping of the bowel because a migrating motor complex and peristaltic signals don't go through the vagus nerve anymore. They're getting stuck at the brain stem. And then because the bowels in stasis, then those dysbiotic bacteria that are in the small bowel now have a better chance to grow and proliferate and get overgrown because the bowels aren't moving, the bacteria is allowed time to come out of its lag phase and enter into log phase growth.

And how common is this endotoxemia? Some of you guys have seen the original study that we did on endotoxemia looking at this huge increase in LPS when seemingly healthy individuals eat. And we found that 55% of the healthy young normals that we screened had severe LPS leaking through. So it's a very common problem. And again, one of the tenants that I had come up with was that whatever drives SIBO has to be pretty common because it's so relevant... it is quite relevant and the prevalence of SIBO is really quite high in populations. And then one of the big problems here is if people have SIBO, they start going away from plant-based foods and start going away from fiber and so on, and they eat more fat and protein because fat doesn't get fermented in their gut and they don't have the bloating and all that, but the problem is increased fat intake may also increase endotoxemia even more. Which means even more LPS is getting through, which then slows down the bowel even more. So that's something just to think about as well.

So when you look at the natural protective mechanisms and when you talk about stomach acid, stress, as I mentioned, reduces stomach acid, H pylori infection, which the CDC and the WHO assume at least 50% of the population has H pylori lower infections. Zinc deficiency and then of course PPI and acid use. And again, if PPIs stop or dramatically reduce stomach acid production, and stomach acid is a critical aspect of preventing SIBO, then using a PPI should induce CBO. And so this meta-analysis paper shows that several meta-analysis and systemic reviews have reported that patients treated with PPIs as well as post gastrectomy patients have a higher frequency of small intestinal bacterial overgrowth compared to patients who lack the aforementioned conditions. So at this time they concluded PPI induced dysbiosis is considered a type of SIBO.

So you stop stomach acid production, you're likely going to end up with SIBO. Why is that? Well that's because the stomach acid is killing all of the dysbiotic bacteria that you're swallowing from your mouth every single minute of every single day. It's providing that barrier function. So if we compromise stomach acid, those dysbiotic microbes end up in the small bowel in a viable state. And especially if they're entering into a small bowel that's not moving. That gives them a great chance to metabolize food and to grow their numbers pretty high and then shift that part of the microbiome from gram positive to gram negative. Here's another paper showing increase in incidence small intestinal bacterial overgrowth during proton pump inhibitor therapy. Studies show that SIBO was detected in 50% of patients that use PPIs. 50%. Half of the patients that use PPIs have SIBO.

And 24 and a half percent of patients with IBS and 6% of the healthy control subjects. So 50% of patients using PPIs end up with SIBO. Compare that to the same age match population, only 6% of healthy control subjects will develop SIBO. That is huge. That is a huge difference between the two. So clearly compromising stomach acid makes you susceptible to SIBO. There was a statistical significant difference between patients using PPIs and those with IBS or healthy control subjects. I mean, so it's really quite crazy because we, again, associate

IBS with SIBO when only 24.5% of patients with IBS were properly diagnosed with SIBO where it's just using a PPI means you're likely have SIBO.

The other mechanism of action is... Sorry. The other protective mechanism is bile, right? But bile, bile acid secretion and recycling can be compromised by a number of things. For example, gallbladder removal. Think about how many people a year just have their gallbladders snipped out. Obstruction of the bio ducts, liver dysfunction, and dysbiosis. And that's why to me, here's another very common thing that can drive SIBO risk is liver dysbiosis, or removal of the gallbladder. Just as PPI use is a common thing that has a very high association with SIBO. So does liver dysfunction and removal of gallbladder.

Let's focus on just the liver dysfunction itself. This paper shows that some studies reinforce the concept that small intestinal bacterial overgrowth plays an important role in the pathogenesis of non alcoholic fatty liver disease through endotoxins of bacteria and tumor necrosis factor as effective mediators. Remember TNF activation and endotoxemia, which is the translocation of LPS endotoxins into circulation, was a big driver of stasis in SIBO. And then that also allows for further and further taxa shift so you have more and more gram negative bacteria in the small intestine, which means more LPS leaking through.

That LPS leaking through also makes its way into the liver through the portal circulation, which then causes a significant toxicity to the liver, and plays a role in the pathogenesis of non-alcoholic fatty liver disease. So SIBO and liver disease are tied, are tied in there really closely. And when you look at the data and prevalence rate, it really becomes quite clear. So in this paper, they looked at 372 eligible patients. 141 of those or 37.9% had tested positive for SIBO. That's called a study group. And 231, which is 62% were negative for it. So, that's a control group. They then they looked at the prevalence of non-alcoholic fatty liver disease. Non-alcoholic fatty liver disease occurred in 45.4% of the study groups.

So those are the people with SIBO. And of the control group, they were only present in 17% of the people. So a significantly higher, almost two and a half times more risk of developing non-alcoholic fatty liver disease if you also had SIBO. So they're all tied. Patients in this study group were found to have higher rates of elevated aspartate aminotransferase, that's a liver enzyme. And alanine aminotransferase, again, this is a common liver enzyme. Of course, type 2 diabetes. Remember the connection there between the oral microbe, SIBO, type 2 diabetes is tied into all of this mechanism as well. And then hypertension, and hypertension again is also part of the metabolic syndrome. So, these are all the underlying drivers and conditions that are associated with or drivers of SIBO.

So when you look at the peristalsis and migrating motor complex, which is an important natural protective mechanism, here are some of the things that end up reducing that is gastroparesis, celiac disease, enteropathy, diabetes, hypochlorhydria, which is the lack of stomach acid. And then of course, LPS as well. And we know that a key aspect here is when you're looking at the treatment of SIBO is you have to address the liver because the liver in most people with SIBO is dysfunctional, the bile acid pool, the stasis in the bowel, and then also the issue its stomach HCL. And remember, all of these people also have that taxa shift so they have a predominance of gram negative bacteria in the small intestine, which means that their small intestines producing a lot of LPS. That LPS is leaking through. That's making it to the dorsal vagal complex shutting down the peristaltic activity. And then that LPS further goes to harm and create toxicity to the liver because it enters through the portal circulation damages the liver.

Now, when the livers damaged, it produces less bile. That negates another one of those really important protective mechanisms. And when you produce less bile, what happens? You get your bacteria overgrowing more. And if you've had a taxa shift that overgrowing bacteria is making more LPS. That more LPS makes your gut even more leaky, lodges itself deeper into the dorsal vagal complex, thereby again stopping the bowel, and further harming the liver again. All the while, because all of these symptoms are setting in, you're taking PPIs and antacids and all that because you're feeling reflux and so on. And so that in itself is destroying the barrier that protects the small bowel from getting continuously inoculated by pathogens from the mouth.

So in addition to when you look at comprehensive placebo treatment, in addition to targeting the overgrowth with antibiotics and antimicrobials, it becomes important to address the underlying issue of that stasis, which involves LPS, which is LPS mediated, systemic TNF alpha upregulation, and the central motility aberration that follows that. Prokinetics don't help in that case because those study on LPS lodging itself in the dorsal vagal complex, inducing an inflammatory response which then stops the signals from the brain to the gut. In those studies, they tried to use prokinetics to try to stimulate the gut to move and it did nothing. And the reason why is because prokinetics stimulate the brain, and the brain then sends a signal down to the gut to start moving. And if the communication between the gut and the brain is disrupted, then the prokinetic is not going to do much.

Low HCL and gastroparesis must also be addressed. Gastroparesis is lo slow gastric emptying time. So again, that slows down the whole movement of food through the GI tract. And that low HCL allows for dysbiotic bacteria to survive through and make it into the small intestine. And of course, liver support is absolutely crucial and critical, because not only do we need to give the liver the bandwidth to deal with all of the toxins coming through, but we also need to count on the liver for producing a really strong, heavy bile acid pool, which it won't do and it'll decline from doing as the gut becomes more leaky and as more LPS ends up there.

So to reduce the risk of comorbidities, mucosal damage, and mucosal inflammation has to be addressed as well. And then all of the poor colonic, saccharolytic bacteria, all of those awesome friendly bacteria including the keystone species like [Faecalum bacter 01:07:04] or Bifidobacterium longum, they're not getting the food that they need to provide the benefits to the host. And the food that they need are the fibers and FODmaps and so on. That's what they consume in order to proliferate their activity in the large bowel, which is the production of short chain fatty acids and metabolism and breakdown of compounds. And then of course working and stimulating the immune system as well.

So in thinking about SIBO, we came up with a few solutions to address some of these root cause issues that we think are driving the problem. And when you think about everything I've said, it starts to become clear why SIBO in itself is not a condition, because SIBO comes about because of an opportunistic situation where a shifting microbial population in your large bowel is now favored to grow because of a number of dysfunctions. And those just functions are liver dysfunction, stomach acid, HCL dysfunction, dysfunction in your gallbladder, or the bile ducts are not releasing the bile properly.

Also leakiness in the gut and the stasis in the bowel that occurs from leakiness in the gut and LPS lodging itself in the dorsal vagal complex. All of those things on their own are problems for your overall health and wellness. They also do happen to lead to bloating. And so when we start looking at the success, or trying to measure the success of SIBO protocols, our knee jerk reaction is to go, how quick did the bloating stop? Or did the bloating stop? When in reality, we should be saying, how healthy is your liver? We need to be supporting the liver because it's inundated with toxicity. We need to compete against the gram negative bacteria that are in the small bowel. We need to improve bio flow. We need improve stomach acid production and secretion. Those are the key things that have to happen in order to get SIBO under control.

And we also have to deal with the oral microbiome because if your mouth is sending in really high levels of these kind of pathogenic organisms, not only is that bad for your gut, but that's a poor indication for your mouth as well. Because remember people with gingivitis which 94% of Americans are confirmed, or not confirmed, sorry, cause we didn't talk to everyone of the 94% of Americans, but studies show in population trials that up 94% of Americans have some degree of gingivitis. And that is also driven by high LPS gram negative strains in the oral cavity. And that LPS is leaking directly into the blood. And in the blood, it can go and drive inflammation in the heart, in the brain and the hundreds of different places. So, mouth dysbiosis and the leakiness in the gums are also associated with chronic illness.

And so all of this put together means that there are a number of issues at play here that lead to bloating, but the bloating is in itself not the condition. All of these other issues are issues that will drive other risk factors in

chronic illness. So your liver becoming dysfunctional over time because of the bloat, because of the SIBO that leads to the bloat. To me, it becomes so much more important to pay attention to what's happening to the liver and start helping and supporting the liver, and start helping and supporting the lining of the small intestine and the stomach acid production than it is to worrying about the bloat all the time, because dysfunctions in those other systems are going to drive other chronic diseases. And then also dealing with your oral microbiome, oral hygiene to reduce some of that opportunistic pathogen load in the mouth or the oral cavity. That in itself can help.

So we created when it comes to SIBO, when we looked at these mechanisms and we looked at the things that were going wrong in a typical SIBO gut, and we looked at the underlying root causes that could to be driving this, we came up with a few things that we needed to address. So number one, ginger root extract. Ginger root is fantastic for calming and soothing the gut. But with the high concentration ginger root extract, it accelerates gastric emptying and soothes out the nausea and their irritable bowel like feeling. And so that gastric emptying becomes important because the bowels have to move. Gut guard is a licorice flavonoid that will protect the gastric mucosa by balancing H pylori levels. That remember is so important because about 50% of the population has elevated H pylori and elevated H pylori compromises stomach acid production.

And then we also found this artichoke leaf extract, which can actually stimulate bile production and balance cholesterol levels. So this becomes so important because rememberable bile is a very important aspect of maintaining low growth levels in the small intestine. So when we look at going beyond the bloat, our overall recommended protocol is if you are using an antimicrobial, and in my view, you don't necessarily need an antimicrobial to deal with this, but let's say you are using one, you would use a MegaIgG and HU58 during the antimicrobial phase. Now why use these? Well, because when you use an antimicrobial it's going to kill everything. It's going to kill the good and the bad bacteria. There's a risk that bad bacteria come back faster than the good as the antimicrobials slowed down, tapered off or even stopped.

The continuous use of HU58. We haves looking at how HU58 negates the opportunistic growth after an antibiotic. So it would certainly do that after an antimicrobial. So, that's there to protect your gut from severe dysbiosis once the antimicrobial is out of the picture. The other thing is the IgG binds up toxins. So it binds mold toxins and a whole bunch of bacterial toxins and neutralizes microbes and viruses itself. So if there's any killing going on in the beginning, you definitely need some IgG in there to neutralize all of those viral and bacterial particles to get it out of the system so they don't trigger autoimmune and aberrant immune responses. So if you're taking antimicrobials, you're deciding to take antimicrobials, then I would start with these two products during your course of antimicrobial therapy. I would also start with Mega Guard before all of your meals. You take it about 10 to 15 minutes before each meal, and you'll feel a significant difference in how the bowels move and feel after that meal.

Because again, we're improving secretion, bile acid secretion, gastric emptying, and the migrating motor complex peristaltic activation. And then as you get through, if you're doing antimicrobials if you get through it, then towards the end of that phase you want to start with Mega Spore and Mega Mucosa, because Mega Spore of course will increase the diversity within the microbiome, will resolve that leaky gut so that LPS stops leaking through. Remember LPS being big culprit here for creating the stasis in the bowel. So Mega Spore takes care of that. Mega Mucosa will take care of the thinning of the mucus lining which tends to happen in SIBO as well. We want nice thick mucus barriers on top of our intestinal epithelium and Mega Muco-

PART 2 OF 4 ENDS [00:50:04]

Kiran Krishnan:

... Barriers on top of our intestinal epithelium, and MegaMucosa is going to be critical for doing that. In SIBO people, you could see that the mucosal layer is damaged and shrinking, right? So that makes things easier to

leak through and cause more problems, cause more havoc and inflammation. And then finally, as symptoms start to improve significantly, where you don't have to completely eat a very restrictive, almost no carbohydrate kind of diet, once you start getting significantly better, then you start using the MegaPre product, because the MegaPre is a set of oligosaccharides that predominantly make it to the large intestine.

But what happens is all of those years of either a low FODMAP diet or antimicrobials or antibiotics, years of that will lead to dysbiosis in the large intestine. So the large intestine needs to start seeing some love from this protocol, because if the large intestine becomes completely dysbiotic, then that's going to surface as a bigger problem to the bowels and to overall health than just the small intestine being dysbiotic and dysfunctional, so it becomes at some point important to start taking a prebiotic as well.

So this is kind of the basic Going Beyond the Bloat protocol that we look at with SIBO. The other things I do is you could look at intermittent fasting, which will try to help the situation, and then of course you can also do oral care, so you reduce that opportunistic pathogen load in the mouth. You can also take supplemental HCL. I recommend that to a lot of people, if they're dealing with SIBO and bloating and IBS-like symptoms, that supplemental HCL can make all the difference. And if your liver is not producing the level of bile that you want, even when you're supporting it, the other thing you can look at is ox bile as a supplement, right? So you can get some HCL into the system and get some ox bile into the system to help with those protective mechanisms as you're trying to rebuild the small intestine. So I think that's it. Hopefully that made sense to everyone, and I'm guessing, I'm sure that there's questions.

PART 3 OF 4 ENDS [01:15:04]

Michael Roesslein:

There's so many questions that I'm going to have to track you down after this to schedule something in January to maybe do some Q and A. So yes, there are questions. We'll try to get to a few, at least a few, but I haven't taken notes that quickly and frantically since I was in grad school. So I have four pages of typed notes in size nine font.

Kiran Krishnan:

Wow.

Michael Roesslein:

I'm going to try to turn that into a PDF guide that I'm going to create and send out to everybody, but that made a lot of sense. I'd like to mention that also you guys created the FODMATE, which one of the problems, because we did that webinar last year, and one of the problems that you mentioned during that presentation was that the SIBO prevents you from being able to eat these foods that contain all these valuable prebiotics that help out the large intestine and the overall healing of the situation, so then we go restriction, restriction, restriction, restriction.

Kiran Krishnan:

Yeah.

Michael Roesslein:

So I've actually recommended to a lot of people that deal with bloating and SIBO-like symptoms to try the FODMATE when they're eating, and if that resolves their symptoms, it's probably pretty likely that they're dealing with a SIBO situation and some sort of small bowel bacterial overgrowth, right?

Kiran Krishnan:

Right, [crosstalk 01:18:45].

Michael Roesslein:

And that can help symptom management while you're doing larger scale... Like digestive enzymes, you didn't mention in here, those are, for those who don't know, the FODMATE are like specialized digestive enzymes that relate specifically to FODMAP foods, because the idea there is to help people be able to tolerate eating certain foods that they usually can't tolerate, so that they can get the benefits from those foods while they're working to heal the underlying dysfunction.

So that wasn't in this presentation, but I want to throw it in there as a suggestion for those who deal with the bloating with the eating. Now, we have, yes, there's a... All right, hold on. Please put the questions in the Q and A, I'm going to... Let's see, we're already at an hour and a half. I'm kind of almost out of time, but there's literally like 50 questions.

Kiran Krishnan:

Let's try to do rapid fire. [crosstalk 01:19:38]

Michael Roesslein:

We can do some rapid fire. There's no way we're going to get through them all, but I will... The hydrogen and methane SIBO is basically a creation of the breath test, I think, but is there a difference in recommendations based on hydrogen or methane SIBO? That was like four of the questions.

Kiran Krishnan:

I can't rationalize in my mind, I'm just putting this up so people see what the FODMATE looks like, I cannot rationalize why there would be a difference in approach, right? Because I don't think that the hydrogen or methane has a different approach in how the condition developed. I think it's just which bacteria ended up getting in there and proliferating, and what gas did they produce. It's still small intestinal bacterial overgrowth. All the underlying mechanisms are still at work here, where you have liver issues, you've got stomach HCL production issues, you've got peristalsis issues, migrating motor complex issues. All of those things are still present in both. It's just a thing, yes, in the breath test, to distinguish, and then for some reason they treat it slightly differently.

So to me, it doesn't matter what you have as far as whether it's hydrogen or methane dominant. I would just still address all the same things. Because I haven't seen any science that says that in hydrogen, this is what all the problems are, in methane, this is what the problems are.

Michael Roesslein:

Okay, that makes sense. About seven people asked, what if you don't have a gallbladder? You talked about that in the presentation, that that does inhibit bioproduction and bio recycling and all of that stuff. You mentioned ox bile as a supplement. Whenever I worked with clients before, if somebody didn't have a gallbladder, I generally recommended ox bile and lipase as a digestive enzyme, because they're going to struggle digesting fat. Would you add anything to that comment?

Kiran Krishnan:

Yeah, I think that's the key. I think ox bile is a key there if you don't have a gallbladder. There's no way to escape the missing organ that is so important to release bile into the system, so you have to just take supplemental bile, and the dosing of it, you'll have to adjust around.

Michael Roesslein:

Okay. Sorry, I'm answering one of them type. Okay, testing for low stomach acid is really invasive. There's some that believe that you can just take a whole bunch of stomach acid or [inaudible 01:22:17] HCL and see at what point it burns or whatever, or there's... I've actually done a test where you swallow a pill on a string or something, and then it tests a strip of... It sucks, and I gagged, and it's pretty invasive and it's not fun.

Usually, I just go on symptoms of indigestion and bloating and difficulty. High stress almost guaranteed low stomach acid. Any sort of nervous system dysregulation to being sympathetic almost guaranteed low stomach acid. Disrupted circadian rhythm almost guaranteed low stomach acid. Eating on the fly type stuff, most people in this culture and society have low stomach acid. So testing's invasive. You don't want to swallow that thing, I promise. Best way to increase bile naturally, you mentioned the HCL Guard product you guys formulated for that.

Kiran Krishnan:

MegaGuard, yeah. Mm-hmm (affirmative). T.

Michael Roesslein:

There's bitter foods too, right? [crosstalk 01:23:21]

Kiran Krishnan:

Yep. Yeah, bitters can help with that to a certain degree. This artichoke extract we found that we work with is actually a prescription product in parts of Europe, like Germany, that is specifically for increasing bile flow. So that's why we put it into the MegaGuard. So that's something, you take that and it's going to start stimulating bile.

Michael Roesslein:

Okay. What type of fat could make SIBO worse? The fat that triggers more LPS production if there's bacteria there is saturated fat, right?

Kiran Krishnan:

Yeah. Mm-hmm (affirmative). So if you have SIBO and you're taking a bunch of coconut oil in your smoothies and all that in the morning to try to get some calories in, because you're not eating a lot of things, that's actually going to make the underlying drivers worse.

Michael Roesslein:

If antibiotics start the chain of events leading to SIBO, or can, it seems to be one of many. It seems like this is a destination with many roads that lead to it, and many doorways that people can come in, and they all tend to start a cycle where one contributes to the other, contributes the other. So it's widespread. Would glyphosate come into play here, which is an antibiotic? I would guess so.

Kiran Krishnan:

Yeah, absolutely. I mean, anything that can start causing disruption to the microbiome, that leads to the leakiness in the gut and LPS translocation, certainly can. And then I think the lack of adequate stress response, because you're dysbiotic, and that continuous HPA activation, that compromises stomach acid production, then that allows more and more the dysbiotic oral bacteria to inoculate the gut, or poor oral hygiene.

It's a number of factors. That's why when I first looked at it, and I was making all these connections between drivers of this condition, it became clear that it is multifactorial, because there are numerous factors that drive each other and each of those factors drives the formation of SIBO itself, right? And to me, the scariest part of it all is that the liver is continuing to become dysfunctional, right? The gut is continuing to become more leaky. More LPS is leaking through. The good beneficial bacteria in the large bowel, that are the ones that repair all of this damage, they're not getting the food they need, right? And H pylori is increasing over time.

So when you look at all of those things, to me, those are the scarier things, and more important things to pay attention to than bloating, right? So that's why I said in the beginning, looking at the bloat as the success of a treatment is something that has caused us to negate the best approach to this problem, right? Because if a SIBO person takes something and the bloat doesn't reduce in the first two or three weeks, they're going to be less interested in that as a solution, right? So if we follow this kind of protocol, you're going to start addressing lots of the stuff that is driving it at the root cause. The bloat may come down in the short term, or it may not, right?

Certainly, with the FODMATE, people experience a bloat reduction almost immediately, taking it, so that is an important aspect of it. But in general, you need to do these kinds of things to improve all of the other drivers, because the bloat in itself is not the condition. That's just of one of the symptoms

Michael Roesslein:

Makes sense. Acid reflux, we actually have another presentation when... I don't even remember if it was a presentation, but it was a webinar. Send me an email at Michael@rebelhealthtribe.com, I'll get you the recording to it where we talked a lot more about acid reflux. There's several questions in here about acid reflux, but that's a whole 'nother presentation, because there's questions about PPIs and acid reflux, and there's a lot of the similar mechanisms in play, and we did a really good webinar on that. It was probably almost two years ago. Maybe we'll do another one next year on that, but I'll send you a replay if you email me. I'm trying to... Gallbladder removed, we already did that one. So many gallbladders removed. The licorice in the MegaGuard is not the type that causes high blood pressure or increases stress hormones, right?

Kiran Krishnan:

That's right, yeah. So it's a fraction from normal licorice extract that does not cause that blood pressure increase. It's a flavanoid, specifically, that has that anti H pylori effect, but doesn't cause the high blood pressure.

Michael Roesslein:

Okay. How does MegaGuard affect stomach acid levels? I can't take anything that increases some... Yeah, someone's gastritis situation, where anything increasing stomach acid is bad. I would guess they would need to heal that before being able to treat the SIBO, but I'm not sure.

Kiran Krishnan:

Yeah. I mean, I think you'd have to look at the root cause of what is driving the gastritis. The MegaGuard won't impact gastritis in a negative or a positive way, so you could still take it with that, even if you have an overproduction of HCL, but yes, you'd have to address the overproduction of HCL as well at some point.

Michael Roesslein:

You mentioned doing this protocol if you're going to go with antimicrobials, but how does the protocol change if you're not doing antimicrobials? Would you just skip the first two things?

Kiran Krishnan:

You could, or what we do with some people is we actually keep them on those first two things to address any pathogens that may be present, right? Because these things, both the IgG and the HU58, will be very specific in going after overgrowing pathogenic organisms. And so you could do it as a kind of an intelligent anti pathogen, or anti opportunistic component to the phase, but you can also jump right into the MegaSpore. But we often will, people who have been on multiple antibiotics, multiple rounds of the rifaximin, and have had the SIBO rebound, they likely have more and more aberrant growth in their gut. So for those people it might be good to have this, and then also anyone that has had mold exposure issues in addition to SIBO and IBS, right? So the MegaIgG really helps take care of that, to a certain degree.

Michael Roesslein:

Okay. Any rough ballpark on how long these phases, you usually recommend them for, of this, like the antimicrobial with the MegaGuard HU58, and the IgG? It says towards the end of the antimicrobial phase. This is generally going to be run by a practitioner, and these instructions are for practitioners. So we can't give specific, this is what you need to do as a person doing this on your own. But I don't know, is there any ballpark, [crosstalk 01:31:14]?

Kiran Krishnan:

You go by feel, right? So let's say you decided to start with the MegaIgG and HU58. You start taking those together. If you're getting to a point where you're significantly reducing the impact of certain pathogens in the gut, you'll feel that as a difference. You'll feel things like you're sleeping better, and your body does agree with food better. You get less cramping, less bloating, less discomfort, maybe less soft stool, if that's one of your primary problems. So you'll start noticing kind of positive changes in your gut, which will then have positive changes systemically in terms of sleep and mood and so on.

And then once you feel like, okay, things have progressed quite a bit for a couple of weeks, then you could start on the next phase, right? And from the beginning, you should be using MegaGuard with your meals, right? And FODMATE as well, especially if there's going to be even a single FODMAP in your meal. You want to start using these two with your meals and then moving through those other phases by feel.

Michael Roesslein:

Okay. All right, I can answer a lot of the questions that are in the chat. So I still have the chat questions from the last webinar all listed that I've been trying to find time to go through to answer some of them. I'm going to put these with those. I'm way over the time that I'm supposed to be here, so I'm going to have to go. I've been on Zoom for close to nine hours today, so I need [crosstalk 01:32:54].

I see a lot of oral microbiome questions. I'm actually, if you know anyone, I know there's some really good functional dentists that talk a lot about oral microbiome, I might hit you up for a connection if you know anybody doing really good work there, because we want to have someone do an oral microbiome specific webinar.

Kiran Krishnan:

Yeah, for sure.

Michael Roesslein:

So I think that'd be really valuable, given the connections here and the connections to everything else, and huge connections just to heart disease and heart attacks and all kinds of other things related to the mouth. You mentioned the LPS from the bacteria in the gums get in the blood. And the last thing is, do you have an opinion, and like four people asked about it, and it's something I've taken, is TUDCA, T-U-D-C-A, for liver support, do you know much about the mechanism of that or how it affects bile production?

Kiran Krishnan:

I don't, no. I'm not familiar with that.

Michael Roesslein:

Okay. No worries. Okay. I am going to copy this Q and A and do the best I can to answer a bunch of them. I took four pages of notes. We may try to wrangle you in in a couple months to a Q and A comeback, where we just do Q and A to cover some of these from this one and the last one. I think that someone's going to email me, they know a perfect guy to do oral microbiome. Perfect. Oil pulling, yes. Dr. Kevin Stock. Okay, I got a bunch of names. Shoot me emails, people, michael@rebelhealthtribe.com, and I will get them and I will try to find the right people to come in and talk about things.

So we're at hour 45. Thank you so much, the presentation is awesome. I, like I said, took four pages of notes. My goal was to get this PDF put together by Friday and send it out. We will see how feasible that is. I want to make it more readable than what my shorthand, sloppy, ridiculous notes are. It's not much good if you can't understand it, but we'll get the recording out this week. We'll get the PDF, we'll get the transcript, and I'm going to probably create some sort of product bundle based on this presentation and throw it on sale for the weekend, for those who want to stock up. I didn't do that. I usually do that for the presentations, but I had no idea which direction it was going to go, so I couldn't prepare anything.

Kiran Krishnan:

Right.

Michael Roesslein:

So we'll cover that later this week. Thanks for all the well wishes, and we're grateful, I mean, we had 160 people on here live and no drop off for an hour and 45 with a professional-level presentation that doctors get at medical conferences. So I'm always amazed by our audience and the questions that you ask and the energy you bring, and how everybody stays so engaged for the entire time, even the people that are in places that are extremely late time zones. So thank you, Kiran.

Kiran Krishnan:

Of course.

Michael Roesslein:

Awesome, as always.

Kiran Krishnan:

My pleasure.

Michael Roesslein:

If I don't talk to you, you and your family have a great holiday. My folks said, I'm at their place, they said to say hi and-

Kiran Krishnan:

Awesome.

Michael Roesslein:

... They often reminisce over the time that you guys went to dinner, and you tried like 19 things on the menu for science. Yeah, for science.

Kiran Krishnan:

[crosstalk 01:36:14] That was great. Yeah, we had a lot of fun. Tell them I said hello as well, please, and happy holidays, everybody, if we don't talk to you. Thank you all for your time. Really appreciate it.

Michael Roesslein:

Have a great night or morning, everybody. Yes, the recording will go out later this week. Thanks, everyone.

Kiran Krishnan:

Cheers.

Michael Roesslein:

Bye.

PART 4 OF 4 ENDS [01:36:32]