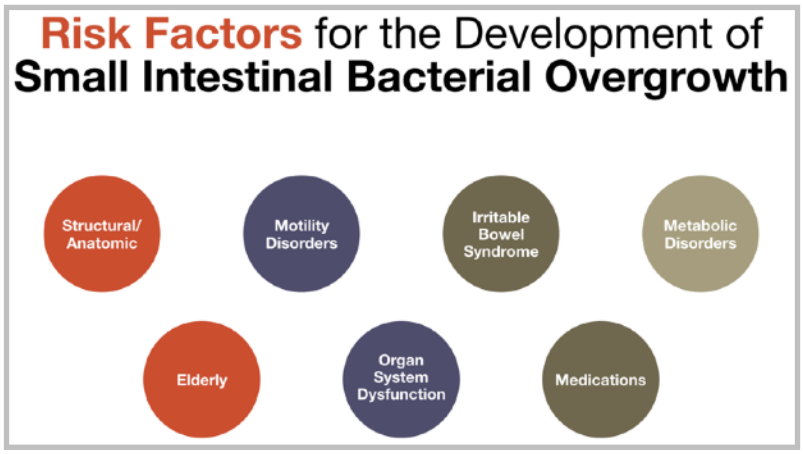
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

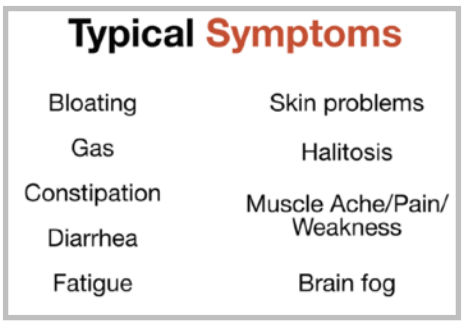
Gut Diagnosis SIBO Review

SIBO is defined as the presence of excessive bacteria in the small intestine. It develops when the normal homeostatic mechanisms that control small intestinal bacterial populations are disrupted.



In functional medicine practice, three primary processes that contribute to SIBO are:

1. Gastric acid secretion
    a. Low stomach acid in particular. This is because stomach acid suppresses the growth of ingested bacteria.
2. Small intestine dysmotility
    a. Disruption of the migrating motor complex and the peristaltic wave in the gut, which normally has a cleansing action and prevents the overgrowth of bacteria.
3. Disrupted gut microbiome
    a. Dysbiosis in the colon that leads to overgrowth of bacteria in the small intestine.
    b. It is well-established that antibiotic use can lead to disrupted gut microbiome and in turn SIBO.



Symptoms are diverse, nonspecific, **and not limited to the gut.** Patients may present only with non-GI symptoms such as fatigue, skin issues, or muscle aches/pains. In one study, up to 50 percent of SIBO patients didn't have gut symptoms, but 100 percent of fibromyalgia patients had SIBO.

Complications include: malabsorption, nutrient deficiency, metabolic bone disorders, and small intestine inflammation.

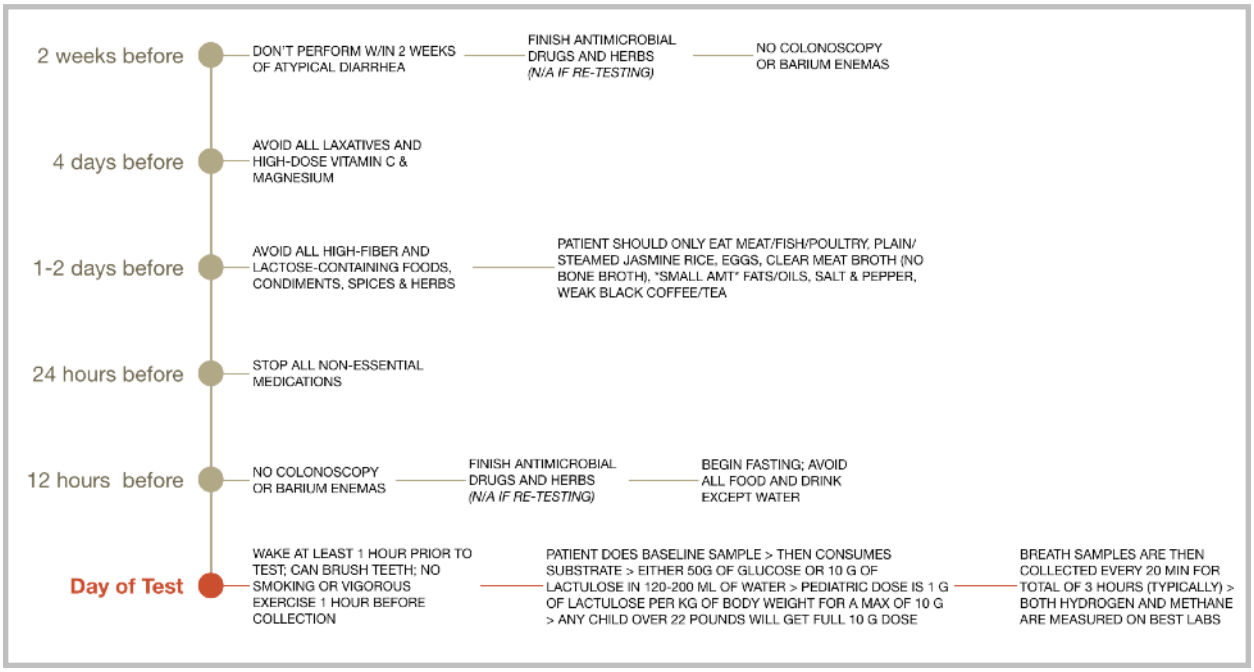
For example, SIBO is known to cause B12 deficiency because B12 is absorbed in the small intestine. In addition, SIBO can lead to fat malabsorption. This can lead to a decline in fat-soluble vitamin absorption, which leads to low vitamin D and low vitamin K2, which can cause osteoporosis. Also, vitamin A deficiency can lead to night blindness and retinopathy. In addition, patients may have prolonged clotting times due to vitamin K deficiency.

SIBO DIAGNOSIS:

There are two main tests for SIBO:

1. One is an endoscopy with bacterial culture, where they're quantifying the levels of bacteria in the sample they take.
    a. Very invasive procedure, so there is some risk involved.
    b. Costly.
    c. Many microbial species that inhabit the small intestine; cannot be effectively cultured.
    d. The endoscope and catheter can be contaminated.
2. Breath test
    a. More commonly used as it is noninvasive and easy to perform at home.
    b. Based on the premise that bacteria in the intestines metabolize carbohydrates like lactulose, glucose, sucrose, or xylose and produce gases like hydrogen and methane, which can be measured in the breath.

SIBO TEST PREPARATION:



ORIGINAL TESTING CRITERIA

- Lactulose breath test
  - SIBO: Rise in hydrogen at least 15 minutes before the substrate enters the colon. A second peak results once it enters the colon.
  - Healthy: Rise in hydrogen once the substrate reaches the colon but not before.
- Glucose breath test
  - SIBO: Early rise in hydrogen of about 15 ppm above baseline.
  - Normal: No rise in hydrogen (since glucose is absorbed prior to reaching the colon).

2003 PIMENTEL REVISED TESTING CRITERIA

- Revised criteria proposed by Dr. Pimentel in 2003.
- Any rise in hydrogen before 90 minutes or any rise of more than 20 ppm over the course of 180 minutes of measurement.
  - The magnitude of abnormal rise under 90 minutes not specified, but Pimentel stated later that most patients had a rise of 20 parts per million or more within that first 90-minute period.

2017 NORTH AMERICAN CONSENSUS

- An increase in hydrogen greater than or equal to 20 parts per million **before** 90 minutes is positive.
    - The "double peak" has no validity and should not be used.
    - A rise in hydrogen that occurs **after** 90 minutes is **not** a positive result.
- A methane level greater than or equal to 10 parts per million **at any point** during the test is considered positive for methane.

GLUCOSE VERSUS LACTULOSE AS SUBSTRATES

Substrate	Advantage	Disadvantage	Risk
Glucose	More specific	Greater risk of *false negative*	Under-treatment
Lactulose	More sensitive	Greater risk of *false positive*	Over-treatment

Glucose is absorbed in the proximal small intestine and the duodenum, so if overgrowth of bacteria is occurring in the jejunum or ileum, you may get a false negative. Lactulose is not absorbed at all in the small intestine. It is fermented by bacteria in the colon.

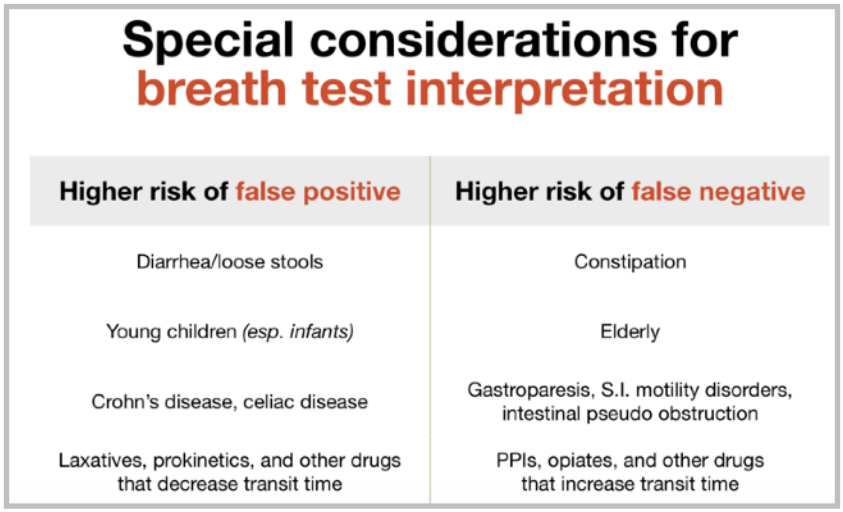
The issue with lactulose as a substrate is that the lactulose breath test is based on the idea that orocecal transit time, or the amount of time it takes for a substance to go from the mouth to the cecum, which is the first part of the colon, in healthy people is always 90 minutes.
However, there's a problem with this because studies have shown that orocecal transit time in healthy people averages from 72 to 85 minutes. Further complicating this problem is that lactulose has a laxative effect. It accelerates transit time, so even someone who normally has an orocecal transit time of 90 minutes, if they take lactulose, it might reach the colon in less than 90 minutes, and that could generate a false positive.

Despite its drawbacks, Chris prefers lactulose substrate because potential benefits of treatment, coupled with the general safety of the treatment interventions outweigh the potential risk under-treating with a false negative. However, the risk of a false positive is that you may miss other underlying issues. If the patient is treated and does not improve, you should reconsider whether there might be something else going on that is driving the bacterial overgrowth.

CONSIDERATIONS FOR WHICH LABS TO USE FOR BREATH TESTING:

1. Labs should use Quintron machine
2. Test for both H_2 and CH_4
3. Follows 2017 North American Consensus

- **BioHealth 900-C (lactulose)**
  - The only lab that has completely updated their criteria to meet the 2017 Consensus
  - Test timing is every 15 minutes for 135 minutes total collection time
  - Be sure you select 900-C (not plain 900, which is the old test)
  - Turn around time is 5-6 days
- **BioHealth 901-C (glucose)**
  - Updated with an increase in 20 parts per million more for hydrogen values as per the Consensus
- **Genova SIBO Breath Test**
  - Have adopted the 2017 Consensus criteria but lack a 90-minute value
  - Test timing is every 20 minutes for either 120 or 180 minutes
  - To estimate a 90-minute value, look at the 80-minute and 100-minute values and half the increase between them
  - Turn around time is about 7 days
- **NUNM (NCNM)**
  - As of the release of this handout, they have not updated their criteria to match the 2017 Consensus
  - Chris stopped using this lab in 2018
- **Commonwealth Lab**
  - Chris does not currently use them - had issues with their billing practices in the past



Patients with lactose allergies should not do lactulose breath testing. If it's just a lactose intolerance, if it isn't IgA-mediated, most patients can do the test, but they may experience some discomfort. That said, a lot of people with SIBO also experience discomfort with lactulose because it's a fermentable carbohydrate, so we typically will tell patients with lactose intolerance that they can do the test but just to be prepared for some discomfort, and after the test, they can take some Lactase or something that helps with breakdown of lactose.

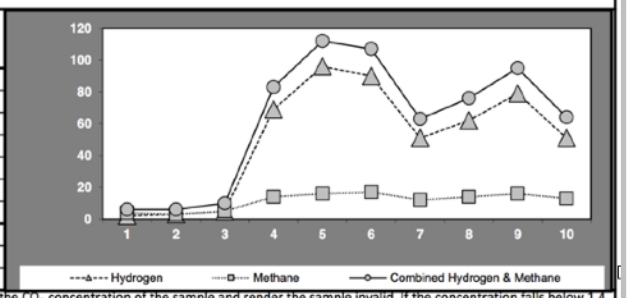
IMPROPER TEST PREP:

- High levels of baseline hydrogen can be a result of SIBO, but it can also be a result of improper test preparation. Typically, when you see improper test prep, you'll see a high baseline level of hydrogen and maybe high at 20 minutes, and then it drops down into the normal range.
- High levels of baseline methane can be normal, and it's usually not caused by improper test preparation. Most often it indicates a positive result.

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	2	4	6	OK
2	20 min	3	3	6	OK
3	40 min	5	5	10	OK
4	60 min	69	14	83	OK
5	80 min	96	16	112	OK
6	100 min	90	17	107	OK
7	120 min	51	12	63	OK
8	140 min	62	14	76	OK
9	160 min	79	16	95	OK
10	180 min	51	13	64	OK



*Dilutions of the sample may occur during the sampling procedure which may decrease the CO_2 concentration of the sample and render the sample invalid. If the concentration falls below 1.4 %, the entry for CO_2 will be marked as Quantity Not Sufficient (QNS) and the entries for H_2 and CH_4 will be highlighted. If the sample is otherwise unusable the entry for CO_2 will be marked as Not Available (N/A) and the entries for H_2 and CH_4 will be highlighted. See notes section for details if cells are highlighted and blank or highlighted and contain N/A or QNS.

Analysis

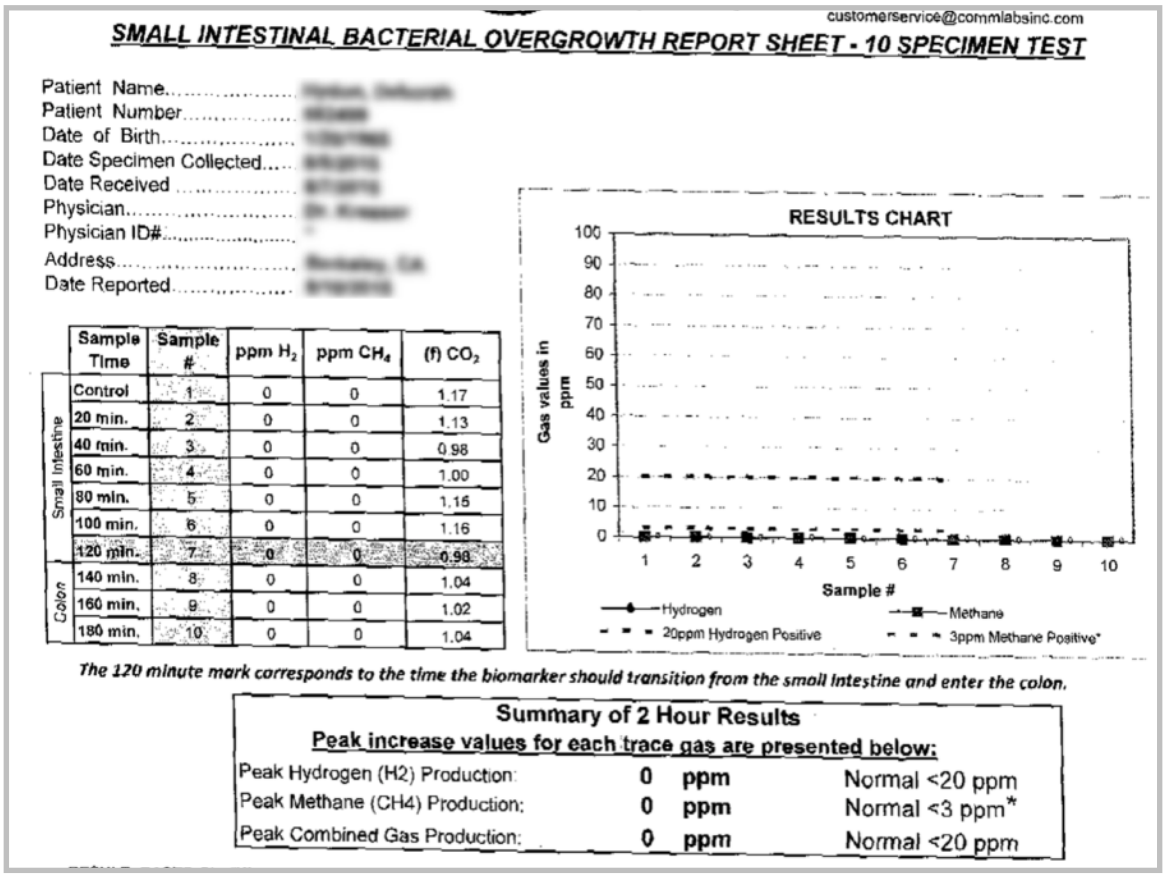
Combined baseline total =	6	-	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	94	H	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	14	H	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	106	H	≤15ppm

Interpretation

SIBO Suspected - Elevated Hydrogen	Increases of hydrogen greater than 20ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**POSITIVE**
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**POSITIVE**
SIBO Suspected - Elevated Combined Hydrogen & Methane Gasses	Increases in combined hydrogen and methane gas values greater than 15ppm over the lowest preceding value are indicative of bacterial overgrowth.	**POSITIVE**

THE ABOVE EXAMPLE SHOWS:

- Strong positive result for hydrogen. It increases from 5 parts per million, which is normal at 40 minutes, up to 69 parts per million at 60 minutes, and then a peak value of 96 parts per million at 80 minutes. Then it drops down again, and then it goes up again as the lactulose enters the colon, so this is a classic double peak.
- Also see that there's an increase of 4 parts per million at baseline of methane to 14 parts per million at 60 minutes, and then a peak value of 17 parts per million at 100 minutes, so that would be a positive for methane as well.
- Also positive for combined hydrogen and methane.



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SMALL INTESTINAL BACTERIAL OVERGROWTH REPORT SHEET - 10 SPECIMEN TEST

Patient Name.....
Patient Number.....
Date of Birth.....
Date Specimen Collected.....
Date Received .....
Physician.....
Physician ID#.....
Address.....
Date Reported.....

	Sample Time	Sample #	ppm H_2	ppm CH_4	(f) CO_2
Small Intestine	Control	1	0	0	1.17
	20 min.	2	0	0	1.13
	40 min.	3	0	0	0.98
	60 min.	4	0	0	1.00
	80 min.	5	0	0	1.15
	100 min.	6	0	0	1.16
	120 min.	7	0	0	0.98
Colon	140 min.	8	0	0	1.04
	160 min.	9	0	0	1.02
	180 min.	10	0	0	1.04

The 120 minute mark corresponds to the time the biomarker should transition from the small intestine and enter the colon.

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

Peak Hydrogen (H2) Production:	**0 ppm**	Normal <20 ppm
Peak Methane (CH4) Production:	**0 ppm**	Normal <3 ppm*
Peak Combined Gas Production:	**0 ppm**	Normal <20 ppm

There are a couple different possibilities for a result with zeros across the board as seen above:

1. The patient is severely constipated, and the lactulose has been in the small intestine this entire time.
2. There is production of other types of gases that aren't measured by this test.
    a. Studies show that patients with lower methane production, like zeros here, can have higher concentrations of sulfate-reducing bacteria, and the product of sulfate reduction is hydrogen sulfide. Hydrogen sulfide should be removed by first-pass detoxification in the liver, but if detox mechanisms are impaired, the hydrogen sulfide can accumulate in the small intestine and the colon.
    b. The sulfate-reducing bacteria consume all of the hydrogen that would normally have been produced by bacteria, and there's nothing left for methanogens to consume, so the methanogens get starved out. This results in zero for both hydrogen and methane levels.

Currently, if we see these zeros and if the patient has a lot of signs and symptoms of SIBO, then we will generally do a therapeutic trial and treat them and see how they respond.