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ReachMD

www.reachmd.com
info@reachmd.com
(866) 423-7849

Navigating the Complexities of Small Intestinal Bacterial Overgrowth

Dr. Buch:

This is *GI Insights* on ReachMD, and I'm your host, Dr. Peter Buch. Today's topic for discussion is small intestinal bacterial overgrowth, or SIBO for short, which is a condition in which a small bowel is colonized by excessive aerobic and anaerobic microbes. Here to help us navigate the complexities of SIBO is Dr. Mark Pimentel. Dr. Pimentel is the Director of the Medically Associated Science and Technology Program at Cedars Sinai in Los Angeles. He's also the author of an article titled "ACG Clinical Guideline Small Intestinal Bacterial Overgrowth," which was published in the *American Journal of Gastroenterology* in 2020. And he has many, many, many other accolades. Dr. Pimentel, welcome to the program.

Dr. Pimentel:

It's such a pleasure to be here. Thanks for inviting me.

Dr. Buch:

To start us off, Dr. Pimentel, would you kindly address the controversies in SIBO testing?

Dr. Pimentel:

SIBO testing began in the 1980s, maybe even sooner, but with an instrument that only measured hydrogen. Hydrogen is a gas that is only produced by bacteria; humans don't produce hydrogen. So it was believed that any gas or hydrogen that you were detecting in the human's breath was coming from the bacteria of the gut. And that's true. The controversies came when we were starting to equate the positive breath test with irritable bowel syndrome and other conditions. And people were saying, "Well, yeah, but maybe the hydrogen is coming from the colon, not from the small bowel. Do we really know where the hydrogen is coming from?" And then methane was introduced. And people were like, "Well, what does methane mean?" It was just added to the test. But all of those controversies in 2021 are completely gone because a lot of the breath test has been validated against modern techniques of culture, modern techniques of sequencing of the small bowel. And we now know that the breath test actually truly does represent bacterial overgrowth and that the hydrogen that we're measuring is actually coming from the small bowel.

Dr. Buch:

So Dr. Pimentel, how would you compare the accuracy of breath testing these days as opposed to a small bowel aspiration and culture?

Dr. Pimentel:

So traditionally, the notion was if you could do aspirate and culture, that was "the gold standard." The challenge is every time we make a new advancement, we challenge the old dogma. The problem with culture is we have instruments like an endoscope that we can put into the stomach, go into the small bowel, and take juice out. But as you're going, you're dirtying the scope from all mouth and other places, so you have to have a special device to go inside the scope to collect the sample. The second thing is the small intestine is 15 feet, 20 feet long. So where do you take your sample from? So while it's correct those who study this suggests that the gold standard is culture. Even culturing itself has problems. Where do you take the sample from? Who's culturing? What media do you use for culture and so on? Now with sequencing we're finding all sorts of organisms we didn't even know existed in the small intestine. And those organisms are, in part, contributing to SIBO and we can't even culture those. So everything's changing with time.

But what I can tell you is we did publish a paper last year that compared the breath test to culture and to deep sequencing. And that paper shows that the breath test is quite good at confirming overgrowth that we can see on duodenal aspirate for SIBO and culture, and it correlated with sequencing, and it correlated with symptoms. And finally, it correlated with checking metabolic function in the small bowel, and in those who are positive on breath test, their gut bugs in the small bowel were upregulated in hydrogen-producing

pathways. So that paper really kind of puts it all together and says, look, breath testing, nothing's perfect, but breath testing is pretty good at picking up SIBO.

Dr. Buch:

And that's a wonderful segue into the next question. Do we need some further future tests to make a more accurate diagnosis of SIBO than what we have right now?

Dr. Pimentel:

Well, it's ironic you asked that question because we do have some new technologies that have just emerged. So the biggest challenge going back to your first question of, 'Well, what does hydrogen mean?' Well, hydrogen, actually, despite thousands of breath tests that we've done, if your hydrogen on your breath test is abnormal, and let's say the number is 100, you're abnormal, you're believed to have overgrowth, but let's say your number is 50. You're also abnormal, and you're believed to have overgrowth, but the person with 100 is not more symptomatic than 50. So how does that help you? And what sense does that make? Well, the problem is hydrogen is just one of four gases produced by bacteria. The four gases are hydrogen, methane, carbon dioxide, and hydrogen sulfide. Carbon dioxide humans produce, so you can't know who's producing it, you or the bacteria, so you can't use that. But you can use hydrogen, methane, and hydrogen sulfide. And hydrogen is the fuel for the bugs that make methane and the bugs make hydrogen sulfide. So if you don't measure all three gases, and those are the only gases that bacteria ferment and produce, you don't know the full story. So recently, we've been part of this discovery to create an instrument that can measure all four. It can measure hydrogen, methane, CO₂, and hydrogen sulfide. And it turns out methane correlates with constipation. And hydrogen sulfide correlates with diarrhea. So for the first time, we have the actual gases of SIBO that are correlating with the actual symptoms that patients present with.

Dr. Buch:

Thank you. And if we move on to treatment, Dr. Pimentel, should probiotics be used to treat SIBO?

Dr. Pimentel:

So one of the challenges with trying to understand the microbiome is that most of the work has been done on stool. And we now know that the 15 feet of small bowel, the microbiome is completely different. But there's things that we're learning about the microbiome, and in particular the small bowel, that there are bugs that are what we call disruptors. They go in, and they take over in a way that may not be beneficial. *E. coli* and *klebsiella* are the two organisms of SIBO. Now once they're there, they're like weeds, and they move everybody out of the way and disturb the network. It turns out, we're starting to think that *lactobacillus* for example, which is a probiotic, does that also. So the problem with the word pro and biotic is that it suggests by the P-R-O, pro, that it's beneficial. But it may not be. And in SIBO, we have an accumulation of bacteria-producing gas. And so you're adding more bacteria to pro, which potentially could produce more gas. And I'll leave you with this other thought. The final way to look at it is you know, I live in Los Angeles now. It has doctors, plumbers, lawyers, bankers, all these folks that make the city cohesive and functioning. So you can't add a million lawyers to Los Angeles every day and expect that that's a good thing. And so similarly, single probiotics have never been clearly shown to improve IBS or functional GI disorders or SIBO as an individual organism like *lactobacillus* or *bifido*. If you pull all the studies together, there's some signal, but it's not as dramatic as we once thought or hoped.

Dr. Buch:

Thank you. For those just joining us, this is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and here to discuss small intestinal bacterial overgrowth is Dr. Mark Pimentel.

Now Dr. Pimentel, there are many therapies for irritable bowel syndrome. So at what point should we consider antibiotic therapy for those who have SIBO?

Dr. Pimentel:

Well as you may know, Rifaximin is an antibiotic that is FDA approved now for the treatment of irritable bowel syndrome with diarrhea. And it's on this basis of a microbiome derangement in IBS. And in fact, a recent study that was a pleasure for me to be part of showed that in the last trial of Rifaximin, breath tests were done in some of those patients. In the patients where if you didn't know if they had a positive breath test or not, 44% of people responded to Rifaximin. But if your breath test was positive in that trial, 56% responded, and if the Rifaximin made the breath test normal, 76% responded. So SIBO and IBS are all intertwined in the sense that if you have a positive breath test in IBS, you probably should be getting an antibiotic approach. If you're not responding to the antibiotic approach, then the other therapies are probably a better choice for you.

Dr. Buch:

So summarizing, your approach is antibiotics first if SIBO is present, and if that doesn't do anything, then move on to other therapies.

Dr. Pimentel:

I think that's probably true for most cases, and you can give empiric antibiotics, and within two weeks, you'll know. If a patient responds great, then that's the approach you should be taking with that patient. If they don't, then you can always try alternatives. The problem with some of the other alternative therapies for IBS with diarrhea is they have some side effects that can make it challenging to use. And so the simpler approach might be to give Rifaximin. But remember Rifaximin is a non-absorbed antibiotic, doesn't go into your bloodstream except for 0.4 percent, so it's almost nothing. And it doesn't create any kind of stable resistance. So it's been very successful for many, many years now in not creating resistance as well.

Dr. Buch:

Thank you. Let's move on to this. Do you believe some patients with SIBO deserve prophylactic antibiotics?

Dr. Pimentel:

Well, this is a newer area of where we're working. We think that this whole story of IBS and SIBO, at least in the majority of cases, starts from food poisoning. This used to be called post-infectious IBS. And some people still use that term. But essentially a toxin in food poisoning, which we helped to identify as CdtB leads to autoimmunity to a protein called vinculin, which is important for nerve integrity of the gut. And you develop these antibodies, and then the gut doesn't flow correctly. And then you get this buildup of bacteria. So as a consequence of that sequence of events, that's where you get small intestinal bacterial overgrowth. And as we're continuing to learn how that happens, we can actually measure these antibodies and diagnose IBS on this basis. And it accounts for about 60% of irritable bowel syndrome. So these are some really exciting new developments in terms of a pathophysiology of IBS.

Dr. Buch:

And before we sign off, are there any other messages you wish to share with our audience?

Dr. Pimentel:

I would like to say that there's a lot of hope in IBS. I mean because of this story of food poisoning leading to this cascade of events, we almost know more about what started IBS, SIBO, and these problems than we do about what is the trigger for Crohn's or ulcerative colitis. And so much more money has been spent in those areas. So my point is IBS affects one billion people worldwide. It's the most expensive, most significant gastrointestinal disorder by prevalence and incidence. And so now that we have these targets, now that we have this inciting event known, it's going to get easier and easier. New therapies are going to start to emerge, and I'm really excited about the future of this area.

Dr. Buch:

Well, that's all the time we have for today. And I really appreciate those final takeaways. I want to thank our guest, Dr. Mark Pimentel, for sharing his insights regarding small intestinal bacterial overgrowth. Dr. Pimentel, it was great speaking with you today.

Dr. Pimentel:

Oh, it was my pleasure. Thank you so much.

Dr. Buch:

For ReachMD, this is Dr. Peter Buch. To access this episode as well as others from this series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening and see you next time.