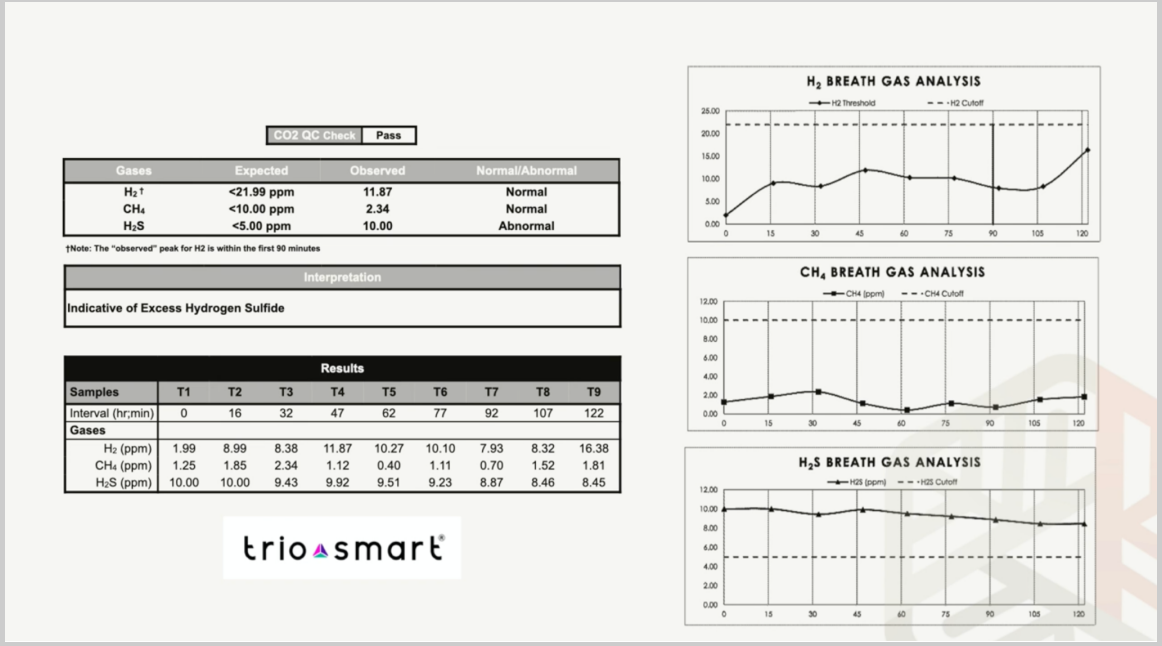
Identifying Gut Pathologies: Small Intestinal Bacterial Overgrowth Breath Test (Part 8)



CO2 QC Check: Pass

Gases	Expected	Observed	Normal/Abnormal
H_2†	<21.99 ppm	11.87	Normal
CH_4	<10.00 ppm	2.34	Normal
H_2S	<5.00 ppm	10.00	Abnormal

†Note: The "observed" peak for H2 is within the first 90 minutes

Interpretation
Indicative of Excess Hydrogen Sulfide

Results

Samples	T1	T2	T3	T4	T5	T6	T7	T8	T9
Interval (hr:min)	0	16	32	47	62	77	92	107	122
Gases									
H_2 (ppm)	1.99	8.99	8.38	11.87	10.27	10.10	7.93	8.32	16.38
CH_4 (ppm)	1.25	1.85	2.34	1.12	0.40	1.11	0.70	1.52	1.81
H_2S (ppm)	10.00	10.00	9.43	9.92	9.51	9.23	8.87	8.46	8.45

trio smart

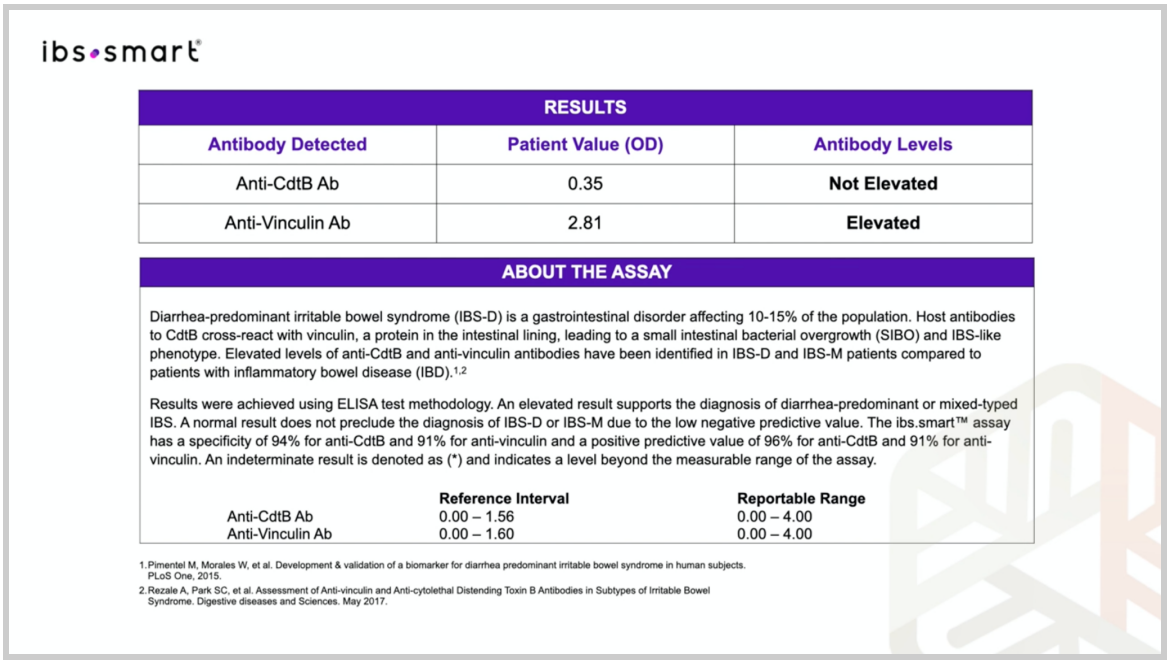
Here we have a trio-smart test showing hydrogen sulfide excess with a gas value of 10. The test does max out at 10 parts per million for hydrogen sulfide. You'll also see that methane is negative and hydrogen is also negative on this test, which is a common presentation for hydrogen sulfide excess, with the level starting high at baseline and staying high throughout the testing samples, similar to what you see with methane levels. This particular test is from a 42-year-old female [with] complaints of gastric reflux, loose stool, gas, fatigue, and excess weight. You can see another example of hydrogen sulfide excess here with the [maximum] value of 10 also being reported at baseline and at the 60-minute mark. This is another patient with mixed [irritable bowel syndrome] (IBS), alternating constipation and diarrhea, food sensitivities, skin rashes, and histamine reactions.

While the typical bowel patterns for hydrogen sulfide excess are diarrhea, I don't find that to be a hard and fast rule in [the] clinic. Same with methane. While constipation tends to be the common pattern associated with methane and diarrhea with hydrogen sulfide excess, it doesn't always happen, so we have to consider the whole patient, their symptoms, [and] their history when deciding when and how to test and treat.

Lastly, I want to touch on the IBS-smart test and how it can be used in SIBO and IBS patients. The IBS-smart test is a blood test that was designed to detect two biomarkers: anti-[cytolethal distending toxin B] (CdtB) and anti-vinculin. The idea behind this test is that studies have shown these markers to be elevated in the majority of patients with [IBS with diarrhea] (IBS-D) and [IBS mixed] (IBS-M), and the presence of these markers indicates the cause was infectious gastroenteritis. This has not been labeled an autoimmune condition at the time of this recording, but the process in which this happens is an autoimmune process. I should say that Dr. Pimentel does not use this test for people with constipation because the mechanism of how the toxins work [isn't] supported with that bowel pattern. However, clinically, I have used this test for people with constipation that have very persistent SIBO and other IBS symptoms, like abdominal pain, bloating, and gas, and I have had some come back positive. So I'm not entirely sure what all this means just yet. It's a little hard to ignore the fact that I am having some patients with constipation with positive results, so I would say to maybe consider it in some of those patients that fit the profile in every other way.

This process starts with a foodborne pathogen, most commonly *Campylobacter*, *Shigella*, *Salmonella*, and [*Escherichia*] *coli*, that release[s] the CdtB. Our body's immune response then generates anti-CdtB antibodies to target that toxin that start to rise within weeks of infection. Then, because of molecular mimicry, often months later, anti-vinculin is produced. Anti-vinculin attacks vinculin proteins in the gut that lead to nerve damage and dysmotility. The result of this cascade of events is an impaired migrating motor complex, and typically IBS with the diarrhea component or with the typical symptoms of diarrhea, abdominal bloating, and pain.

This test is used as a test of inclusion for the diagnosis of IBS. I'll link to the podcast between Dr. Pimentel and Chris where they talk about this in much more detail in this section. So let's talk about how the IBS-smart test is connected to SIBO diagnosis and treatment. When you have a patient with persistent SIBO [who] has had a history of foodborne illness and presents with IBS-D or IBS-M, I think this is a good test to do in addition to stool and SIBO breath testing. If you have positive antibody tests, then you have an idea that impaired motility and autoimmunity are likely playing a role in the person's digestive symptoms and persistent or recalcitrant SIBO. We'll cover more about the impact of these results during SIBO treatment in that treatment section.



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RESULTS		
Antibody Detected	**Patient Value (OD)**	**Antibody Levels**
Anti-CdtB Ab	0.35	**Not Elevated**
Anti-Vinculin Ab	2.81	**Elevated**

ABOUT THE ASSAY

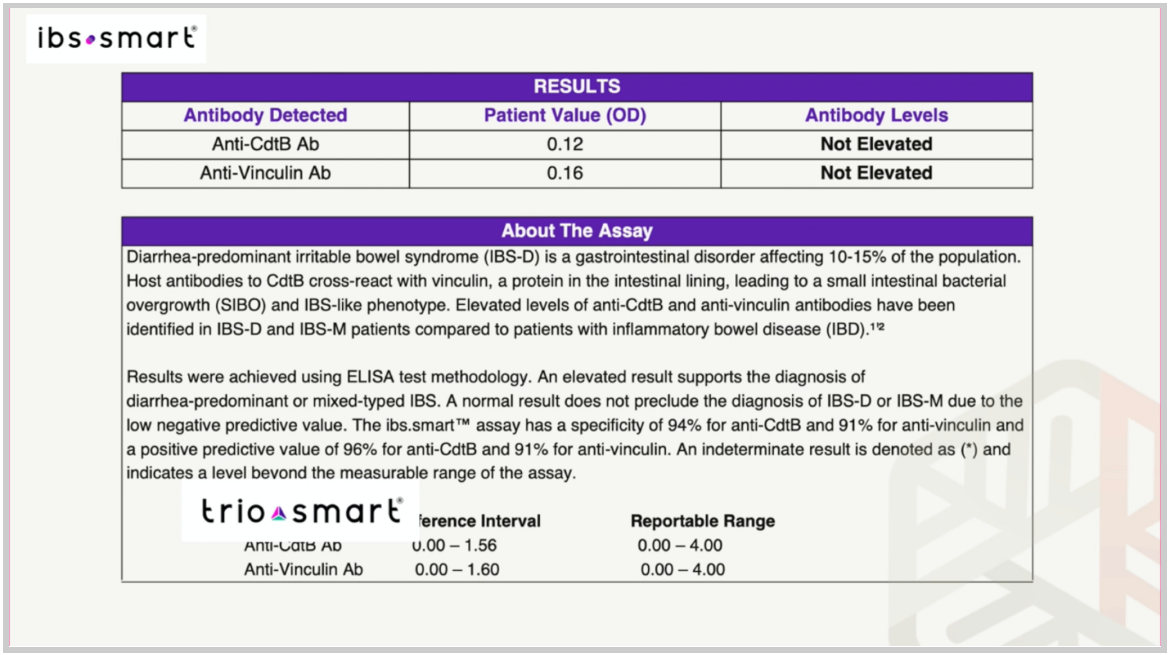
Diarrhea-predominant irritable bowel syndrome (IBS-D) is a gastrointestinal disorder affecting 10-15% of the population. Host antibodies to CdtB cross-react with vinculin, a protein in the intestinal lining, leading to a small intestinal bacterial overgrowth (SIBO) and IBS-like phenotype. Elevated levels of anti-CdtB and anti-vinculin antibodies have been identified in IBS-D and IBS-M patients compared to patients with inflammatory bowel disease (IBD).[1,2]

Results were achieved using ELISA test methodology. An elevated result supports the diagnosis of diarrhea-predominant or mixed-typed IBS. A normal result does not preclude the diagnosis of IBS-D or IBS-M due to the low negative predictive value. The ibs.smart™ assay has a specificity of 94% for anti-CdtB and 91% for anti-vinculin and a positive predictive value of 96% for anti-CdtB and 91% for anti-vinculin. An indeterminate result is denoted as (*) and indicates a level beyond the measurable range of the assay.

	Reference Interval	Reportable Range
Anti-CdtB Ab	0.00 – 1.56	0.00 – 4.00
Anti-Vinculin Ab	0.00 – 1.60	0.00 – 4.00

1. Pimentel M, Morales W, et al. Development & validation of a biomarker for diarrhea predominant irritable bowel syndrome in human subjects. PLoS One, 2015.
2. Rezale A, Park SC, et al. Assessment of Anti-vinculin and Anti-cytolethal Distending Toxin B Antibodies in Subtypes of Irritable Bowel Syndrome. Digestive diseases and Sciences. May 2017.

This is an example of a positive anti-vinculin antibody result, and a pretty high value at that. I think when we are seeing numbers above two, it can mean that the person has likely had repeated events of infection or poisoning or has had a really significant event and really significant response. When talking to Dr. Pimentel, he also has mentioned that a value between 0.8 [and] 1.6 may be more of a gray area. So, if symptoms fit, then you could consider moving forward with addressing this as a cause. So even when we see elevated anti-vinculin antibodies, we suspect motility is impaired, and intervention with a promotility agent is necessary.



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RESULTS		
Antibody Detected	**Patient Value (OD)**	**Antibody Levels**
Anti-CdtB Ab	0.12	**Not Elevated**
Anti-Vinculin Ab	0.16	**Not Elevated**

About The Assay

Diarrhea-predominant irritable bowel syndrome (IBS-D) is a gastrointestinal disorder affecting 10-15% of the population. Host antibodies to CdtB cross-react with vinculin, a protein in the intestinal lining, leading to a small intestinal bacterial overgrowth (SIBO) and IBS-like phenotype. Elevated levels of anti-CdtB and anti-vinculin antibodies have been identified in IBS-D and IBS-M patients compared to patients with inflammatory bowel disease (IBD).[1,2]

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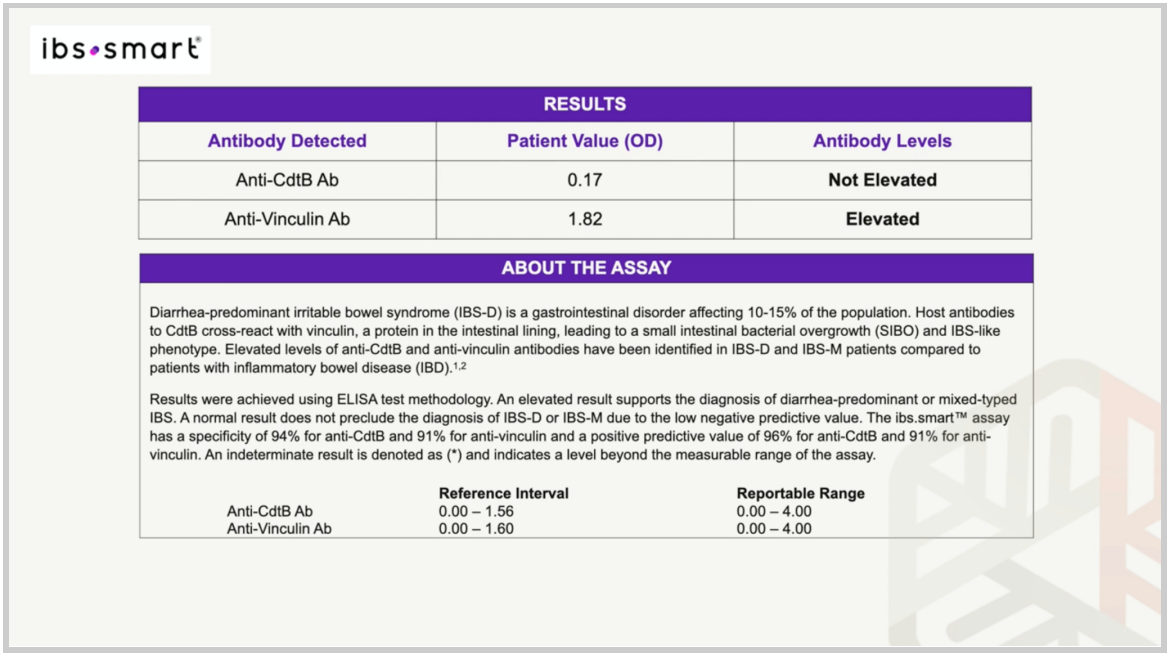
	Reference Interval	Reportable Range
Anti-CdtB Ab	0.00 – 1.56	0.00 – 4.00
Anti-Vinculin Ab	0.00 – 1.60	0.00 – 4.00

Here's a normal result for the IBS-smart test. Both the anti-CdtB and anti-vinculin antibodies are not elevated, so that would essentially rule out a post-infectious cause of IBS or SIBO for this patient based [on] what we know at the time of this recording.



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RESULTS		
Antibody Detected	**Patient Value (OD)**	**Antibody Levels**
Anti-CdtB Ab	0.17	**Not Elevated**
Anti-Vinculin Ab	1.82	**Elevated**

ABOUT THE ASSAY

Diarrhea-predominant irritable bowel syndrome (IBS-D) is a gastrointestinal disorder affecting 10-15% of the population. Host antibodies to CdtB cross-react with vinculin, a protein in the intestinal lining, leading to a small intestinal bacterial overgrowth (SIBO) and IBS-like phenotype. Elevated levels of anti-CdtB and anti-vinculin antibodies have been identified in IBS-D and IBS-M patients compared to patients with inflammatory bowel disease (IBD).[1,2]

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	Reference Interval	Reportable Range
Anti-CdtB Ab	0.00 – 1.56	0.00 – 4.00
Anti-Vinculin Ab	0.00 – 1.60	0.00 – 4.00

Here's another example of a positive anti-vinculin antibody at 1.82 with a negative anti-CdtB. This is a 34-year-old female with IBS-M. Persistent SIBO that did not respond well, or responded

briefly, I should say, to multiple treatments and complained of [a] full feeling all the time. It's also important to provide patient counseling about future food poisoning events because having had a previous event and autoimmunity can potentially increase [the] risk [of] future events when traveling or in general, and could increase the anti-vinculin antibody levels further with another incidence of infectious gastroenteritis.

Scenarios

Anti-CdtB	Anti-Vinculin	Clinical Association
Low	Low	No recent infection and no autoimmune basis for functional symptoms
High	Low	Recent infection and may be developing IBS
Low	High	Infection long past, now autoimmunity driving condition with IBS
High	High	Recent with or without remote infection, now autoimmune with IBS
Either	Very High	Pseudo-obstruction (neuropathy)

Adapted from: Dr. Pimentel's presentation with Gemelli Labs

You may be asking yourself why I haven't shown you a positive anti-CdtB lab result. Well, the answer is that I haven't seen one yet. This is still a newer to the market test, so [it's] possible [that] we will see one soon. But an elevated anti-CdtB antibody level with a normal anti-vinculin antibody is often indicative of a recent infection that could develop into IBS. But the autoimmune response has not happened yet, so there's [a] better prognosis for recovering from IBS. When the anti-CdtB is low and anti-vinculin is high, that means the infection is long past and autoimmunity is often driving the condition. If you see them both elevated, then this means a recent infection with or without remote infection and also [an] autoimmune component to IBS. Dr. Pimentel reports that when you have really high levels, into the threes of either, you should look at pseudo-obstruction as a possible mechanism of disease. There was also some discussion about high anti-CdtB antibodies being present in people with functional dyspepsia. All right, that's it for the SIBO testing and diagnosis section.

To summarize this presentation, as you can see, there's a lot of gray area in SIBO testing; it's not black and white. There's tremendous uncertainty, more than typically acknowledged in

discussions about SIBO testing from what we've seen. The interpretation of the results depend[s] on the lab you use, the substrate, whether glucose or lactulose, transit time, the patient, whether they follow the prep diet properly, and several other factors.

At this point, I think it's difficult to get a result that you may be 100 percent confident in. I see it more as a spectrum. Some of the earlier results that we looked at in the presentation were maybe negative or close to equivocal positive, as you can get with some SIBO breath tests, whereas some of the results that we looked at were a lot more reliable and were true positive[s]. So the decision on whether to treat includes evaluation of the patient signs and symptoms, clinical history, and other labs.

But the good news is, as I've said a number of times now, that the treatment for SIBO, I think, is relatively safe, and that's true for both the botanical protocol we're going to teach and the pharmaceutical protocol. This is why many clinicians, including myself and Chris, consider a therapeutic trial if the breath tests are equivocal and symptoms match. This is the valid method of diagnosis in medicine and does have its role. It's also true that as you'll see when we start doing the full case studies, we're rarely treating SIBO alone, and we're often treating other gut conditions simultaneously. And you can choose a treatment that will be effective for all of the different conditions that you're treating. So any one of the conditions' presence or lack of presence becomes less significant from a practical perspective because it's not really going to alter your treatment plan drastically. We'll discuss that in more detail when we get to the section on treating gut conditions, all of these things that we're also learning to help diagnose.

Okay, that's it for now. Next, we're going to talk about microbial organic acid testing.