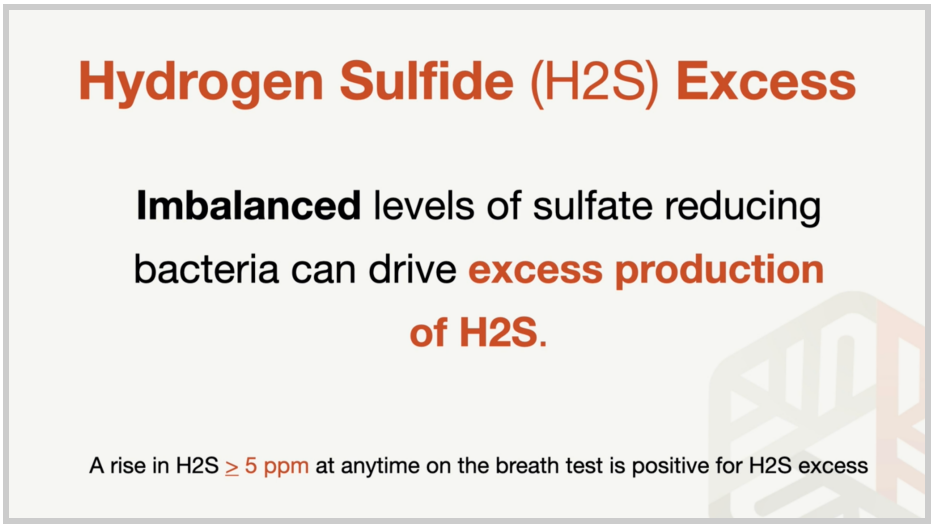
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

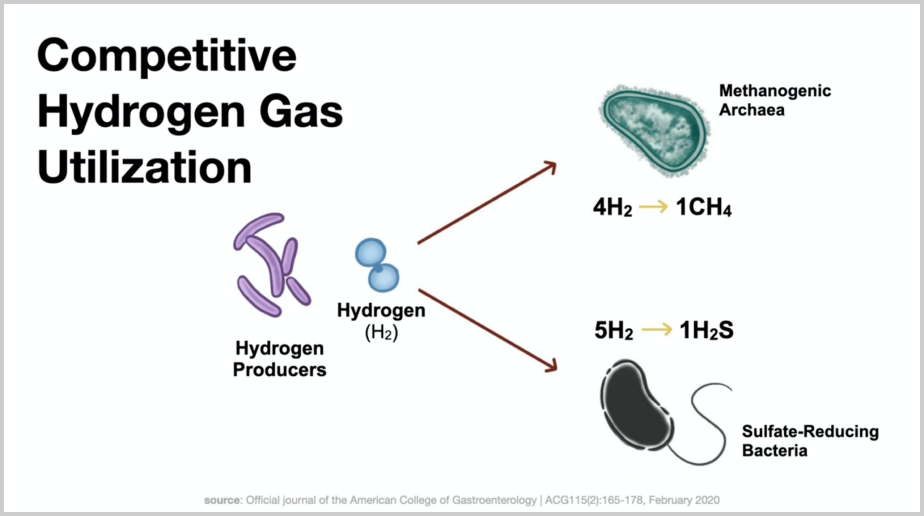
Identifying Gut Pathologies: Small Intestinal Bacterial Overgrowth Breath Test (Part 3)



The third subtype of [small intestinal bacterial overgrowth] (SIBO) that has just recently become more recognized due to the ability to test for it is hydrogen sulfide excess. The presence of hydrogen sulfide gas and bacteria that produce these gases aren't necessarily a problem per se when they're present in appropriate amounts and are important players in the immune response by reducing inflammation and more. Much like most other processes in the body, it's the levels of these sulfate-reducing bacteria that impact symptoms and potentially even cause cellular damage, inflammation, and upregulation of the immune activity. The mechanism behind this particular type of bacterial overgrowth is still unknown. And we don't have an exact understanding yet of why it happens. There are some theories out there to help explain this imbalance. One of those is sulfur intolerance that may be caused by toxic burdens, like heavy metals or glyphosate toxicity, genetic variance in the cystathionine B-synthase enzymes that impact sulfur metabolism, and more, all of which are thought to impact sulfation, glucuronidation, and glutathione S-transferase.

Essentially, the idea is that sulfur production is reduced, so as a compensatory mechanism, the body encourages overgrowth of sulfate-reducing bacteria. The sulfur-reducing bacteria metabolize sulfur and end with hydrogen sulfide as the end product, hence, the hydrogen sulfide production on the breath test. Again, at the time of this recording, it's just a theory. Not everyone's on board. Although, I will say there's a lot of proponents of this theory who are treating hydrogen sulfide SIBO as a sulfur intolerance and metabolism problem. So there's not as much research that I know of disproving or proving this theory.

Hydrogen sulfide SIBO has very similar symptoms to other subtypes of SIBO but is more commonly linked to diarrhea and foul "sulfur smelling gas." I've had mixed experiences of this in [the] clinic. Meaning when people have this combination of symptoms along with high sulfur food sensitivities, I see it commonly result in a positive hydrogen sulfide SIBO breath test, but again, [this is] not a hard and fast rule. And I see people with positive hydrogen sulfide tests that don't necessarily complain of these specific symptoms. Per [Dr.] Pimentel's research and the diagnostic criteria set by Gemelli Labs, the lab that's running the hydrogen sulfide SIBO test, a rise that's greater than or equal to five parts per million at any time on the breath test is positive for hydrogen sulfide.



As I mentioned before, methanogens consume hydrogen in the gut. Hydrogen sulfide-producing organisms also use hydrogen and bacterial breakdown of sulfur compounds. I alluded to this previously, but understanding the competitive nature for resources of these organisms is important. You may hear Dr. Pimentel refer to this as the "fox and wolves analogy." He equates methanogens to foxes and hydrogen sulfide producers as wolves that are both competing to eat the "rabbits," or hydrogen. Typically, we see methanogens and hydrogen sulfide-producing

organisms competing for hydrogen as a food source or as an element for [the] bacterial metabolism of sulfur. This can be represented on the SIBO breath test as a low hydrogen value with a positive methane or hydrogen sulfide value. That is more typical of what we see in [the] clinic. There are times, though, when we see a combination of methane and hydrogen, or hydrogen sulfide and hydrogen, on the breath test. I think this is indicative of overgrowth of both organisms. But we maybe just haven't depleted the hydrogen at that stage of testing. So it's not as typical to see both methane and hydrogen sulfide predominant. But I've seen this a handful of times in [the] clinic. And I just haven't found a great explanation for it just yet. But I will say that most of the time, the patient will present their symptoms leaning toward one way or the other. And that might be what I lean toward when it comes to treatment.

Let's move on to testing and diagnosis. This is really the bigger question when it comes to SIBO, in my opinion. There's been a huge focus on it in the Functional Medicine community, and so many patients are being treated for SIBO. And certainly, if they really do have SIBO, and it's really causing their pathology, it's appropriate, and it's important. But I think there are some uncomfortable realities around the diagnosis and treatment of SIBO that we should be aware of as clinicians. So number one is that we still don't have a perfectly reliable test and a consensus on how to interpret the tests that are being used. As I mentioned, there was a lot more controversy up until 2017, when the North American Consensus guidelines came out for interpretation. I think that's made things a little less murky. More and more research is coming out. But I still think there isn't a firm agreement on what the best criteria are. And there are still some labs using those older criteria for interpreting. So I'm going to review all of this in the slides that follow and tell you what tests we've decided to use and that we continue to use with some caveats and considerations. And then we'll move into revealing some results and cases.

As I said before, there are two main tests for SIBO. The gold standard is an endoscopy with small bowel aspirate and culture where they are quantifying the levels of bacteria in the sample they take. And the second one is a breath test. It's really important to understand that SIBO can't be diagnosed with a stool test or a urine test. Bacterial culture is the most direct method. It's done by endoscopy. And they take an anaerobic and aerobic count of the small intestine luminal contents. There are a lot of problems with this method. The first is that the small intestine has to be intubated. A catheter is passed into the distal duodenum through an endoscope. Then fluid is aspirated for culture, and that's a very invasive procedure. It's costly, and there's some risk involved. The other thing is that many species that inhabit the small intestine, many species of microbes, cannot be effectively cultured. So any kind of quantitative culture will underestimate [the] bacterial population in the small intestine as a result. The endoscope and catheter can be contaminated as the instrument is passed through the digestive tract. And that can also cause

problems for the patients and for the dependability of the test result. So it's also time-consuming and expensive.

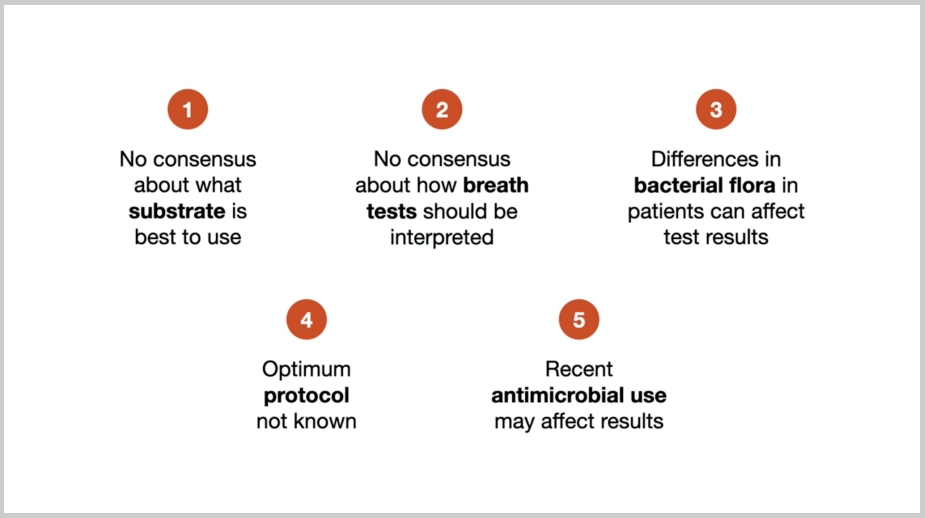
SIBO is known to be patchy in distribution. So let's say they take a sample of an area of the small intestine where there isn't any bacterial overgrowth, and that returns a negative result, where just next to that area, there was a slice of small intestine that did have bacterial overgrowth, and they missed it. And I think this can happen frequently. Then prompt and proper specimen handling is needed to get accurate results. So all of these shortcomings explain why endoscopy is rarely used now in clinical practice for SIBO testing. I see it mostly in research settings at this point and in some hospitals. Historically, a level of greater than or equal to 10 to the power of five CFUs per milliliter had been used for identifying pathological bacterial infections in humans, including a diagnosis of SIBO. However, in the case of SIBO, this cut-off appears to maybe be a little too stringent and even lacks some validation. [In] more recent studies, healthy controls have shown people with less than or equal to 10 to the power of three in the small bowel and concentrations above 10 to the power of five are almost exclusively seen in patients with gastrectomy. A concentration of greater than or equal to 10 to the power of three CFUs per milliliter is now generally considered diagnostic of SIBO and has also been backed and recommended by the North American Consensus.

Source: http://u.jimdo.com/www400/o/s0778412baad3f3a7/img/i1d73a4999b5c8e7a/1344427880/orig/image.gif

All of these various challenges led to the development of a different method of testing for SIBO, which is breath testing. This is by far more commonly used, especially in Functional Medicine. It's non-invasive. It's safe. It's easy to perform at home. And it's relatively cheap. The basic premise is that human cells are incapable of producing hydrogen and methane gases. But because bacteria in the intestines can metabolize carbohydrates, like lactulose, glucose, sucrose, or xylose, and

produce gases like hydrogen and methane, we feed those to the bacteria and then produce the gases, which can be measured in the breath.

Breath testing has become the de facto testing for SIBO, particularly in the clinical setting. And it does certainly [have an] advantage over culture. But it's far from perfect and can be problematic. In fact, much more so than is commonly acknowledged, I think, maybe even by some experts.



The first issue is that there's no consensus about the best substrate to use in testing. Some argue that glucose is best. Others argue that lactulose is best. There [are] pros and cons to both substrate[s], which we're going to cover in detail. Second, there's a lack of agreement on the consensus about how breath tests should be interpreted. We're going to cover more throughout the presentation. Third is that differences in bacterial flora in patients can affect test results. For example, 10 percent of adults and 15 percent of kids don't produce hydrogen at all. They only produce methane. So if you're not testing for methane, you might miss some of those people. And some people don't produce much methane or hydrogen at all. And they actually produce more hydrogen sulfide. That's only measured by one lab at the time of this recording. So that could be a potential problem. Fourth is the optimal protocol for timing, collection, and method of administering [the] breath test is not really known or agreed upon. Fifth is recent antimicrobial or antibiotic use may impact results. But the proper antimicrobial-free interval prior to doing the test is not known. We've used retesting intervals of anywhere from two to four weeks in our clinic. And I've recently settled on four weeks between antimicrobials or antibiotics and retesting based [on] the North American Consensus. In short, the breath test is an easy test to perform. But it can have its difficulties when interpreting the results.

I mentioned on the last slide that each of the substrates that are used clinically, lactulose and glucose primarily at this point, has its own pros and cons. Let's start with glucose. The main problem with glucose is that it's absorbed in the proximal intestine in the duodenum. So if overgrowth of bacteria is occurring in the jejunum or the ileum, you may get a false negative with the glucose breath test. That said, the Rome Consensus Conference, which was an earlier guideline, recommends [the] glucose breath test over [the] lactulose breath test, while the North American Consensus recommended either substrate for testing. According to a systematic review, the sensitivity of lactulose has ranged from 31 percent to 68 percent. And specificity has ranged from 44 percent to 100 percent. Whereas the sensitivity of glucose test results has varied from 20 percent to 93 percent and specificity from 30 percent to 86 percent when compared with cultures of aspirates from the small bowel. The lactulose breath test has been criticized for high false-positive results because of accelerated transit and colonic fermentation in some individuals. Alternatively, the glucose breath test for being absorbed in the proximal duodenum and therefore having low sensitivity for detecting distal SIBO, in other words, missing overgrowth in [the] distal small bowel.

Let me elaborate a little bit more on this.