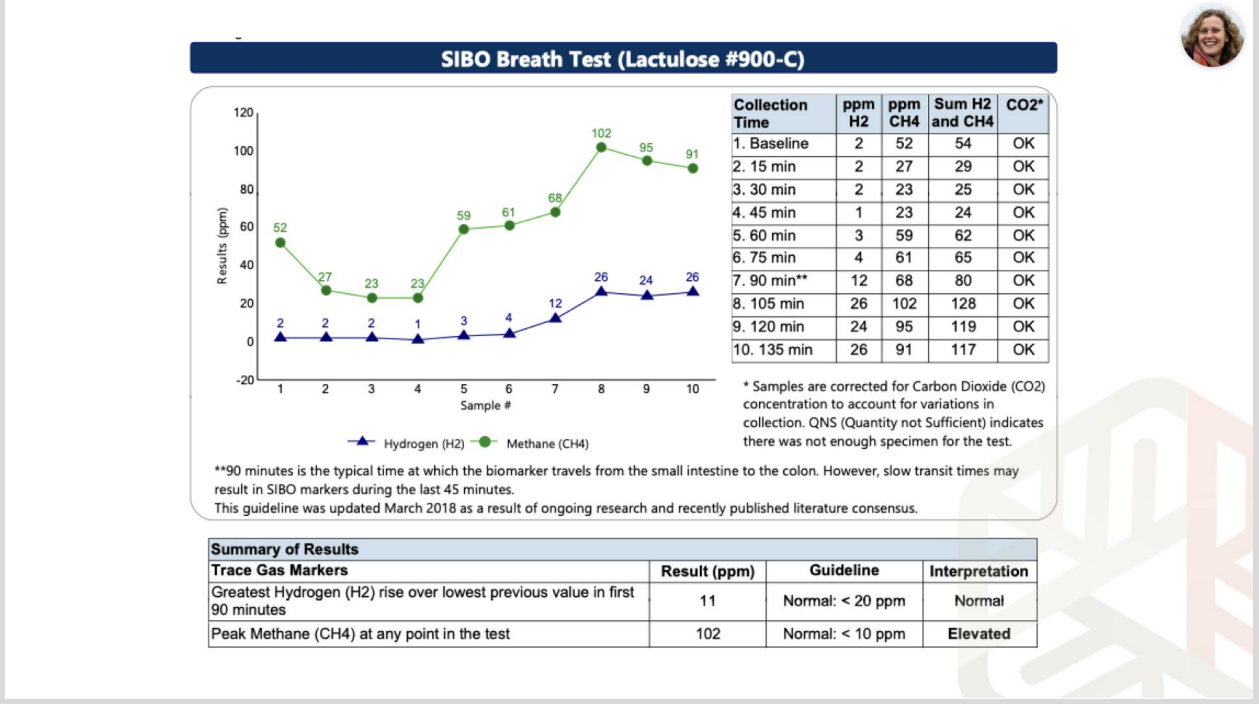
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Gut Case Studies, Part 5

CASE #9: 45-YEAR-OLD FEMALE

Next is a 45-year-old female with chief complaint[s] of nasal congestion and constipation. She'd been diagnosed with hypothyroidism several years ago, but it seemed to be under control pretty well with thyroid replacement. Red wine seems to be the only observed trigger for nasal congestion. [She] has done some elimination diets before, and that seems to help with both congestion and constipation. But as soon as she adds any food back in, symptoms return, which is fairly common for us to see, especially if the underlying imbalance isn't addressed. She had been diagnosed with [small intestinal bacterial overgrowth] (SIBO) in the past and has been through two different antimicrobial or botanical-type protocols prior to coming to see me and was inquiring about pharmaceutical treatments specifically. This happens quite often, actually. Now that SIBO and functional [gastrointestinal] disorders are starting to become a little more well-known, I find that people have often already tried some sort of treatment by the time they've gotten to me. We review what they've done in the past. We double-check the dose, type of treatment, and aim to make sure that we can confidently call it, quote, "A failed treatment," before we decide to not repeat [it]. So, for her, I felt pretty good about what she had tried with her previous provider. The protocols were similar to what we would have done, so it did seem to make sense to assume that those treatments were ineffective.



SIBO Breath Test (Lactulose #900-C)

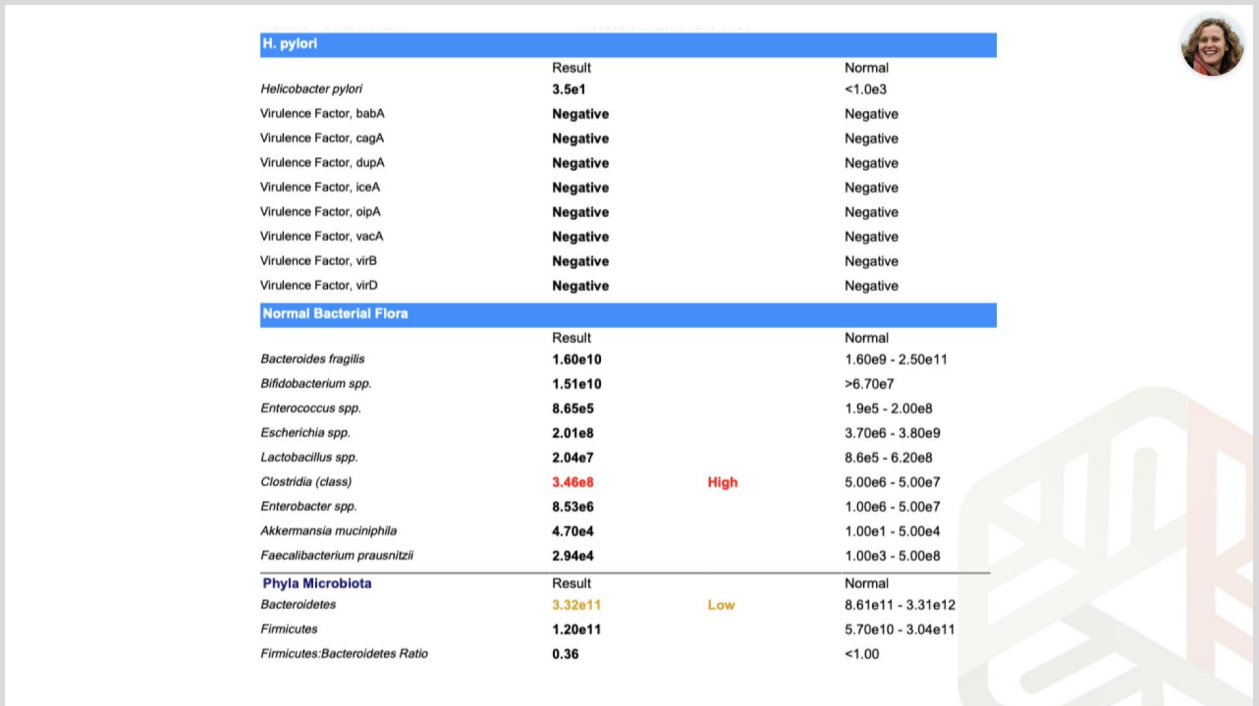
Collection Time	ppm H2	ppm CH4	Sum H2 and CH4	CO2*
1. Baseline	2	52	54	OK
2. 15 min	2	27	29	OK
3. 30 min	2	23	25	OK
4. 45 min	1	23	24	OK
5. 60 min	3	59	62	OK
6. 75 min	4	61	65	OK
7. 90 min**	12	68	80	OK
8. 105 min	26	102	128	OK
9. 120 min	24	95	119	OK
10. 135 min	26	91	117	OK

* Samples are corrected for Carbon Dioxide (CO2) concentration to account for variations in collection. QNS (Quantity not Sufficient) indicates there was not enough specimen for the test.

**90 minutes is the typical time at which the biomarker travels from the small intestine to the colon. However, slow transit times may result in SIBO markers during the last 45 minutes.
This guideline was updated March 2018 as a result of ongoing research and recently published literature consensus.

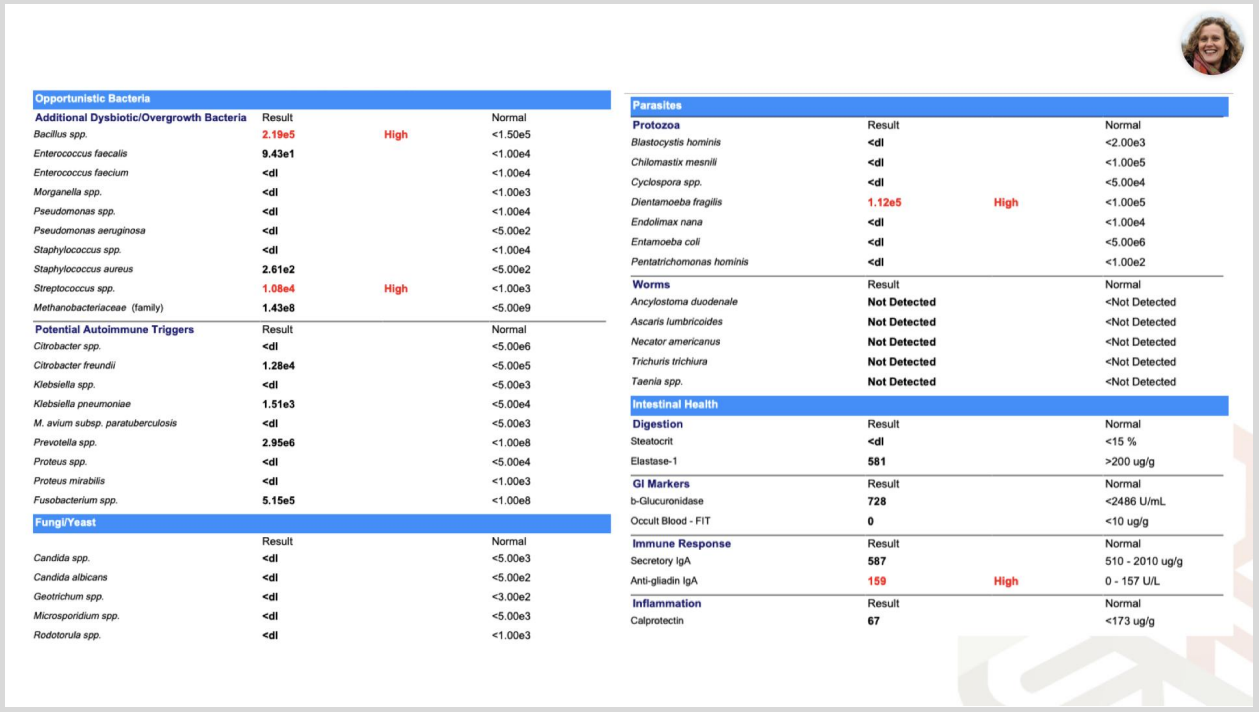
Summary of Results			
Trace Gas Markers	**Result (ppm)**	**Guideline**	**Interpretation**
Greatest Hydrogen (H2) rise over lowest previous value in first 90 minutes	11	Normal: < 20 ppm	Normal
Peak Methane (CH4) at any point in the test	102	Normal: < 10 ppm	**Elevated**

Here are the SIBO results from the Genova SIBO lactulose breath test. You can see that her hydrogen levels were normal, but her methane levels were super high at 102, being the highest value at the 105-minute mark.



H. pylori			
	Result		Normal
Helicobacter pylori	**3.5e1**		<1.0e3
Virulence Factor, babA	**Negative**		Negative
Virulence Factor, cagA	**Negative**		Negative
Virulence Factor, dupA	**Negative**		Negative
Virulence Factor, iceA	**Negative**		Negative
Virulence Factor, oipA	**Negative**		Negative
Virulence Factor, vacA	**Negative**		Negative
Virulence Factor, virB	**Negative**		Negative
Virulence Factor, virD	**Negative**		Negative
Normal Bacterial Flora			
	Result		Normal
Bacteroides fragilis	**1.60e10**		1.60e9 - 2.50e11
Bifidobacterium spp.	**1.51e10**		>6.70e7
Enterococcus spp.	**8.65e5**		1.9e5 - 2.00e8
Escherichia spp.	**2.01e8**		3.70e6 - 3.80e9
Lactobacillus spp.	**2.04e7**		8.6e5 - 6.20e8
Clostridia (class)	**3.46e8**	High	5.00e6 - 5.00e7
Enterobacter spp.	**8.53e6**		1.00e6 - 5.00e7
Akkermansia muciniphila	**4.70e4**		1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**2.94e4**		1.00e3 - 5.00e8
Phyla Microbiota	Result		Normal
Bacteroidetes	**3.32e11**	Low	8.61e11 - 3.31e12
Firmicutes	**1.20e11**		5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.36**		<1.00

Her [Diagnostic Solutions Laboratory] (DSL) GI-MAP stool test had very low levels of [*Helicobacter*] *pylori* without any virulence factors, and her normal bacterial flora section was mostly normal, in my opinion.



Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	2.19e5	High	<1.50e5
Enterococcus faecalis	9.43e1		<1.00e4
Enterococcus faecium	<dl		<1.00e4
Morganella spp.	<dl		<1.00e3
Pseudomonas spp.	<dl		<1.00e4
Pseudomonas aeruginosa	<dl		<5.00e2
Staphylococcus spp.	<dl		<1.00e4
Staphylococcus aureus	2.61e2		<5.00e2
Streptococcus spp.	1.08e4	High	<1.00e3
Methanobacteriaceae (family)	1.43e8		<5.00e9

Potential Autoimmune Triggers	Result	Normal
Citrobacter spp.	<dl	<5.00e6
Citrobacter freundii	1.28e4	<5.00e5
Klebsiella spp.	<dl	<5.00e3
Klebsiella pneumoniae	1.51e3	<5.00e4
M. avium subsp. paratuberculosis	<dl	<5.00e3
Prevotella spp.	2.95e6	<1.00e8
Proteus spp.	<dl	<5.00e4
Proteus mirabilis	<dl	<1.00e3
Fusobacterium spp.	5.15e5	<1.00e8

Fungi/Yeast

	Result	Normal
Candida spp.	<dl	<5.00e3
Candida albicans	<dl	<5.00e2
Geotrichum spp.	<dl	<3.00e2
Microsporidium spp.	<dl	<5.00e3
Rodotorula spp.	<dl	<1.00e3

Parasites

Protozoa	Result		Normal
Blastocystis hominis	<dl		<2.00e3
Chilomastix mesnili	<dl		<1.00e5
Cyclospora spp.	<dl		<5.00e4
Dientamoeba fragilis	1.12e5	High	<1.00e5
Endolimax nana	<dl		<1.00e4
Entamoeba coli	<dl		<5.00e6
Pentatrichomonas hominis	<dl		<1.00e2

Worms	Result	Normal
Ancylostoma duodenale	Not Detected	<Not Detected
Ascaris lumbricoides	Not Detected	<Not Detected
Necator americanus	Not Detected	<Not Detected
Trichuris trichiura	Not Detected	<Not Detected
Taenia spp.	Not Detected	<Not Detected

Intestinal Health

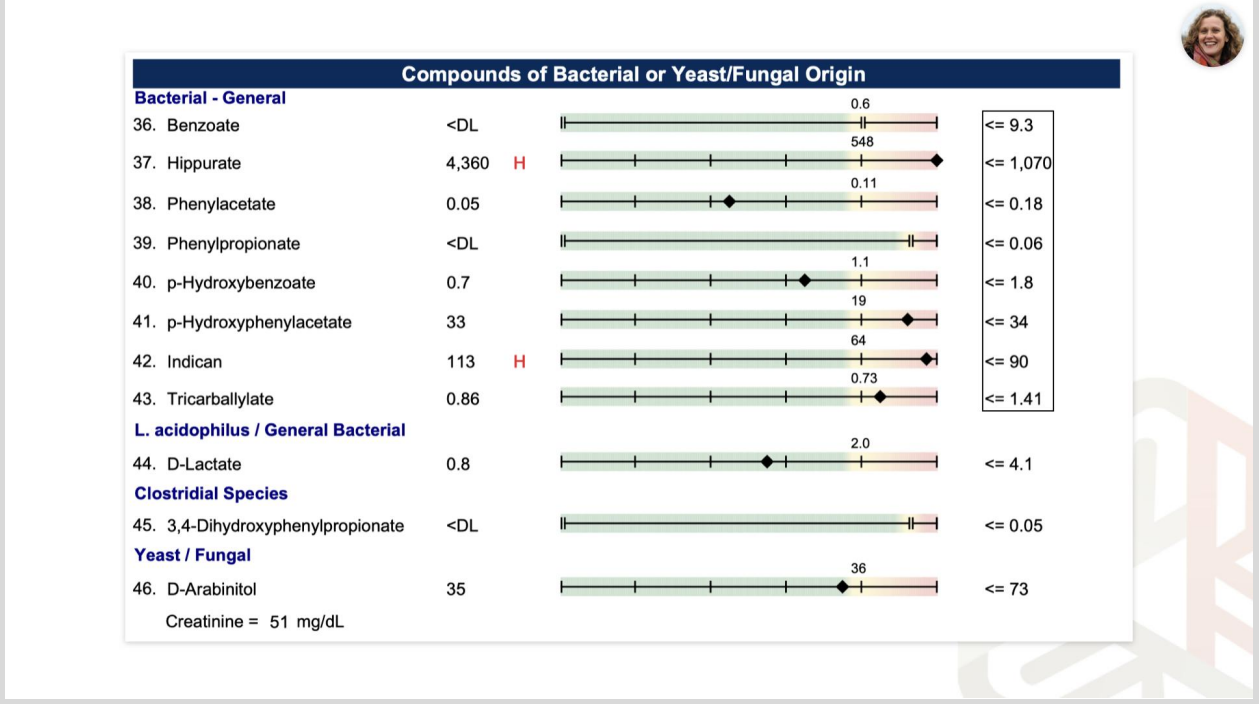
Digestion	Result	Normal
Steatocrit	<dl	<15 %
Elastase-1	581	>200 ug/g

GI Markers	Result	Normal
b-Glucuronidase	728	<2486 U/mL
Occult Blood - FIT	0	<10 ug/g

Immune Response	Result		Normal
Secretory IgA	587		510 - 2010 ug/g
Anti-gliadin IgA	159	High	0 - 157 U/L

Inflammation	Result	Normal
Calprotectin	67	<173 ug/g

She had a few low levels of *Citrobacter* and *Klebsiella*, as you can see here. She has no real personal or family history of autoimmune disease, and her antibodies were normal, and the thyroid ultrasound also came back normal, so I wasn't really planning on chasing these trace amounts of organisms in this section. She did have some [*Dientamoeba*] *fragilis*. Again, [it's] hard to know if this is an issue or something that is transiently passing through that we often see in practice and in the literature. Her fecal anti-gliadin and [immunoglobulin A] (IgA) came back high in her stool. I [confirmed] with her, and she had just come back from vacation where she had been consuming gluten. And she wasn't super strict about it previously and probably has gluten about once or twice a week on average. So we are seeing some immune activity against gluten in this fecal marker.

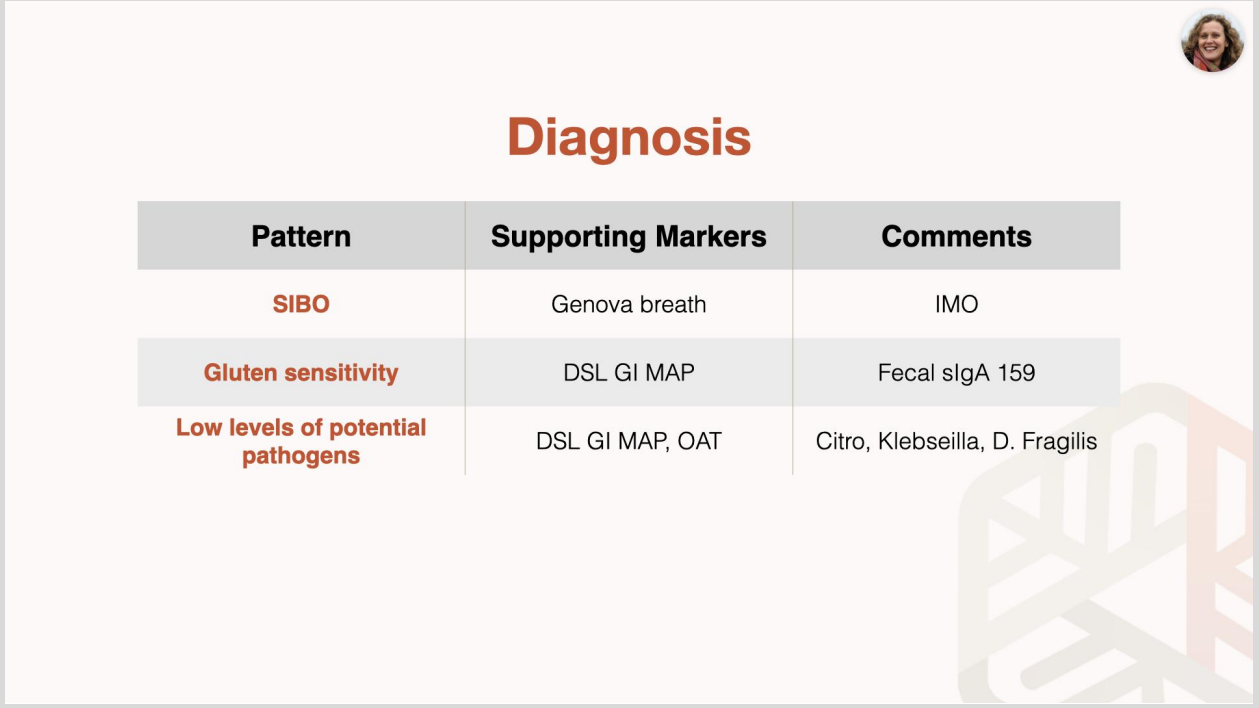


Compounds of Bacterial or Yeast/Fungal Origin

Bacterial - General				
36. Benzoate	<DL		0.6	<= 9.3
37. Hippurate	4,360	H	548	<= 1,070
38. Phenylacetate	0.05		0.11	<= 0.18
39. Phenylpropionate	<DL			<= 0.06
40. p-Hydroxybenzoate	0.7		1.1	<= 1.8
41. p-Hydroxyphenylacetate	33		19	<= 34
42. Indican	113	H	64	<= 90
43. Tricarballylate	0.86		0.73	<= 1.41
L. acidophilus / General Bacterial				
44. D-Lactate	0.8		2.0	<= 4.1
Clostridial Species				
45. 3,4-Dihydroxyphenylpropionate	<DL			<= 0.05
Yeast / Fungal				
46. D-Arabinitol	35		36	<= 73

Creatinine = 51 mg/dL

Here you can see her organic acids test had high indican and hippurate levels.



Diagnosis

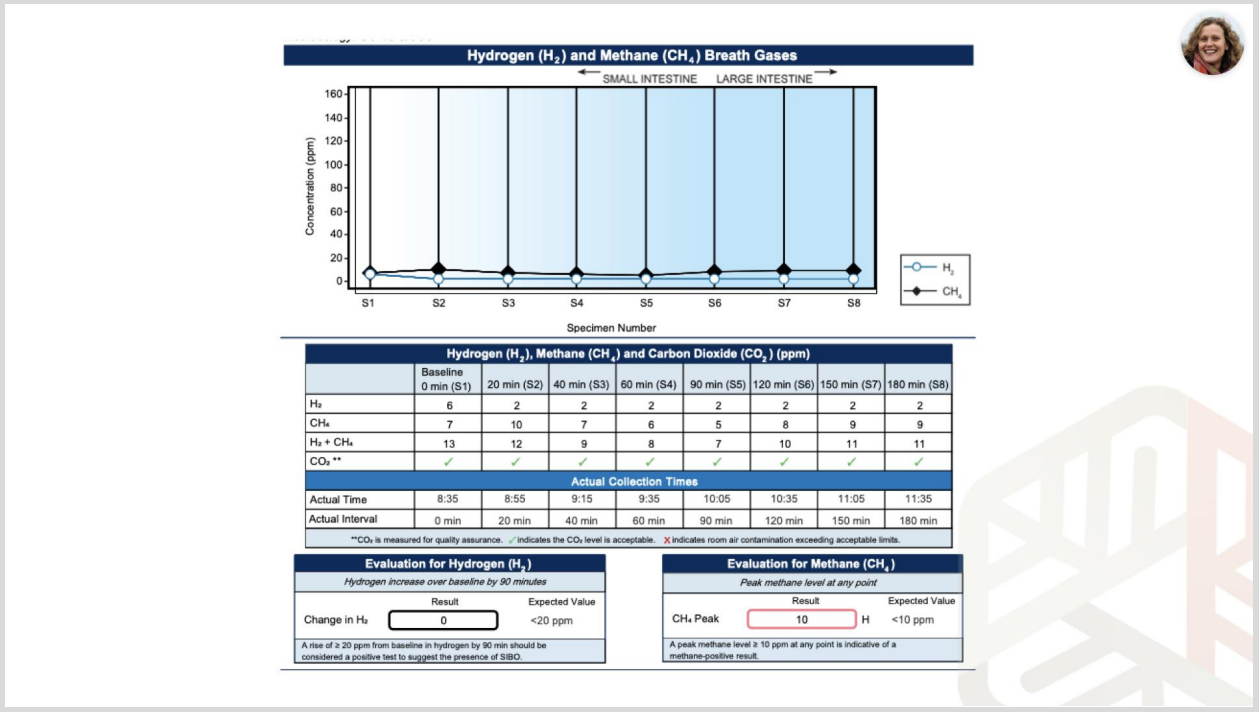
Pattern	Supporting Markers	Comments
SIBO	Genova breath	IMO
Gluten sensitivity	DSL GI MAP	Fecal sIgA 159
Low levels of potential pathogens	DSL GI MAP, OAT	Citro, Klebseilla, D. Fragilis

Here our diagnosis with intestinal methanogen overgrowth is the primary diagnosis, and then gluten sensitivity and the low levels of potential pathogens that I put on here just to make sure it stays on our radar as we track treatment effectiveness, symptoms, and retesting.

Pharmaceutical/combo protocol for SIBO

Therapeutic Agent	Dosage
Rifaximin	550 mg TID for 3 weeks
Neomycin	500 mg BID for 10 days
InterFase Plus	3–4 capsules BID on an empty stomach
SEED	2 capsules before bed
Atrantil	2 capsules TID
PHGG	Take up to one scoop daily mixed with water, with or without food.

We decided to do a bit of a combination protocol for her. She took rifaximin for three weeks with neomycin for 10 days. In addition, I had her take a biofilm disruptor, Atrantil, [partially hydrolyzed guar gum], and Seed. She continued the botanical portion of the protocol for an additional four weeks after the prescriptions were over. So this was that pharmaceutical/botanical combination protocol we've talked about in the previous lessons.



Hydrogen (H_2) and Methane (CH_4) Breath Gases

Hydrogen (H_2), Methane (CH_4) and Carbon Dioxide (CO_2) (ppm)

	Baseline 0 min (S1)	20 min (S2)	40 min (S3)	60 min (S4)	90 min (S5)	120 min (S6)	150 min (S7)	180 min (S8)
H_2	6	2	2	2	2	2	2	2
CH_4	7	10	7	6	5	8	9	9
$H_2 + CH_4$	13	12	9	8	7	10	11	11
CO_2 **	✓	✓	✓	✓	✓	✓	✓	✓
Actual Collection Times								
Actual Time	8:35	8:55	9:15	9:35	10:05	10:35	11:05	11:35
Actual Interval	0 min	20 min	40 min	60 min	90 min	120 min	150 min	180 min

**CO_2 is measured for quality assurance. ✓ indicates the CO_2 level is acceptable. X indicates room air contamination exceeding acceptable limits.

Evaluation for Hydrogen (H_2)

Hydrogen increase over baseline by 90 minutes

	Result	Expected Value
Change in H_2	0	<20 ppm

A rise of ≥ 20 ppm from baseline in hydrogen by 90 min should be considered a positive test to suggest the presence of SIBO.

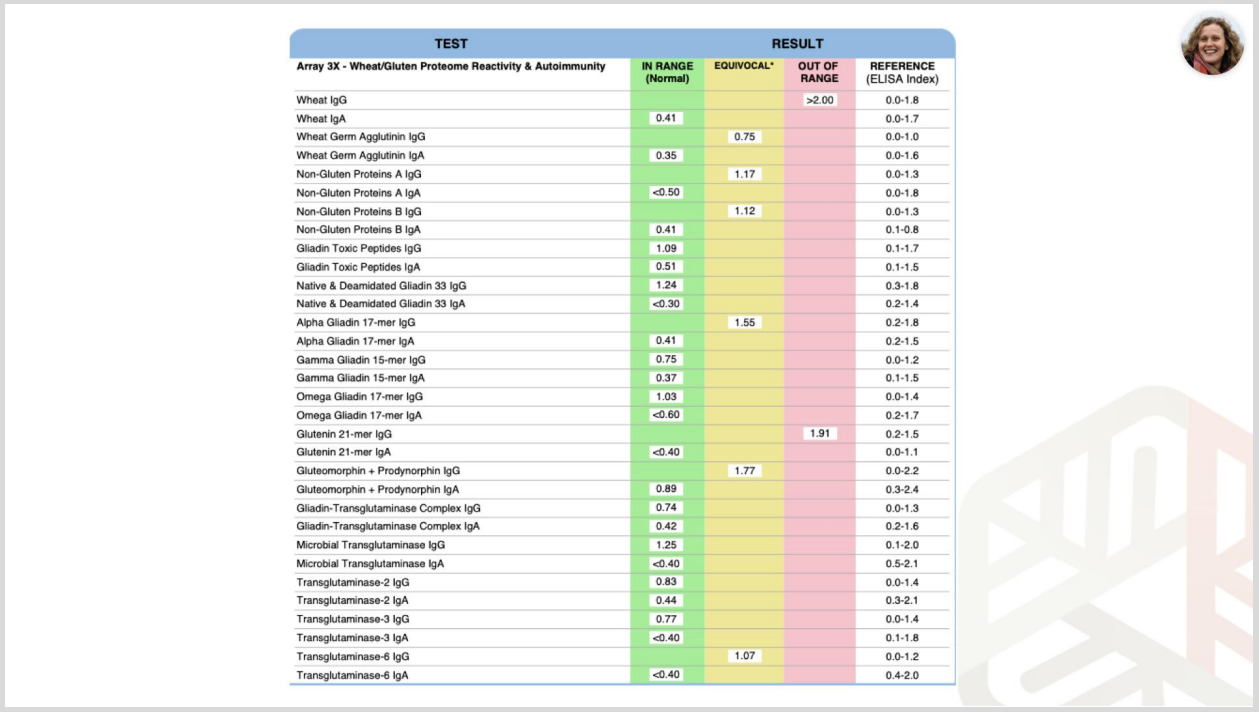
Evaluation for Methane (CH_4)

Peak methane level at any point

	Result		Expected Value
CH_4 Peak	10	H	<10 ppm

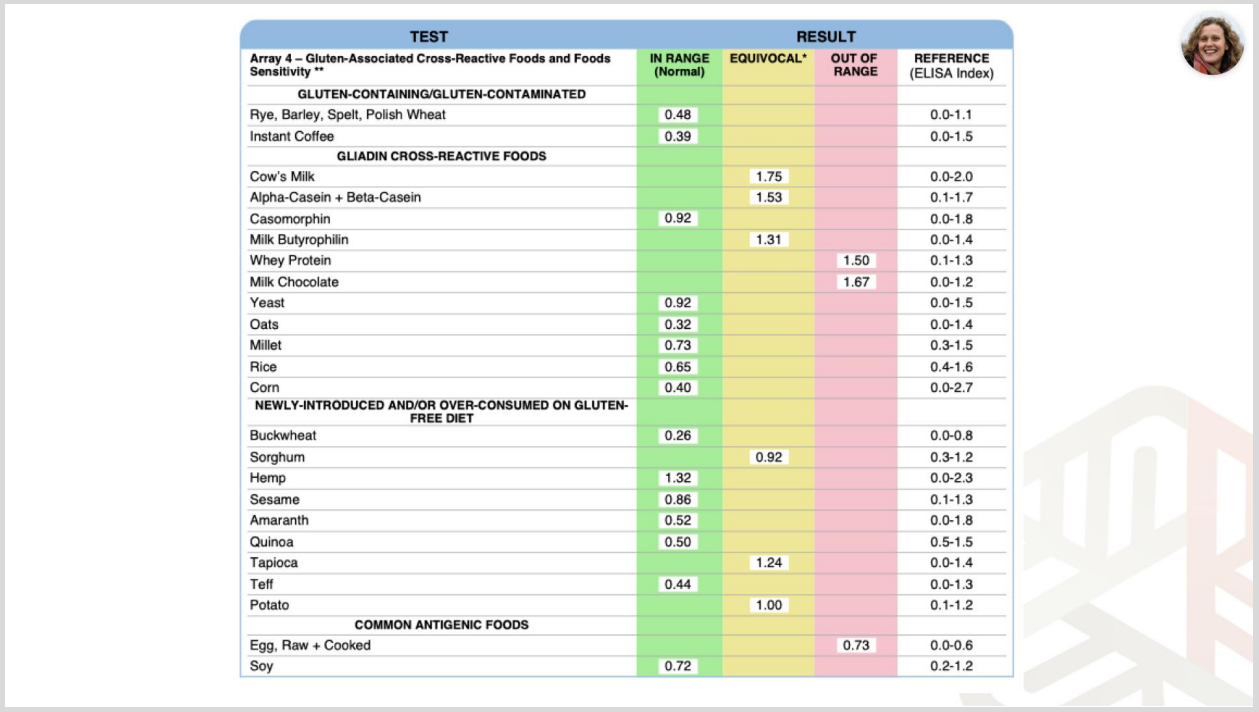
A peak methane level ≥ 10 ppm at any point is indicative of a methane-positive result.

Here's her follow-up for [the] Genova SIBO breath test. I honestly could barely believe that these numbers came down so nicely. For me, it's rare that with the methane level in the hundreds, we're really able to have this level of improvement the first go around, although she had had a couple of other treatments. So [it's] a little tough to know, really. This isn't really considered her first treatment, so that's something to consider. A methane [level] of 10 is still technically positive, but I probably wasn't going to chase this on its own. But [it] just really depended on the presentation of her at this point. She was reporting about 75 percent improvement in constipation. [There was] not much noticeable change in the nasal congestion, though. But still, I'll take the improvement in constipation with this result.



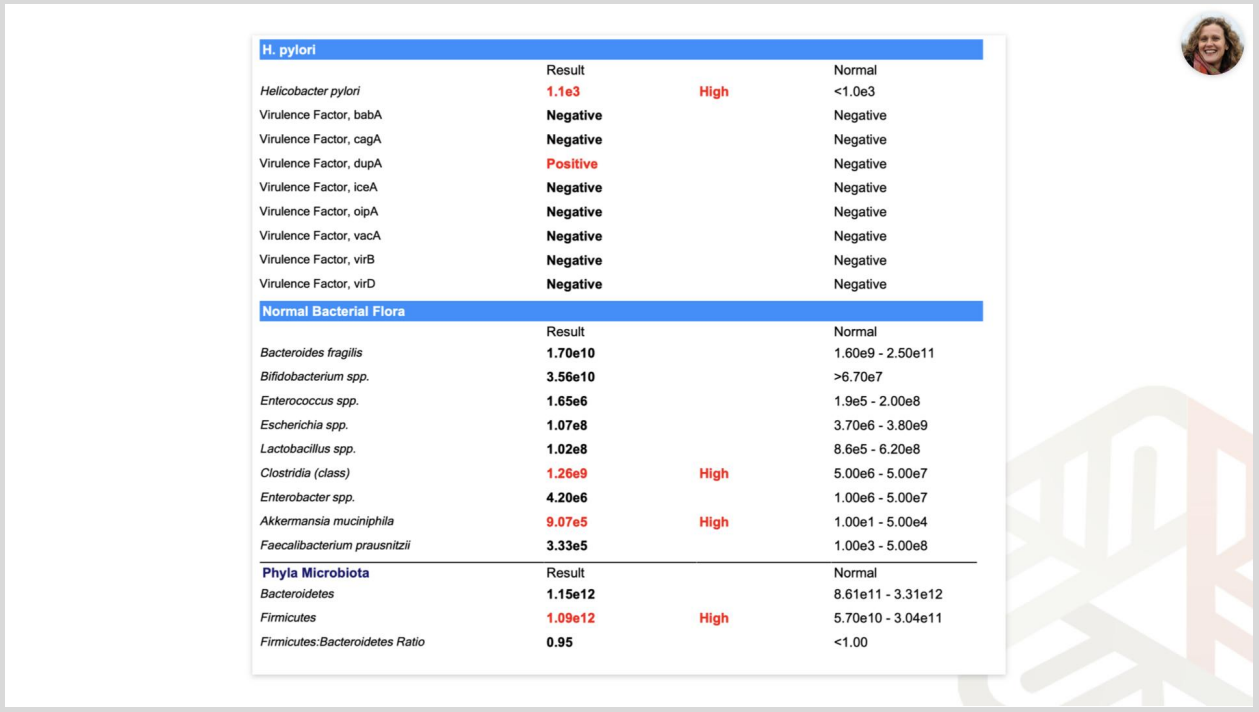
TEST	RESULT			
Array 3X - Wheat/Gluten Proteome Reactivity & Autoimmunity	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Wheat IgG			>2.00	0.0-1.8
Wheat IgA	0.41			0.0-1.7
Wheat Germ Agglutinin IgG		0.75		0.0-1.0
Wheat Germ Agglutinin IgA	0.35			0.0-1.6
Non-Gluten Proteins A IgG		1.17		0.0-1.3
Non-Gluten Proteins A IgA	<0.50			0.0-1.8
Non-Gluten Proteins B IgG		1.12		0.0-1.3
Non-Gluten Proteins B IgA	0.41			0.1-0.8
Gliadin Toxic Peptides IgG	1.09			0.1-1.7
Gliadin Toxic Peptides IgA	0.51			0.1-1.5
Native & Deamidated Gliadin 33 IgG	1.24			0.3-1.8
Native & Deamidated Gliadin 33 IgA	<0.30			0.2-1.4
Alpha Gliadin 17-mer IgG		1.55		0.2-1.8
Alpha Gliadin 17-mer IgA	0.41			0.2-1.5
Gamma Gliadin 15-mer IgG	0.75			0.0-1.2
Gamma Gliadin 15-mer IgA	0.37			0.1-1.5
Omega Gliadin 17-mer IgG	1.03			0.0-1.4
Omega Gliadin 17-mer IgA	<0.60			0.2-1.7
Glutenin 21-mer IgG			1.91	0.2-1.5
Glutenin 21-mer IgA	<0.40			0.0-1.1
Gluteomorphin + Prodynorphin IgG		1.77		0.0-2.2
Gluteomorphin + Prodynorphin IgA	0.89			0.3-2.4
Gliadin-Transglutaminase Complex IgG	0.74			0.0-1.3
Gliadin-Transglutaminase Complex IgA	0.42			0.2-1.6
Microbial Transglutaminase IgG	1.25			0.1-2.0
Microbial Transglutaminase IgA	<0.40			0.5-2.1
Transglutaminase-2 IgG	0.83			0.0-1.4
Transglutaminase-2 IgA	0.44			0.3-2.1
Transglutaminase-3 IgG	0.77			0.0-1.4
Transglutaminase-3 IgA	<0.40			0.1-1.8
Transglutaminase-6 IgG		1.07		0.0-1.2
Transglutaminase-6 IgA	<0.40			0.4-2.0

I should mention that we also ran a Cyrex [Array] 3X and [a Cyrex Array] 4, considering her elevated levels of fecal anti-gliadin and IgA on the GI-MAP. And she wasn't super strict about eliminating previously, so we really wanted to know what level of involvement [we are] dealing with and for her to know how compliant to be. Since she had just [come] back from vacation, [and] had been eating it regularly, I thought it was a good time to check in on these foods. So you can see here that there are quite a few markers out of range. And I would even categorize the high normal or equivocal markers as out of range also, especially since they're on the high end of that range. So make sure to go back and review the Cyrex panel lesson for more information on how to interpret these labs. But I am considering her gluten-sensitive at the very least here, and we could consider additional celiac [disease] testing if she really wanted to pursue it.



TEST	RESULT			
Array 4 – Gluten-Associated Cross-Reactive Foods and Foods Sensitivity **	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
GLUTEN-CONTAINING/GLUTEN-CONTAMINATED				
Rye, Barley, Spelt, Polish Wheat	0.48			0.0-1.1
Instant Coffee	0.39			0.0-1.5
GLIADIN CROSS-REACTIVE FOODS				
Cow's Milk		1.75		0.0-2.0
Alpha-Casein + Beta-Casein		1.53		0.1-1.7
Casomorphin	0.92			0.0-1.8
Milk Butyrophilin		1.31		0.0-1.4
Whey Protein			1.50	0.1-1.3
Milk Chocolate			1.67	0.0-1.2
Yeast	0.92			0.0-1.5
Oats	0.32			0.0-1.4
Millet	0.73			0.3-1.5
Rice	0.65			0.4-1.6
Corn	0.40			0.0-2.7
NEWLY-INTRODUCED AND/OR OVER-CONSUMED ON GLUTEN-FREE DIET				
Buckwheat	0.26			0.0-0.8
Sorghum		0.92		0.3-1.2
Hemp	1.32			0.0-2.3
Sesame	0.86			0.1-1.3
Amaranth	0.52			0.0-1.8
Quinoa	0.50			0.5-1.5
Tapioca		1.24		0.0-1.4
Teff	0.44			0.0-1.3
Potato		1.00		0.1-1.2
COMMON ANTIGENIC FOODS				
Egg, Raw + Cooked			0.73	0.0-0.6
Soy	0.72			0.2-1.2

Here's her Cyrex [Array] 4. Also, [there are] a lot of out-of-range markers. We talked about this before, and I would recommend you go back to the section for a brush-up on the Cyrex panel results. But when I see this many markers out of range for cross-reactivity, I consider something more along the lines of polyreactive or hyperreactive immune system in these cases, in addition to gluten sensitivity or a celiac [disease] diagnosis driving the high amount of cross-reactive foods on Cyrex [Array] 4. So we start with [a] strict elimination of gluten and dairy, including whey products. She already wasn't eating a lot of eggs, so we took that out as well for 60 days and then plan[ned] to go from there. Help restore the gut lining, make sure there [weren't] any intestinal permeability issues, and then decide on when and if to reintroduce.

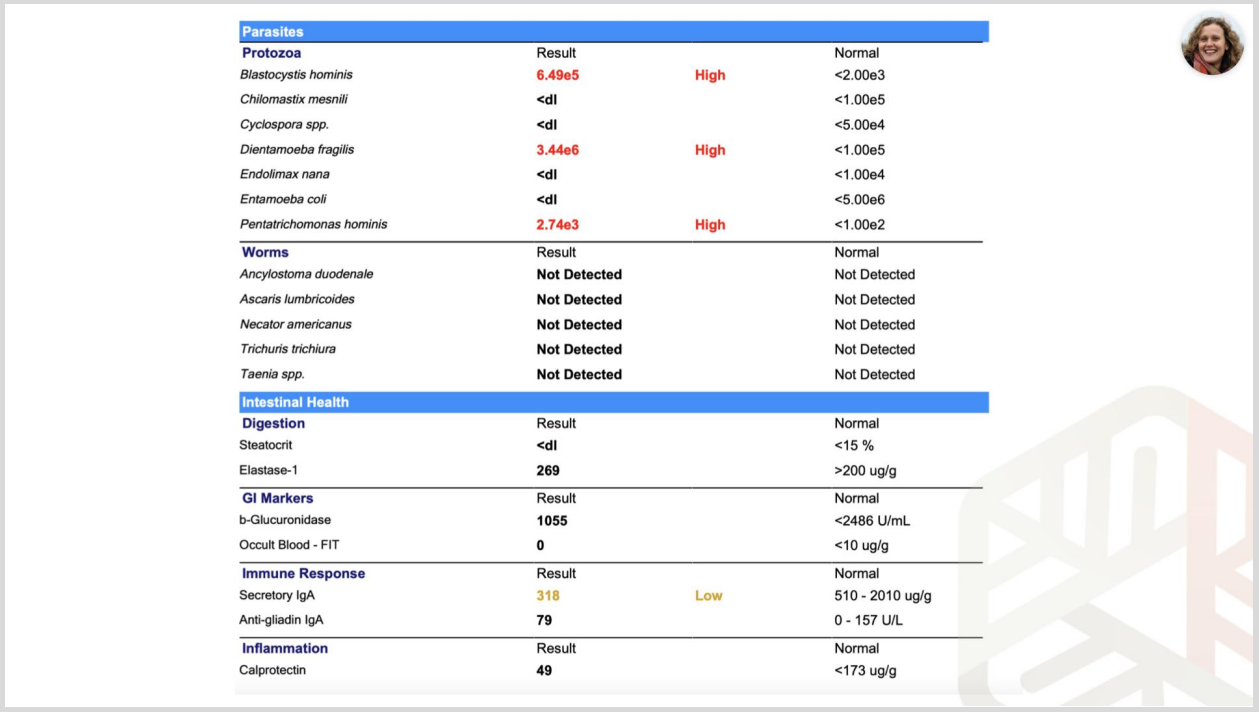


H. pylori			
	Result		Normal
Helicobacter pylori	1.1e3	High	<1.0e3
Virulence Factor, babA	Negative		Negative
Virulence Factor, cagA	Negative		Negative
Virulence Factor, dupA	Positive		Negative
Virulence Factor, iceA	Negative		Negative
Virulence Factor, oipA	Negative		Negative
Virulence Factor, vacA	Negative		Negative
Virulence Factor, virB	Negative		Negative
Virulence Factor, virD	Negative		Negative

Normal Bacterial Flora			
	Result		Normal
Bacteroides fragilis	1.70e10		1.60e9 - 2.50e11
Bifidobacterium spp.	3.56e10		>6.70e7
Enterococcus spp.	1.65e6		1.9e5 - 2.00e8
Escherichia spp.	1.07e8		3.70e6 - 3.80e9
Lactobacillus spp.	1.02e8		8.6e5 - 6.20e8
Clostridia (class)	1.26e9	High	5.00e6 - 5.00e7
Enterobacter spp.	4.20e6		1.00e6 - 5.00e7
Akkermansia muciniphila	9.07e5	High	1.00e1 - 5.00e4
Faecalibacterium prausnitzii	3.33e5		1.00e3 - 5.00e8

Phyla Microbiota	Result		Normal
Bacteroidetes	1.15e12		8.61e11 - 3.31e12
Firmicutes	1.09e12	High	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	0.95		<1.00

Here's her follow-up of the GI-MAP. So this follow-up with a little more, should I say frustrating to me. [laughter] So her follow-up of *H. pylori* test levels not only went up in quantity but also now have a virulence factor that appear[s]. So you can see why I have some concerns about the utility of this test. There's just some variability that happens that I have some questions about. And it's possible after treatment that there's more activity, more material within the stool sample. [It] could just be the sampling process. Either way, I'll make a note of this change and make sure to interpret [it] in the context of this patient and what we decide to do moving forward. She also had some additional parasites show up on the retest. So now, as we've discussed before, these parasites often come together. So it's possible that the previous test just missed these other two and only showed the *Dientamoeba fragilis*. So either way, they're now being shown on this test.

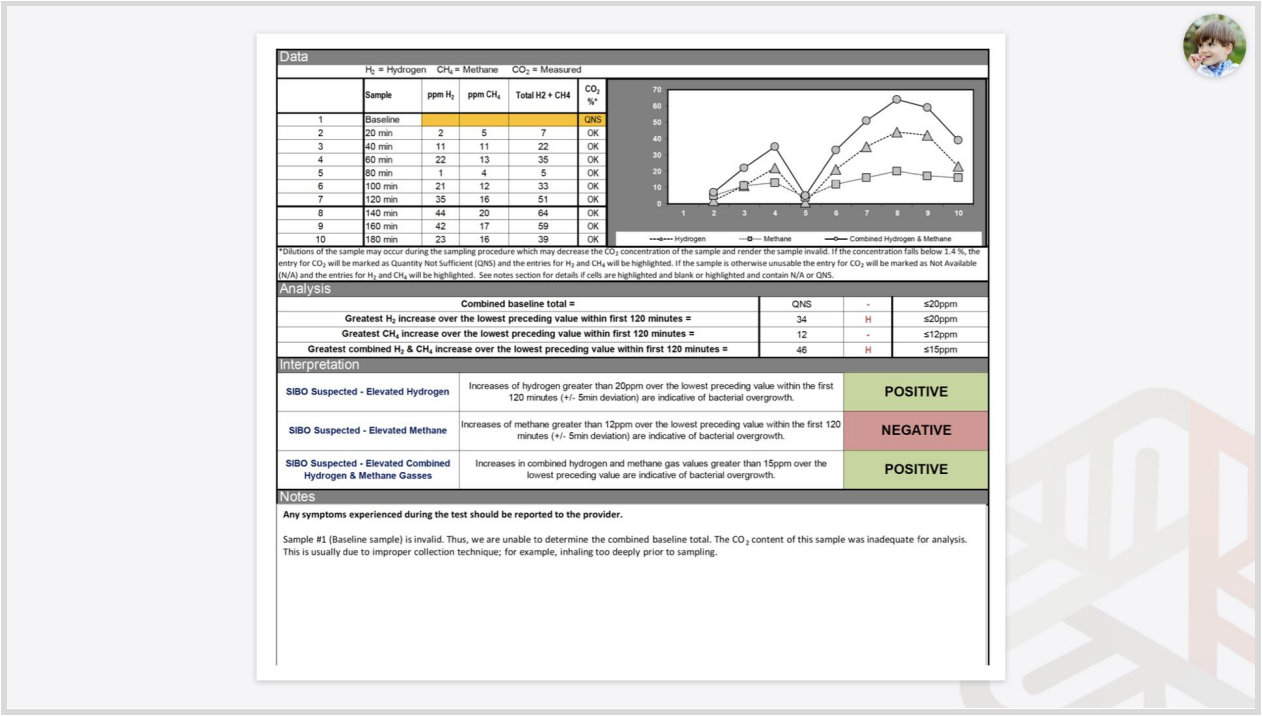


Parasites			
Protozoa	Result		Normal
Blastocystis hominis	6.49e5	High	<2.00e3
Chilomastix mesnili	<dl		<1.00e5
Cyclospora spp.	<dl		<5.00e4
Dientamoeba fragilis	3.44e6	High	<1.00e5
Endolimax nana	<dl		<1.00e4
Entamoeba coli	<dl		<5.00e6
Pentatrichomonas hominis	2.74e3	High	<1.00e2
Worms	Result		Normal
Ancylostoma duodenale	Not Detected		Not Detected
Ascaris lumbricoides	Not Detected		Not Detected
Necator americanus	Not Detected		Not Detected
Trichuris trichiura	Not Detected		Not Detected
Taenia spp.	Not Detected		Not Detected
Intestinal Health			
Digestion	Result		Normal
Steatocrit	<dl		<15 %
Elastase-1	269		>200 ug/g
GI Markers	Result		Normal
b-Glucuronidase	1055		<2486 U/mL
Occult Blood - FIT	0		<10 ug/g
Immune Response	Result		Normal
Secretory IgA	318	Low	510 - 2010 ug/g
Anti-gliadin IgA	79		0 - 157 U/L
Inflammation	Result		Normal
Calprotectin	49		<173 ug/g

Her secretory IgA lowered some, but the anti-gliadin and IgA normalize nicely with a gluten-free diet. So overall, at this point in treatment, she was reporting 75 percent improvement in constipation and slowly improving nasal congestion. So I followed up with the stool antigen and urea breath test for *H. pylori*. [I] offered her an antimicrobial protocol for the parasites. I might only do a 30-day protocol for these parasites, and that's what she did want to do. So we ended up doing a comprehensive restoration protocol after a 30-day parasite protocol, and that seemed to help with us waiting for the results to come back.

CASE #10: 4-YEAR-OLD MALE

Our last patient we're going to talk about is a four-year-old male. Chris and I saw this patient a couple of years ago. His parents' chief complaints for him were [attention-deficit/hyperactivity disorder], possible Asperger [syndrome], constipation, food allergies, environmental allergies, and skin rashes for this little guy. So it was a fairly classic presentation for a young child with behavioral or attention disorders. He did have some improvement with a Paleo-type diet that they had tried previously, but they did have a hard time getting him to adhere to it, considering his behavioral issues.



Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline				QNS
2	20 min	2	5	7	OK
3	40 min	11	11	22	OK
4	60 min	22	13	35	OK
5	80 min	1	4	5	OK
6	100 min	21	12	33	OK
7	120 min	35	16	51	OK
8	140 min	44	20	64	OK
9	160 min	42	17	59	OK
10	180 min	23	16	39	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 =	QNS	-	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	34	H	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	12	-	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	46	H	≤15ppm

Interpretation

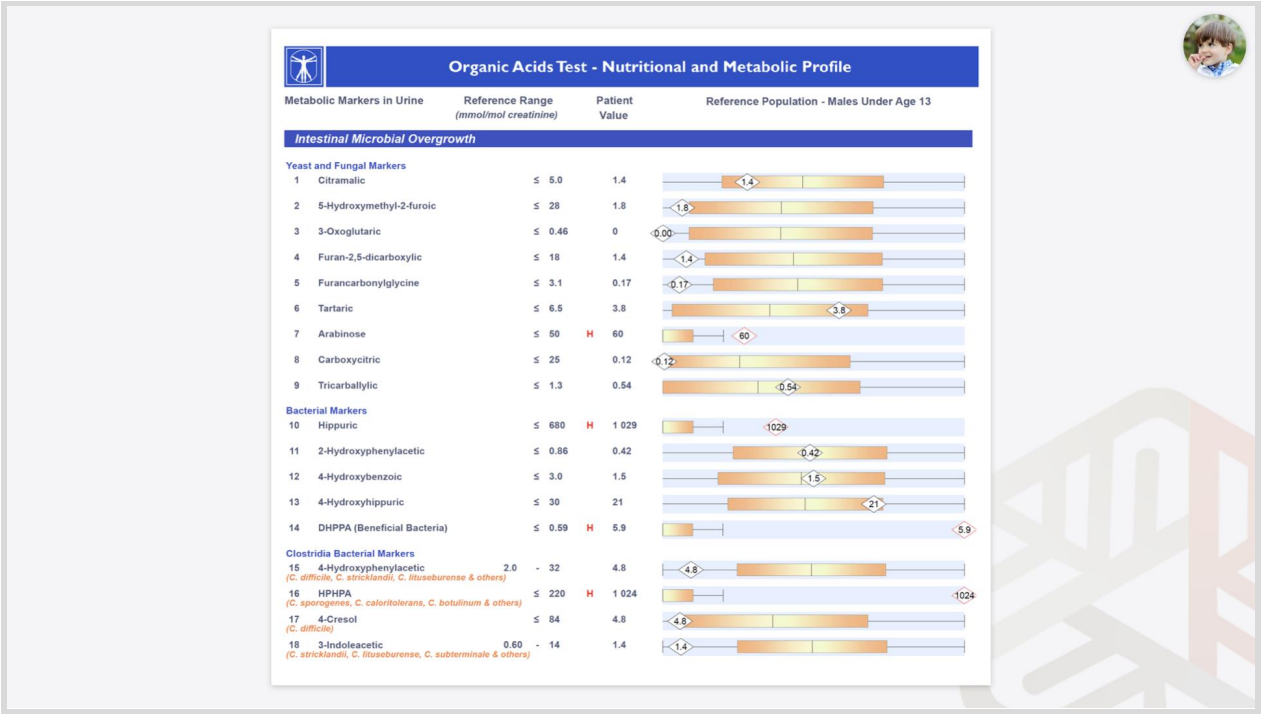
SIBO Suspected - Elevated Hydrogen	Increases of hydrogen greater than 20ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**POSITIVE**
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**NEGATIVE**
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**

Notes

Any symptoms experienced during the test should be reported to the provider.

Sample #1 (Baseline sample) is invalid. Thus, we are unable to determine the combined baseline total. The CO_2 content of this sample was inadequate for analysis. This is usually due to improper collection technique; for example, inhaling too deeply prior to sampling.

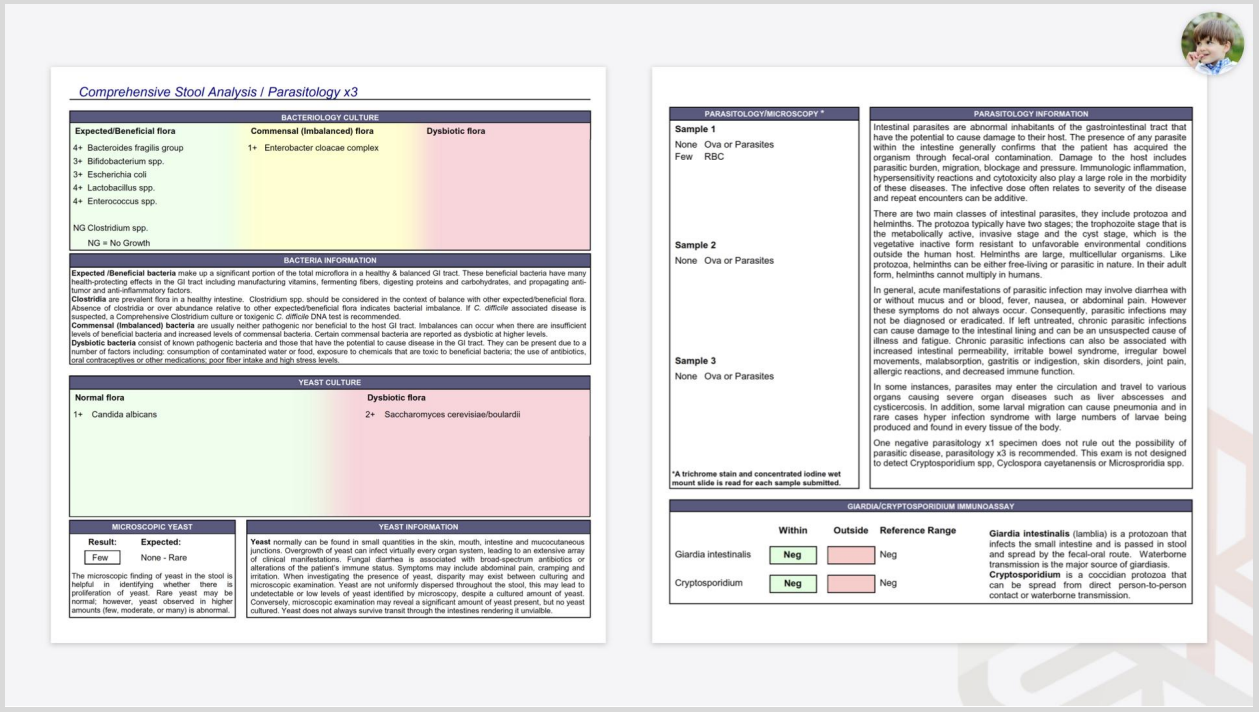
He was positive for SIBO. As a reminder, this test was done prior to the North American Consensus. So it is being interpreted a little bit different[ly] and using the 120-minute mark for hydrogen. He would technically be positive for the North American Consensus with a difference of 20 from the 20-minute mark and the 60-minute sample. Methane was positive for [the] North American Consensus with 20 parts per million at the 140-minute mark. So [I'm] not sure what to make of sample number 5, where he goes from hydrogen of 22 at 60 to 1 at 80 and then goes from methane of 13 to 4. So there's this really pronounced dip there that you can see in the chart. It's possible he didn't blow into the tube correctly. And he did have an invalid sample at number one, but they would have normally marked it invalid if that were the case. So I'm just not sure what happened here. I'm not sure it really matters necessarily in this case. With the constipation he experiences and intestinal methanogen overgrowth being predominant, I think that really makes sense for this patient.



Organic Acids Test - Nutritional and Metabolic Profile

	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth					
Yeast and Fungal Markers					
1	Citramalic	≤ 5.0		1.4	1.4
2	5-Hydroxymethyl-2-furoic	≤ 28		1.8	1.8
3	3-Oxoglutaric	≤ 0.46		0	0.00
4	Furan-2,5-dicarboxylic	≤ 18		1.4	1.4
5	Furancarbonylglycine	≤ 3.1		0.17	0.17
6	Tartaric	≤ 6.5		3.8	3.8
7	Arabinose	≤ 50	H	60	60
8	Carboxycitric	≤ 25		0.12	0.12
9	Tricarballylic	≤ 1.3		0.54	0.54
Bacterial Markers					
10	Hippuric	≤ 680	H	1 029	1029
11	2-Hydroxyphenylacetic	≤ 0.86		0.42	0.42
12	4-Hydroxybenzoic	≤ 3.0		1.5	1.5
13	4-Hydroxyhippuric	≤ 30		21	21
14	DHPPA (Beneficial Bacteria)	≤ 0.59	H	5.9	5.9
Clostridia Bacterial Markers					
15	4-Hydroxyphenylacetic (*C. difficile, C. stricklandii, C. litusebureense & others*)	2.0 - 32		4.8	4.8
16	HPHPA (*C. sporogenes, C. caloritolerans, C. botulinum & others*)	≤ 220	H	1 024	1024
17	4-Cresol (*C. difficile*)	≤ 84		4.8	4.8
18	3-Indoleacetic (*C. stricklandii, C. litusebureense, C. subterminale & others*)	0.60 - 14		1.4	1.4

As I mentioned before, we'll often order the Great Plains Organic Lab test for kids or adults with behavioral issues because it has more markers for *Clostridia* species that are often associated with these kinds of problems. Also, more fungal markers because they're also associated with what we see, especially in children with behavioral issues or who aren't neurotypical. So as you can see, in this case, he had elevated levels of HPHPA. This is an abnormal phenylalanine metabolite produced when byproducts of *Clostridium* bacteria [are] combined with human metabolites. So it inhibits the metabolism of dopamine to epinephrine. High levels of homovanillate and low levels of epinephrine or norepinephrine can lead to altered behavior, a special hyperreactivity. And you can note that his values [are] almost five times the upper limit of [the] lab range. So [the] upper limit was 220, and he was 1,024. His hippuric acid was a little bit elevated, and his arabinose was also just slightly elevated. So although I'm not certain about how those are impacting the clinical picture, we're going to still consider this and keep it on our radar.



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	1+ Enterobacter cloacae complex	
3+ Bifidobacterium spp.		
3+ Escherichia coli		
4+ Lactobacillus spp.		
4+ Enterococcus spp.		
NG Clostridium spp.		

NG = No Growth

BACTERIA INFORMATION

Expected /Beneficial bacteria make up a significant portion of the total microflora in a healthy & balanced GI tract. These beneficial bacteria have many health-protecting effects in the GI tract including manufacturing vitamins, fermenting fibers, digesting proteins and carbohydrates, and propagating anti-tumor and anti-inflammatory factors.
Clostridia are prevalent flora in a healthy intestine. Clostridium spp. should be considered in the context of balance with other expected/beneficial flora. Absence of clostridia or over abundance relative to other expected/beneficial flora indicates bacterial imbalance. If *C. difficile* associated disease is suspected, a Comprehensive Clostridium culture or toxigenic *C. difficile* DNA test is recommended.
Commensal (imbalanced) bacteria are usually neither pathogenic nor beneficial to the host GI tract. Imbalances can occur when there are insufficient levels of beneficial bacteria and increased levels of commensal bacteria. Certain commensal bacteria are reported as dysbiotic at higher levels.
Dysbiotic bacteria consist of known pathogenic bacteria and those that have the potential to cause disease in the GI tract. They can be present due to a number of factors including: consumption of contaminated water or food, exposure to chemicals that are toxic to beneficial bacteria; the use of antibiotics, oral contraceptives or other medications; poor fiber intake and high stress levels.

YEAST CULTURE

Normal flora	Dysbiotic flora
1+ Candida albicans	2+ Saccharomyces cerevisiae/boulardii

MICROSCOPIC YEAST

Result:	Expected:
Few	None - Rare

The microscopic finding of yeast in the stool is helpful in identifying whether there is proliferation of yeast. Rare yeast may be normal; however, yeast observed in higher amounts (few, moderate, or many) is abnormal.

YEAST INFORMATION

Yeast normally can be found in small quantities in the skin, mouth, intestine and mucocutaneous junctions. Overgrowth of yeast can infect virtually every organ system, leading to an extensive array of clinical manifestations. Fungal diarrhea is associated with broad-spectrum antibiotics or alterations of the patient's immune status. Symptoms may include abdominal pain, cramping and irritation. When investigating the presence of yeast, disparity may exist between culturing and microscopic examination. Yeast are not uniformly dispersed throughout the stool, this may lead to undetectable or low levels of yeast identified by microscopy, despite a cultured amount of yeast. Conversely, microscopic examination may reveal a significant amount of yeast present, but no yeast cultured. Yeast does not always survive transit through the intestines rendering it unviable.

PARASITOLOGY/MICROSCOPY *

Sample 1
None Ova or Parasites
Few RBC

Sample 2
None Ova or Parasites

Sample 3
None Ova or Parasites

*A trichrome stain and concentrated iodine wet mount slide is read for each sample submitted.

PARASITOLOGY INFORMATION

Intestinal parasites are abnormal inhabitants of the gastrointestinal tract that have the potential to cause damage to their host. The presence of any parasite within the intestine generally confirms that the patient has acquired the organism through fecal-oral contamination. Damage to the host includes parasitic burden, migration, blockage and pressure. Immunologic inflammation, hypersensitivity reactions and cytotoxicity also play a large role in the morbidity of these diseases. The infective dose often relates to severity of the disease and repeat encounters can be additive.

There are two main classes of intestinal parasites, they include protozoa and helminths. The protozoa typically have two stages; the trophozoite stage that is the metabolically active, invasive stage and the cyst stage, which is the vegetative inactive form resistant to unfavorable environmental conditions outside the human host. Helminths are large, multicellular organisms. Like protozoa, helminths can be either free-living or parasitic in nature. In their adult form, helminths cannot multiply in humans.

In general, acute manifestations of parasitic infection may involve diarrhea with or without mucus and or blood, fever, nausea, or abdominal pain. However these symptoms do not always occur. Consequently, parasitic infections may not be diagnosed or eradicated. If left untreated, chronic parasitic infections can cause damage to the intestinal lining and can be an unsuspected cause of illness and fatigue. Chronic parasitic infections can also be associated with increased intestinal permeability, irritable bowel syndrome, irregular bowel movements, malabsorption, gastritis or indigestion, skin disorders, joint pain, allergic reactions, and decreased immune function.

In some instances, parasites may enter the circulation and travel to various organs causing severe organ diseases such as liver abscesses and cysticercosis. In addition, some larval migration can cause pneumonia and in rare cases hyper infection syndrome with large numbers of larvae being produced and found in every tissue of the body.

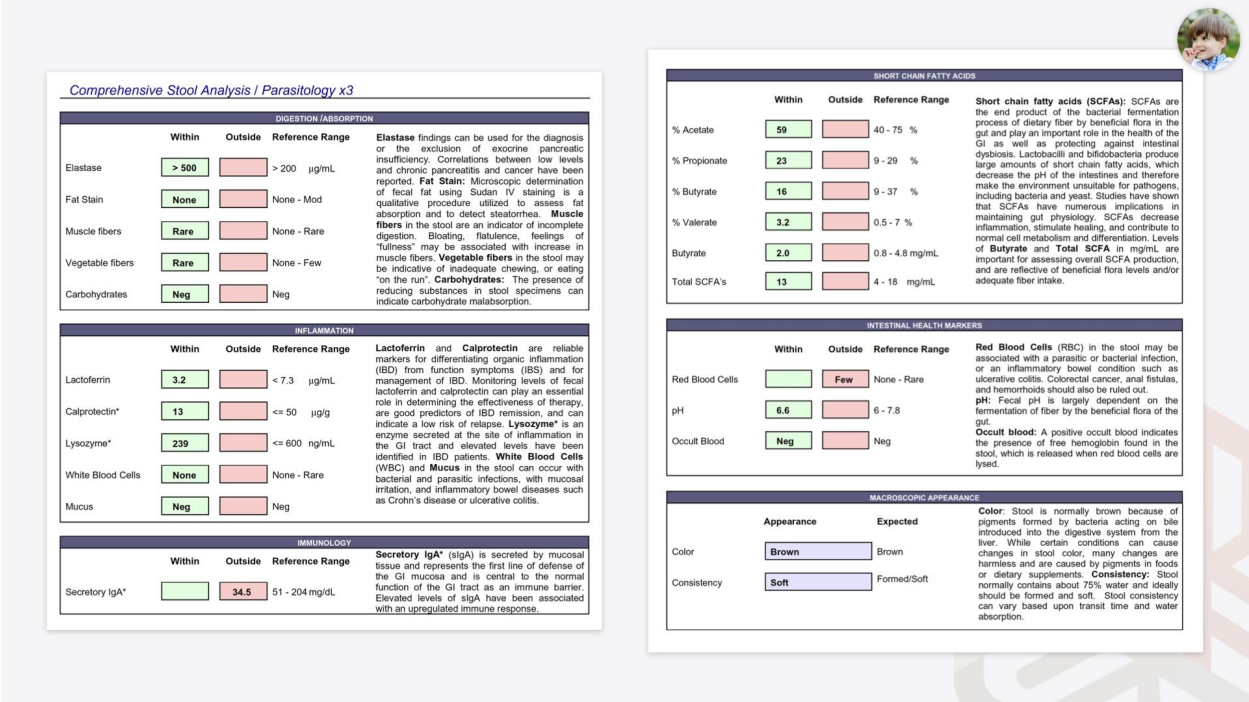
One negative parasitology x1 specimen does not rule out the possibility of parasitic disease, parasitology x3 is recommended. This exam is not designed to detect Cryptosporidium spp, Cyclospora cayetanensis or Microsproridia spp.

GIARDIA/CRYPTOSPORIDIUM IMMUNOASSAY

	Within	Outside	Reference Range
Giardia intestinalis	Neg		Neg
Cryptosporidium	Neg		Neg

Giardia intestinalis (lamblia) is a protozoan that infects the small intestine and is passed in stool and spread by the fecal-oral route. Waterborne transmission is the major source of giardiasis.
Cryptosporidium is a coccidian protozoa that can be spread from direct person-to-person contact or waterborne transmission.

[On] the Doctor's Data stool test, his beneficial bacteria [are] pretty good, which is unusual in a case like this, to be honest. He had only a one plus for commensal bacteria. No dysbiotic flora. But the [inaudible] section was a little tricky here. So he had a two-plus listed in the dysbiotic flora section for *Saccharomyces cerevisiae* or *boulardii*, but he was [taking] that as a supplement prior to the test. So it's, I think, unlikely that that's pathogenic, even though it's listed in the pathogenic column. So you have to be aware of what your patient's supplementing with. He had a one-plus for *Candida*, and then it listed few in the microscopy section. So now while few is considered abnormal, the problem is we don't know whether the few is referring to *Candida albicans*, which is listed in the normal flora section, or *Saccharomyces boulardii*. So we might assume it was the *S. boulardii* since the culture found it in greater amounts than *Candida*, but it's really hard to say. Parasitology was normal, and at the time, we were using BioHealth for parasitology, so that's what we're showing you here as normal.



Comprehensive Stool Analysis / Parasitology x3

DIGESTION /ABSORPTION

	Within	Outside	Reference Range
Elastase	> 500		> 200 µg/mL
Fat Stain	None		None - Mod
Muscle fibers	Rare		None - Rare
Vegetable fibers	Rare		None - Few
Carbohydrates	Neg		Neg

Elastase findings can be used for the diagnosis or the exclusion of exocrine pancreatic insufficiency. Correlations between low levels and chronic pancreatitis and cancer have been reported. **Fat Stain:** Microscopic determination of fecal fat using Sudan IV staining is a qualitative procedure utilized to assess fat absorption and to detect steatorrhea. **Muscle fibers** in the stool are an indicator of incomplete digestion. Bloating, flatulence, feelings of "fullness" may be associated with increase in muscle fibers. **Vegetable fibers** in the stool may be indicative of inadequate chewing, or eating "on the run". **Carbohydrates:** The presence of reducing substances in stool specimens can indicate carbohydrate malabsorption.

INFLAMMATION

	Within	Outside	Reference Range
Lactoferrin	3.2		< 7.3 µg/mL
Calprotectin*	13		<= 50 µg/g
Lysozyme*	239		<= 600 ng/mL
White Blood Cells	None		None - Rare
Mucus	Neg		Neg

Lactoferrin and **Calprotectin** are reliable markers for differentiating organic inflammation (IBD) from function symptoms (IBS) and for management of IBD. Monitoring levels of fecal lactoferrin and calprotectin can play an essential role in determining the effectiveness of therapy, are good predictors of IBD remission, and can indicate a low risk of relapse. **Lysozyme*** is an enzyme secreted at the site of inflammation in the GI tract and elevated levels have been identified in IBD patients. **White Blood Cells** (WBC) and **Mucus** in the stool can occur with bacterial and parasitic infections, with mucosal irritation, and inflammatory bowel diseases such as Crohn's disease or ulcerative colitis.

IMMUNOLOGY

	Within	Outside	Reference Range
Secretory IgA*		34.5	51 - 204 mg/dL

Secretory IgA* (sIgA) is secreted by mucosal tissue and represents the first line of defense of the GI mucosa and is central to the normal function of the GI tract as an immune barrier. Elevated levels of sIgA have been associated with an upregulated immune response.

SHORT CHAIN FATTY ACIDS

	Within	Outside	Reference Range
% Acetate	59		40 - 75 %
% Propionate	23		9 - 29 %
% Butyrate	16		9 - 37 %
% Valerate	3.2		0.5 - 7 %
Butyrate	2.0		0.8 - 4.8 mg/mL
Total SCFA's	13		4 - 18 mg/mL

Short chain fatty acids (SCFAs): SCFAs are the end product of the bacterial fermentation process of dietary fiber by beneficial flora in the gut and play an important role in the health of the GI as well as protecting against intestinal dysbiosis. Lactobacilli and bifidobacteria produce large amounts of short chain fatty acids, which decrease the pH of the intestines and therefore make the environment unsuitable for pathogens, including bacteria and yeast. Studies have shown that SCFAs have numerous implications in maintaining gut physiology. SCFAs decrease inflammation, stimulate healing, and contribute to normal cell metabolism and differentiation. Levels of **Butyrate** and **Total SCFA** in mg/mL are important for assessing overall SCFA production, and are reflective of beneficial flora levels and/or adequate fiber intake.

INTESTINAL HEALTH MARKERS

	Within	Outside	Reference Range
Red Blood Cells		Few	None - Rare
pH	6.6		6 - 7.8
Occult Blood	Neg		Neg

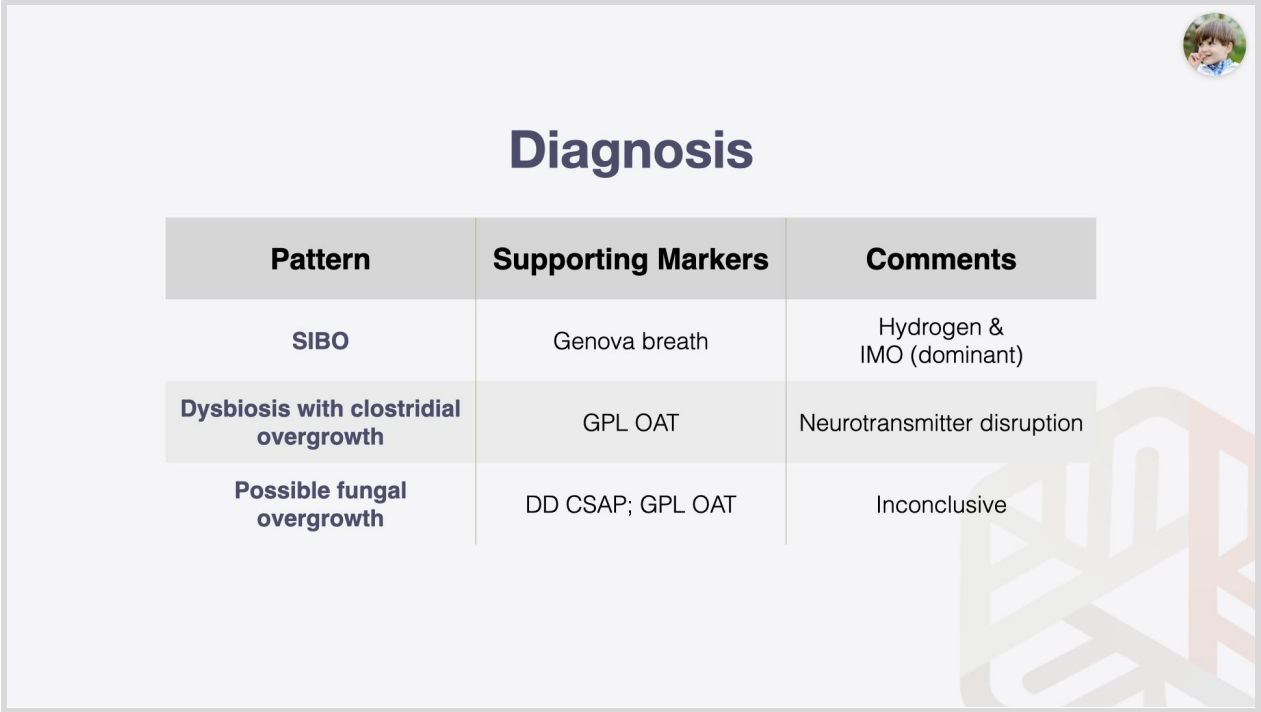
Red Blood Cells (RBC) in the stool may be associated with a parasitic or bacterial infection, or an inflammatory bowel condition such as ulcerative colitis. Colorectal cancer, anal fistulas, and hemorrhoids should also be ruled out.
pH: Fecal pH is largely dependent on the fermentation of fiber by the beneficial flora of the gut.
Occult blood: A positive occult blood indicates the presence of free hemoglobin found in the stool, which is released when red blood cells are lysed.

MACROSCOPIC APPEARANCE

	Appearance	Expected
Color	Brown	Brown
Consistency	Soft	Formed/Soft

Color: Stool is normally brown because of pigments formed by bacteria acting on bile introduced into the digestive system from the liver. While certain conditions can cause changes in stool color, many changes are harmless and are caused by pigments in foods or dietary supplements. **Consistency:** Stool normally contains about 75% water and ideally should be formed and soft. Stool consistency can vary based upon transit time and water absorption.

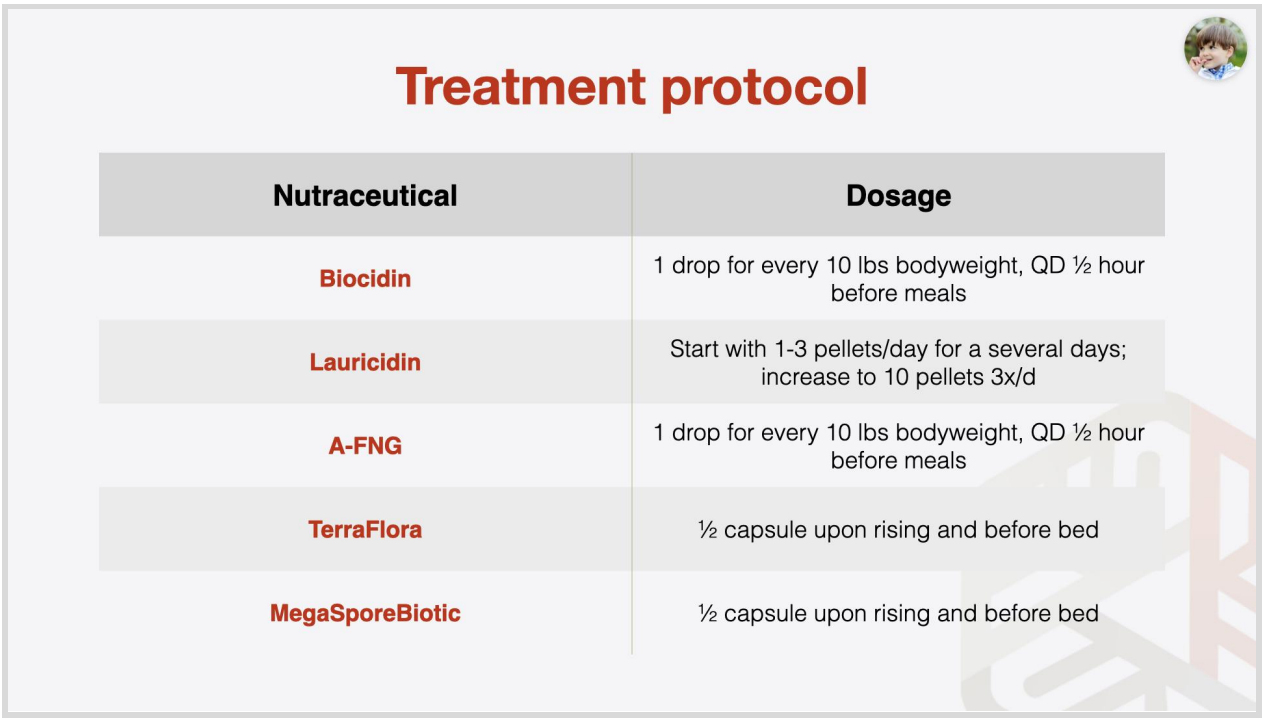
Then [on] the second page, the only thing that was out of range for the secretory IgA. [It] was a little bit low. And then he had some red blood cells in the stool, indicating a little bit of inflammation.



Diagnosis

Pattern	Supporting Markers	Comments
SIBO	Genova breath	Hydrogen & IMO (dominant)
Dysbiosis with clostridial overgrowth	GPL OAT	Neurotransmitter disruption
Possible fungal overgrowth	DD CSAP; GPL OAT	Inconclusive

So the diagnosis here for us was SIBO, both hydrogen and methane, based on the breath test, but intestinal methanogen overgrowth was the dominant presentation. Dysbiosis with clostridial overgrowth based on the Great Plains Organic Acids Test, which was leading to neurotransmitter disruption and probably contributing to his behavioral issues. And then possible fungal overgrowth showed up on both Doctor's Data and Great Plains Lab [tests].



We did a pediatric botanical protocol for him. This was part of the treatment protocol section from earlier. Biocidin, Lauricidin, [AF&G?], Terraflora, and MegaSporeBiotic. We did this for 21 days. Kids often respond a little faster than adults, so sometimes we can do a shorter protocol. He was a pretty new patient at the time that we originally recorded this. So we didn't have any retest results back. But [his] mom had reported that he seemed less distracted. More consistent bowel movements. Skin was better. Allergies had lessened. He was bedwetting before. I don't think I mentioned that on the previous slide, but that had improved significantly, as well. So I don't have the follow-up labs, unfortunately, here on this particular slide. But [a] repeat SIBO test showed improvement in methane levels to 10 parts million at the highest resolution of the high hydrogen levels. He did have a lowering value on the]organic acids test] but did still have markers of possible fungal overgrowth or what we could consider mold exposure. We decided to continue the protocol just a little bit longer since he was tolerating it well and had been in a rhythm and make a few more tweaks for fungal overgrowth. So far, that

treatment turned out [well], and we were just continuing on probably for an additional two to three weeks on this protocol, and then we'll take a break and retest.

Okay. That's it for the gut studies and for the gut unit overall. I hope you got a lot out of that. I'm really looking forward to diving into the [hypothalamic–pituitary–adrenal] (HPA) axis, where Chris and I will go through labs and dysfunction and [have] a lot of really interesting material to cover. I think you're going to find it a fresh perspective on a topic that I think badly needs some updated scientific evidence-based approach. So we'll see you in the HPA axis section.