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Diagnosing Gastrointestinal Conditions with the Hydrogen Breath Test

Dr. Buch: Hydrogen breath tests can help clinicians determine if a patient has conditions that can affect their digestive health, and they're especially important for the diagnosis of carbohydrate maldigestion and small intestinal bacterial overgrowth, which is why today, we'll be taking an in-depth look at breath tests and what we need to know about them.

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And joining me today is Dr. Mark Pimentel, who is a Professor of Medicine at the David Geffen School of Medicine at UCLA and Associate Professor at Cedars-Sinai Medical Center. He's also the head of the Pimentel Laboratory and Executive Director of the Medically Associated Science and Technology Program, which focuses on the microbiome.

Dr. Pimentel, welcome to the program.

Dr. Pimentel:
It's so good to be with you today. Thank you for the introduction.

Dr. Buch:
So, Dr. Pimentel, let's start by looking at the patient. Who would be an appropriate candidate for breath testing?

Dr. Pimentel:
Well, breath testing is becoming more and more popularized, but we have to be careful and do it in the right patient. And I think that the most important patient where you want to do breath testing is somebody who describes symptoms of bloating, especially after eating a meal because breath testing is all about fermentation and the interaction with bacteria—so food plus bacteria equals gas and bloating and abnormal symptoms; that would be the ideal patient. But remember, some of the changes in the bacteria can make you have constipation or diarrhea or both, so it just depends on what the breath test profile looks like.

Dr. Buch:
And subdividing that a little bit and getting into your field, the small intestinal bacterial overgrowth and irritable bowel syndrome as opposed to structural abnormalities, can you go into that a little bit further?

Dr. Pimentel:
Yeah. The developments in terms of the relationship between bacterial overgrowth and IBS have really come a long way in the last few years. We could probably now confidently say, based on culture studies, not just breath testing, that about 60% of patients with IBS with diarrhea have SIBO, or small intestinal bacterial overgrowth, and then on the constipation side of IBS, we now know methane, which is a different type of overgrowth seen on breath test, can be found in constipation-predominant IBS probably in about 60% of cases there as well. So the relationship between these alterations in the gut microbiome that a breath test would be useful to find is about 60% of all of IBS.

Dr. Buch:
And let's get into a little bit of controversy. What's the correct dose of glucose for breath testing?

Dr. Pimentel:
So I was part of the North American Consensus. And consensus statements are not fact. They're opinion based on the literature from experts. So what we did in the North American Consensus is we brought together pretty much anybody who does breath testing research in North America into a room and said, "Let's make some decisions." And one of the decisions was how much glucose should be on a breath test, and that decision was 75 grams of glucose, so that's what people give for a glucose breath test. But there are controversies about which substrate to use for breath testing. Should you use lactulose or glucose? And I think you probably have a question like that today.

Dr. Buch:
And that's the perfect segue. That's exactly the next question, so go ahead and answer it for us, please.

Dr. Pimentel:
I'm happy to. So I don't want to say purists, but there are purists who think that glucose is more accurate. And what that means is that if you are positive, meaning you have a higher hydrogen after glucose, that it's more likely that you truly do have bacterial overgrowth. So let me take that apart a little bit. So glucose gets absorbed so quickly by the human that within 3 feet of the small bowel you're done; the glucose is in your bloodstream. And so the problem with that is you still have another 12 feet of small bowel ahead of you where the glucose never was there, so you could have bacterial overgrowth further down, and the glucose is just flat out going to miss it.

Lactulose, which is a non-absorbed sugar—and that dose is 10 grams—when you drink that, that stuff is getting all the way through the small bowel, but it also gets to the colon, so you're going to sample and determine the bacteria and fermentation of the entire small bowel and the first part of the colon potentially depending upon how far you go. So critics say, "Well, lactulose breath test may show transit," because if you get to the colon, you've got all this bacteria, and all of a sudden you get a big spike, but what we've shown actually is that lactulose is more accurate for predicting and picking up overgrowth. In fact, there are more studies on lactulose, and there are more studies verifying lactulose against culture, against deep sequencing of the small bowel and versus treatment or predicting treatment outcomes, such as rifaximin, such that lactulose actually is a better predictor of who's going to respond to an antibiotic treatment like rifaximin.

Rifaximin in and of itself, by itself, is probably treating an IBS bacterial overgrowth, and we have some studies that are published to suggest that, but rifaximin works in about 44% of IBS patients in the clinical trial, but only 30% of IBS patients test positive on a glucose breath test. So I want you to think about being a patient. You do a glucose breath test. You're negative. But what if you're in the group between 30 and 44%? Now I'm not going to give you something that will be of amazing benefit to you. So even the data on treatment with rifaximin suggests if you do glucose, there are going to be some patients who miss out on treatment that would have benefitted them. So my understanding of the entire literature on this is lactulose really is the preferred substance. The science backs that up.

Dr. Buch:
And talking about rifaximin, is there any data to suggest that rifaximin acts beyond an antibacterial?

Dr. Pimentel:
Well again, the mechanism of action of rifaximin has been suggested to be multifactorial, but really, it's an antibiotic, and what we've shown in the research is that it really gets the bacteria down in the small bowel but really doesn't affect the colon bacteria, again suggesting that all the activity of rifaximin and all the benefits that rifaximin gives to IBS patients is that reduction in specifically 2 organisms: E. coli and klebsiella reductions in the small intestine of patients, so that's what we think is the most likely mechanism of action of rifaximin.

Dr. Buch:
Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Mark Pimentel about the use of breath testing for GI disorders.

So, Dr. Pimentel, what are the limitations of using fructose or sucrose breath tests?

Dr. Pimentel:
So remember, breath testing can be used to determine carbohydrate malabsorption or maldigestion as well, but whether it's fructose, sucrose or lactose, which traditionally had been used on breath testing, the problem is the way breath tests work is you drink a sugar, and if it reaches bacteria, then you didn't absorb the sugar well. That's in patients without overgrowth. But if you have bacterial overgrowth of the small bowel, the sugar is going to reach bacteria early, prematurely, and you're going to have a false-positive result, so the challenge in the North American Consensus, which is from 2018, addresses this very clearly. Yes, you can do a fructose breath test, and if you get a peak later, it could be fructose malabsorption. The same for sucrose. The same for lactose. But you've got to do the lactulose or glucose breath test first because if you have SIBO, the fructose, sucrose, and lactose breath tests become uninterpretable because the bacteria are coming up to the sugar rather than the sugar being malabsorbed and getting to the bacteria in the colon, so that's the challenge with those breath tests. So if you do a lactulose breath test, it's negative, and then you give fructose or sucrose and it's positive, you have fructose or sucrose maldigestion or malabsorption, and so that's the sequence that needs to occur in order to make sure you're doing it the right way.

Dr. Buch:
Thanks for that clarification. That was great. And if we look at this a little bit more broadly, what are the knowledge gaps regarding breath testing?

Dr. Pimentel:
Well, I think what we need to understand now in breath testing is that it's about hydrogen, which is a predictor of overgrowth. It's about detecting methane, which is very clearly now from dozens of studies that methane causes, not only predicts, constipation because the methane gas actually slows transit in the gut. And the third gas, which is now a new breath test that measures all 3 gases, is that hydrogen sulfide on breath test predicts and/or causes diarrhea and urgency and abdominal pain. So we're actually principally doing 3 gas breath tests now in our center for this reason, and this is expanding around the U.S. It's commercially available now. And so what's happening with breath testing is now we're starting to understand the full picture because hydrogen doesn't correlate with symptoms very well even if it correlates with overgrowth because hydrogen is used to make methane and used to make hydrogen sulfide, and so, if you have those other 2 gases and you're not measuring them, you have no idea what's happening because the hydrogen is being used up, and so it can affect the hydrogen levels. So bottom line is if you're going to do breath testing, if you can, you should do all 3 gases.

Dr. Buch:
Thank you. And before we conclude, Dr. Pimentel, what are any other thoughts that you'd like to share with our audience today?

Dr. Pimentel:
Well, I think it's ironic, or interesting I guess is a better way to put it, that breath testing emerged in the 1970s, and it wasn't until the 2000s and the emergence of this blossom of the microbiome and all the technologies to study the microbiome that we began to fully understand breath testing. And now with microbiome research sequencing, new ways of culturing organisms of the gut, we now understand what the breath test is telling us more than we ever have, but the sense of optimism from that is, now that we know that, new treatments will come that will better handle these patients with these multiple illnesses and conditions and symptoms, so there's only optimism to look forward to in the future.

Dr. Buch:
Thank you. Well, this has been a great discussion on the importance of using breath testing in our GI patients. And I want to thank my

guest, Dr. Mark Pimentel, for sharing his insights. Dr. Pimentel, it's been wonderful speaking with you today.

Dr. Pimentel:
Thank you very much.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of the Knowledge. Thanks for listening and see you next time.