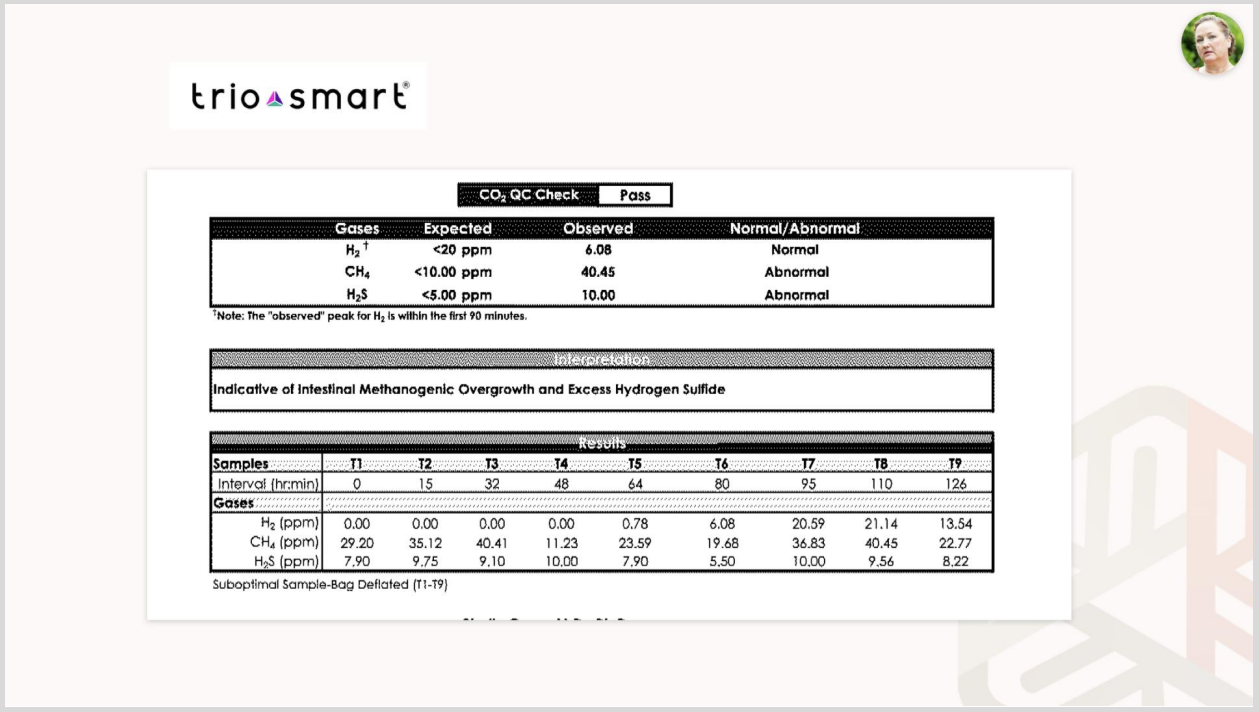
KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Gut Case Studies, Part 1

For this unit, we're going to do full case studies for the gut, including all gut tests run for a particular patient and the treatment that we prescribe. I want to mention that I'm presenting cases and patients [who] we've treated over the years, so some of the treatment plans recommended may differ slightly from what we've recently discussed in the curriculum. I am regularly adjusting the treatment plans and recommendations so that they are current with research, new products on the market, and updated standards of care. So throughout the presentation, you'll see treatment plans that were recommended during the time that the patient was seen. We'll give you a summary of the changes to those protocols at the end of the presentation.

CASE #1: 64-YEAR-OLD FEMALE

Here we have a 64-year-old female, and, of course, a reminder that these aren't the real pictures of our patients, which I think you know, but just a little disclaimer, with primary complaints of bloating, indigestion, abdominal pain, constipation, hypothyroidism, and weight gain. She's had a history of food sensitivities, antibiotic use, and has gained over 30 pounds in the past year or two. Admittedly, her diet isn't great. She had been a vegetarian for some time with high processed food consumption and still struggles with animal protein and fat consumption, but has tried elimination diets for short periods of time with very little success.



trio smart®

CO_2 QC Check	Pass

Gases	Expected	Observed	Normal/Abnormal
H_2 †	<20 ppm	6.08	Normal
CH_4	<10.00 ppm	40.45	Abnormal
H_2S	<5.00 ppm	10.00	Abnormal

†Note: The "observed" peak for H_2 is within the first 90 minutes.

Interpretation
Indicative of Intestinal Methanogenic Overgrowth and Excess Hydrogen Sulfide

Results

Samples	T1	T2	T3	T4	T5	T6	T7	T8	T9
Interval (hr:min)	0	15	32	48	64	80	95	110	126
Gases									
H_2 (ppm)	0.00	0.00	0.00	0.00	0.78	6.08	20.59	21.14	13.54
CH_4 (ppm)	29.20	35.12	40.41	11.23	23.59	19.68	36.83	40.45	22.77
H_2S (ppm)	7.90	9.75	9.10	10.00	7.90	5.50	10.00	9.56	8.22

Suboptimal Sample-Bag Deflated (T1-T9)

Let's start with the [small intestinal bacterial overgrowth] (SIBO) results. As you remember, the trio-smart panel test for all three known types of gasses: hydrogen sulfide, methane, and hydrogen. This test is marked positive for intestinal methanogen overgrowth and hydrogen sulfide excess. The methane at its highest was 40.45, and hydrogen sulfide was 10 parts per million. Hydrogen levels, interestingly, were pretty low until the 95 minutes collection. This could be an example of the competitive gas model that we've discussed, where hydrogen is being used by methanogens and hydrogen sulfide-producing organisms.

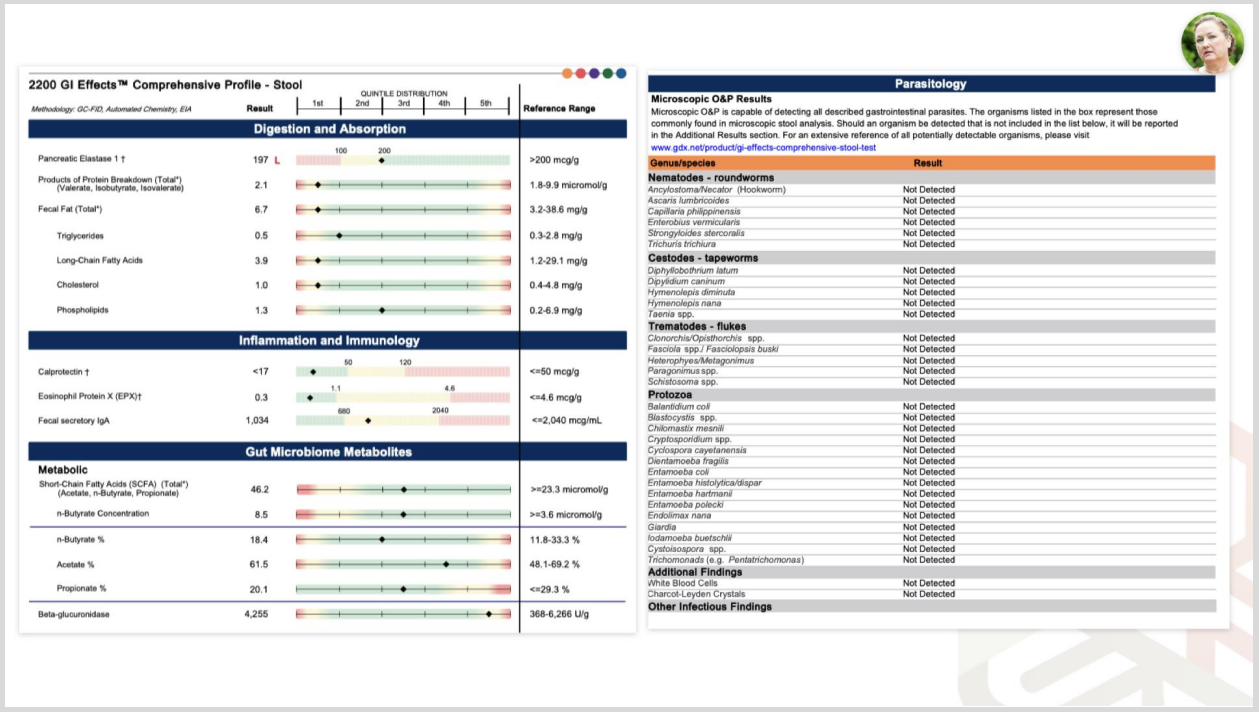
METABOLITE IMBALANCE

Functional Imbalance Scores

Key: <2 : Low Need for Support | 2-3 : Optional Need for Support | 4-6 : Moderate Need for Support | 7-10 : High Need for Support

	Need for Digestive Support	Need for Inflammation Modulation	Need for Microbiome Support	Need for Prebiotic Support	Need for Antimicrobial Support
	MALDIGESTION	INFLAMMATION	DYSBIOSIS	METABOLIC IMBALANCE	INFECTION
	4	0	10	0	0
Biomarkers	Pancreatic Elastase ▽ Products of Protein Breakdown ▽ Fecal Fats ▽	Secretory IgA △ Calprotectin ● Eosinophil Protein X ● Occult Blood ●	Reference Variance ▲ IAD/Methane Score △ Total Abundance △ PP Bacteria/Yeast ●	Beta-glucuronidase △ Total SCFA's ● n-Butyrate Conc. ● SCFA (%) ●	Total Abundance △ Parasitic Infection ● Pathogenic Bacteria ● PP Bacteria/Yeast ●
Therapeutic Support Options	• Digestive Enzymes • Betaine HCl • Bile Salts • Apple Cider Vinegar • Mindful Eating Habits • Digestive Bitters	• Elimination Diet/ Food Sensitivity Testing • Mucosa Support: Slippery Elm, Althea, Aloe, DGL, etc. • Zinc Carnosine • L-Glutamine • Quercetin • Turmeric • Omega-3's • GI Referral (If Calpro is Elevated)	• Pre-/Probiotics • Increase Dietary Fiber Intake • Consider SIBO Testing • Increase Resistant Starches • Increase Fermented Foods • Meal Timing	• Pre-/Probiotics • Increased Dietary Fiber Intake • Increase Resistant Starches • Increase Fermented Foods • Calcium D-Glucarate (for high beta-glucuronidase)	• Antibiotics (if warranted) • Antimicrobial Herbal Therapy • Antiparasitic Herbal Therapy (if warranted) • *Saccharomyces boulardii*

Next, we have the GI Effects Comprehensive Stool results. The good news here is there [weren't] any major pathogens found on the panel, but she did get some dysbiosis markers and a handful of markers of maldigestion. As we've discussed before, I think the beneficial bacteria section is helpful to look at, especially when it comes to patterns, but I've had a hard time correlating symptoms and treatment plans to one specific level of beneficial bacteria. I generally look at this result in the context of symptoms and other lab results. So, for this particular patient, her score was high because of the reference variance, which is based on Genova's algorithm that differentiates healthy and unhealthy commensal patterns.



2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC-FID, Automated Chemistry, EIA

	Result	QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	197 L	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	2.1		1.8-9.9 micromol/g
Fecal Fat (Total*)	6.7		3.2-38.6 mg/g
Triglycerides	0.5		0.3-2.8 mg/g
Long-Chain Fatty Acids	3.9		1.2-29.1 mg/g
Cholesterol	1.0		0.4-4.8 mg/g
Phospholipids	1.3		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<17	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	0.3	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	1,034	680 2040	<=2,040 mcg/mL
Gut Microbiome Metabolites			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	46.2		>=23.3 micromol/g
n-Butyrate Concentration	8.5		>=3.6 micromol/g
n-Butyrate %	18.4		11.8-33.3 %
Acetate %	61.5		48.1-69.2 %
Propionate %	20.1		<=29.3 %
Beta-glucuronidase	4,255		368-6,266 U/g

Parasitology

Microscopic O&P Results

Microscopic O&P is capable of detecting all described gastrointestinal parasites. The organisms listed in the box represent those commonly found in microscopic stool analysis. Should an organism be detected that is not included in the list below, it will be reported in the Additional Results section. For an extensive reference of all potentially detectable organisms, please visit www.gdx.net/product/gi-effects-comprehensive-stool-test

Genus/species	Result
Nematodes - roundworms	
Ancylostoma/Necator (Hookworm)	Not Detected
Ascaris lumbricoides	Not Detected
Capillaria philippinensis	Not Detected
Enterobius vermicularis	Not Detected
Strongyloides stercoralis	Not Detected
Trichuris trichiura	Not Detected
Cestodes - tapeworms	
Diphyllobothrium latum	Not Detected
Dipylidium caninum	Not Detected
Hymenolepis diminuta	Not Detected
Hymenolepis nana	Not Detected
Taenia spp.	Not Detected
Trematodes - flukes	
Clonorchis/Opisthorchis spp.	Not Detected
Fasciola spp./ *Fasciolopsis buski*	Not Detected
Heterophyes/Metagonimus	Not Detected
Paragonimus spp.	Not Detected
Schistosoma spp.	Not Detected
Protozoa	
Balantidium coli	Not Detected
Blastocystis spp.	Not Detected
Chilomastix mesnili	Not Detected
Cryptosporidium spp.	Not Detected
Cyclospora cayetanensis	Not Detected
Dientamoeba fragilis	Not Detected
Entamoeba coli	Not Detected
Entamoeba histolytica/dispar	Not Detected
Entamoeba hartmanii	Not Detected
Entamoeba polecki	Not Detected
Endolimax nana	Not Detected
Giardia	Not Detected
Iodamoeba buetschlii	Not Detected
Cystoisospora spp.	Not Detected
Trichomonads (e.g. *Pentatrichomonas*)	Not Detected
Additional Findings	
White Blood Cells	Not Detected
Charcot-Leyden Crystals	Not Detected
Other Infectious Findings	

Interestingly, she did have high levels of *Methanobrevibacter* and [inaudible] *Vibrio* on the stool test. As we discussed previously, there isn't any evidence to suggest that seeing overgrowth of these in the stool is diagnostic of overgrowth in the small intestine, but on occasion, you may see some clinical correlation in practice. You can see the low levels of pancreatic elastase at 197. This might be considered "Borderline," but anything below 500 is sub-optimal. So considering her symptoms, I do think it's a significant finding. Interestingly, her gut microbiome metabolites, like the short-chain fatty acids, are relatively good, and her products of protein breakdown are on the low side. This could be from a low-protein diet, commensal bacterial abundance issues, SIBO, intestinal inflammation, and a few other things. I also have the OMP portion of the test. You can see that this section was all negative.

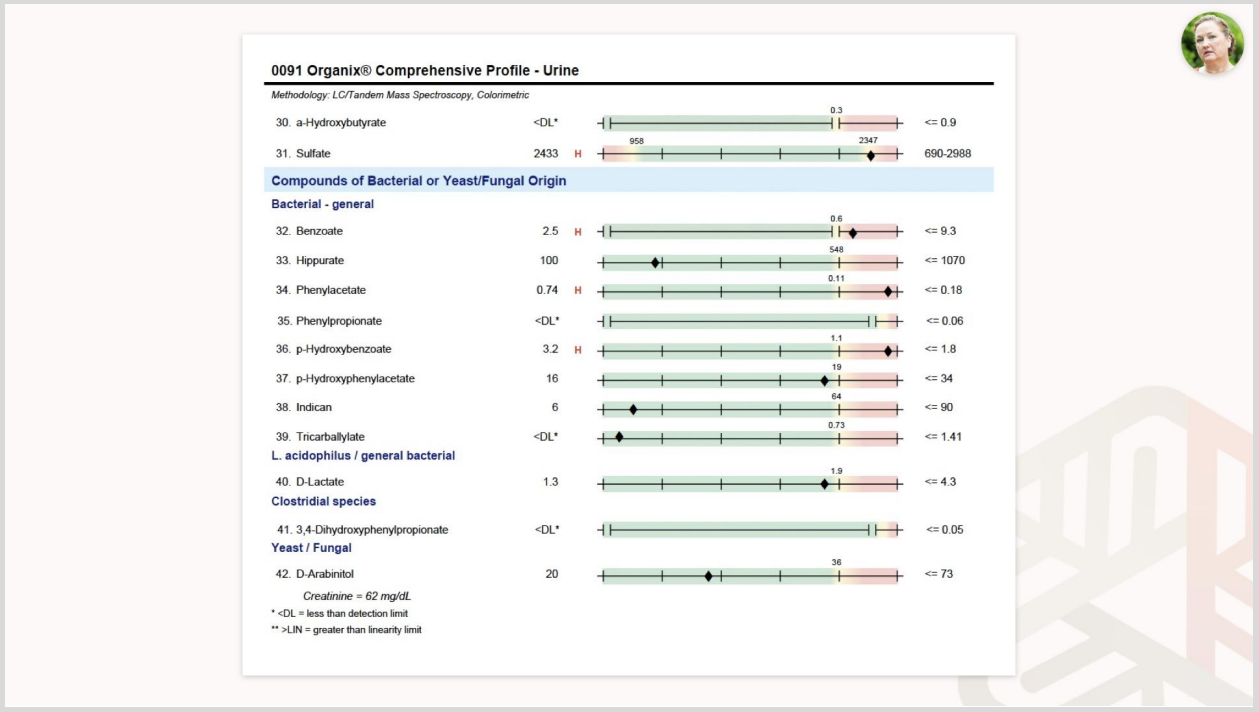
Clinical Info: SRC:ST

H. pylori Stool Ag, EIA

Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
▶ H. pylori Stool Ag, EIA [01]	**Positive**	**Abnormal**			Negative

labcorp

For this patient, we also decided to do stool antigen testing through Labcorp to use insurance. You do have the option of adding the stool antigen test onto the Genova panel, yet this worked out better for this particular patient. And as you can see, she did have a positive [*Helicobacter*] *pylori* stool antigen result.



0091 Organix® Comprehensive Profile - Urine

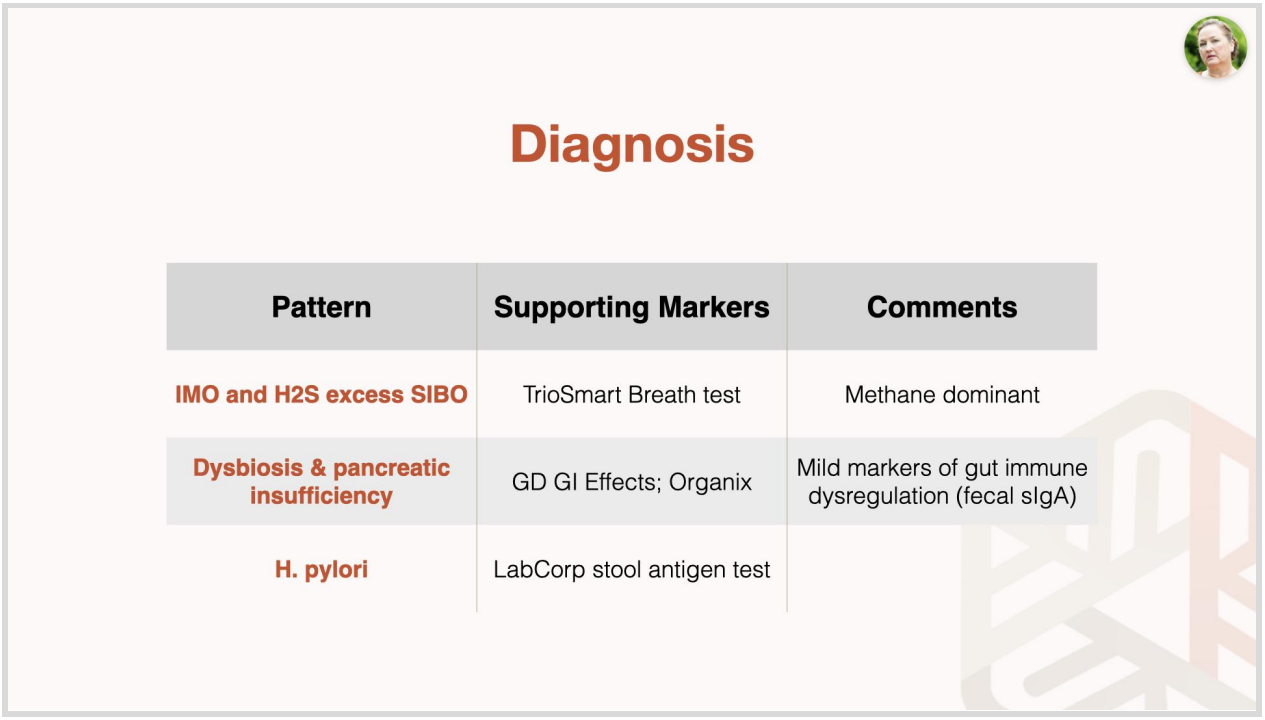
Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

30. a-Hydroxybutyrate	<DL*		0.3	<= 0.9
31. Sulfate	2433	H	958 2347	690-2988
Compounds of Bacterial or Yeast/Fungal Origin				
Bacterial - general				
32. Benzoate	2.5	H	0.6	<= 9.3
33. Hippurate	100		548	<= 1070
34. Phenylacetate	0.74	H	0.11	<= 0.18
35. Phenylpropionate	<DL*			<= 0.06
36. p-Hydroxybenzoate	3.2	H	1.1	<= 1.8
37. p-Hydroxyphenylacetate	16		19	<= 34
38. Indican	6		64	<= 90
39. Tricarballylate	<DL*		0.73	<= 1.41
L. acidophilus / general bacterial				
40. D-Lactate	1.3		1.9	<= 4.3
Clostridial species				
41. 3,4-Dihydroxyphenylpropionate	<DL*			<= 0.05
Yeast / Fungal				
42. D-Arabinitol	20		36	<= 73

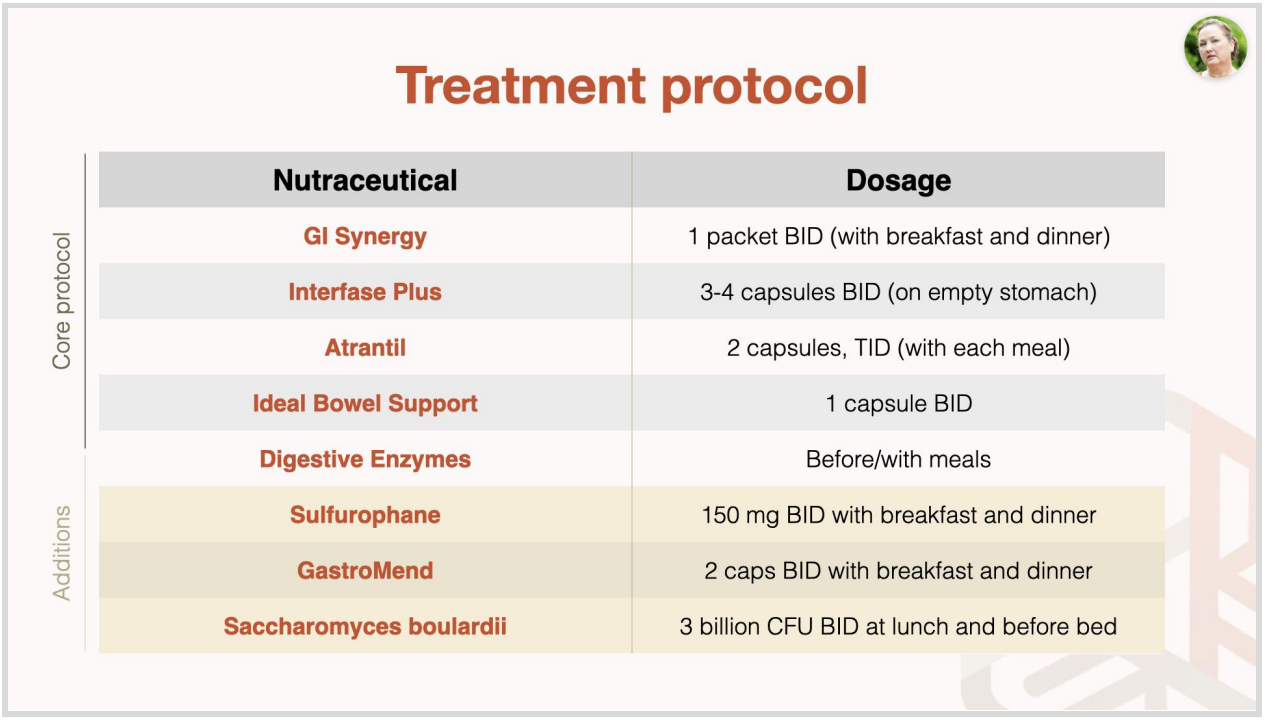
Creatinine = 62 mg/dL

* <DL = less than detection limit
** >LIN = greater than linearity limit

Here's her urine organic acids test. Her benzoate is high normal. [It's] not out of [the] reference range, but on the high normal side. I think we talked about this in the testing section, but high often means high normal. The phenylacetate was also in the elevated range. In this case, it was out of the reference range. And elevations in phenylacetate can cause cognitive, behavioral, and neurological problems. It wasn't a primary complaint that this patient mentioned, but she did have a little bit of that. And then there's fi-hydroxybenzoate, which was also elevated, and that's a sign of microbial overgrowth also.



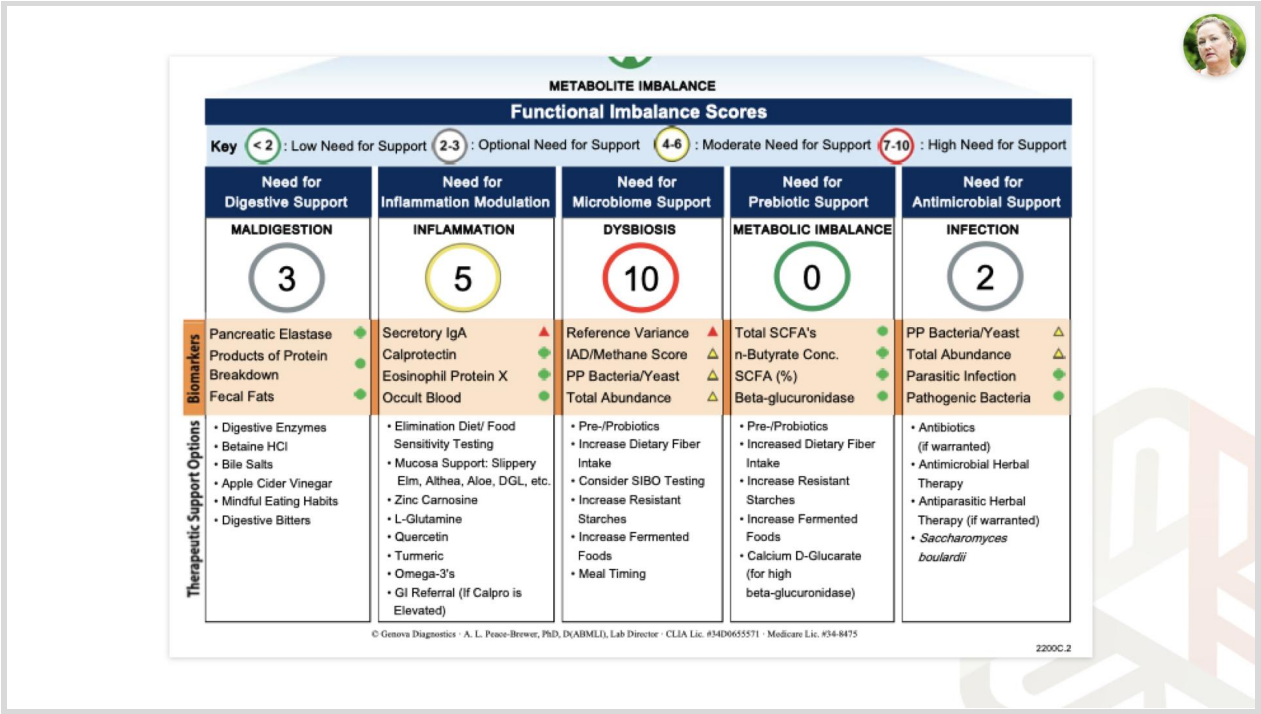
The diagnosis for this patient is intestinal methanogen overgrowth and hydrogen sulfide excess SIBO based [on] the trio-smart breath test. And I would probably call this methane-dominant because of how high the levels are and also with her symptoms of constipation. But they're both significant findings. Then, dysbiosis and pancreatic insufficiency based [on] the Genova GI Effects and organic acids test and *H. pylori* positive based [on] the Labcorp stool antigen test.



Treatment protocol

	Nutraceutical	Dosage
Core protocol	GI Synergy	1 packet BID (with breakfast and dinner)
	Interfase Plus	3-4 capsules BID (on empty stomach)
	Atrantil	2 capsules, TID (with each meal)
	Ideal Bowel Support	1 capsule BID
	Digestive Enzymes	Before/with meals
Additions	Sulfurophane	150 mg BID with breakfast and dinner
	GastroMend	2 caps BID with breakfast and dinner
	Saccharomyces boulardii	3 billion CFU BID at lunch and before bed

Here's the treatment that I used for this patient, starting with some items from the core botanical protocol GI-Synergy and Interfase Plus, then adding Atrantil, an Ideal Bowel Support, for the intestinal methanogen overgrowth, and digestive enzymes for additional digestive support. I also added sulforaphane, GastroMend, and *Saccharomyces boulardii* for *H. pylori*. This is an example of a place [where] I didn't add a lot of probiotics upfront because this patient had a history of not being able to tolerate them. So I waited and slowly introduced them about halfway through the protocol. She was only able to tolerate one MegaSporeBiotic daily, but I was glad we were at least able to get that in. So we did this protocol for about 12 to 15 weeks. It took her a few weeks to get ramped up on the full dose. And we had to make some adjustments and slow down from time to time, but we were able to stick with it and complete the treatment plan.



METABOLITE IMBALANCE

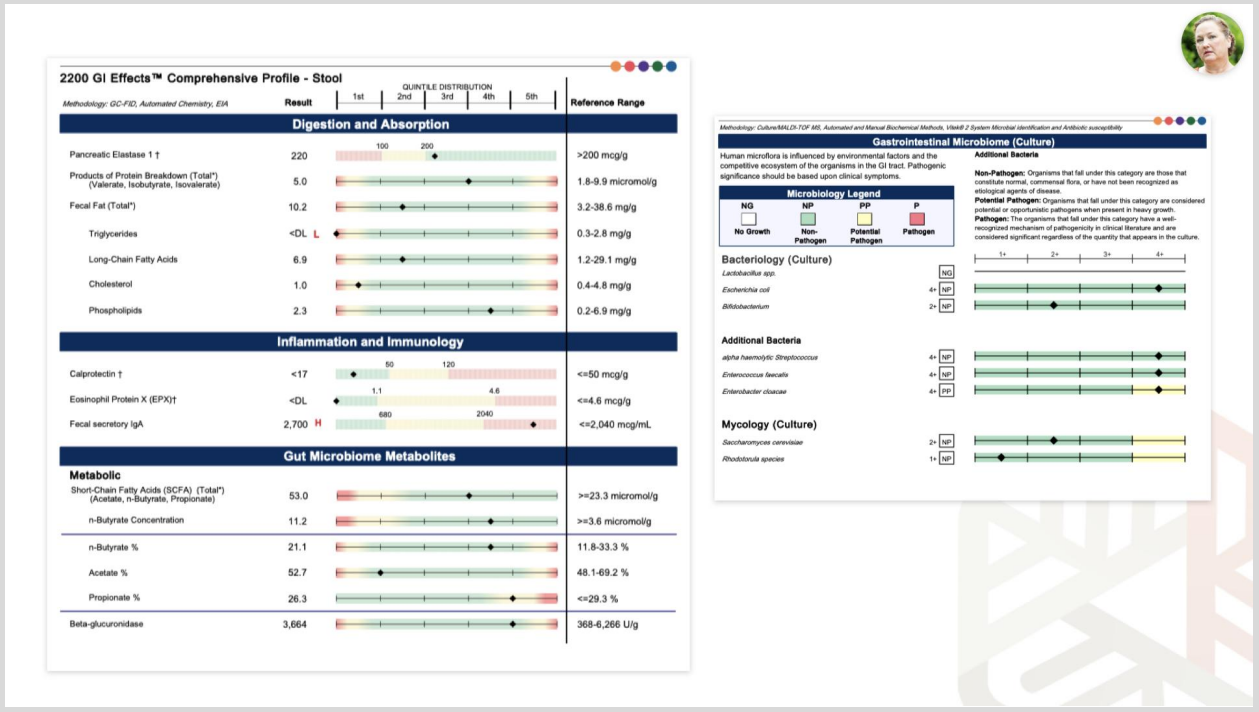
Functional Imbalance Scores

Key (< 2) : Low Need for Support (2-3) : Optional Need for Support (4-6) : Moderate Need for Support (7-10) : High Need for Support

	Need for Digestive Support	Need for Inflammation Modulation	Need for Microbiome Support	Need for Prebiotic Support	Need for Antimicrobial Support
	MALDIGESTION	INFLAMMATION	DYSBIOSIS	METABOLIC IMBALANCE	INFECTION
	3	5	10	0	2
Biomarkers	Pancreatic Elastase Products of Protein Breakdown Fecal Fats	Secretory IgA Calprotectin Eosinophil Protein X Occult Blood	Reference Variance IAD/Methane Score PP Bacteria/Yeast Total Abundance	Total SCFA's n-Butyrate Conc. SCFA (%) Beta-glucuronidase	PP Bacteria/Yeast Total Abundance Parasitic Infection Pathogenic Bacteria
Therapeutic Support Options	• Digestive Enzymes • Betaine HCl • Bile Salts • Apple Cider Vinegar • Mindful Eating Habits • Digestive Bitters	• Elimination Diet/ Food Sensitivity Testing • Mucosa Support: Slippery Elm, Althea, Aloe, DGL, etc. • Zinc Carnosine • L-Glutamine • Quercetin • Turmeric • Omega-3's • GI Referral (If Calpro is Elevated)	• Pre-/Probiotics • Increase Dietary Fiber Intake • Consider SIBO Testing • Increase Resistant Starches • Increase Fermented Foods • Meal Timing	• Pre-/Probiotics • Increased Dietary Fiber Intake • Increase Resistant Starches • Increase Fermented Foods • Calcium D-Glucarate (for high beta-glucuronidase)	• Antibiotics (if warranted) • Antimicrobial Herbal Therapy • Antiparasitic Herbal Therapy (if warranted) • *Saccharomyces boulardii*

2200C.2

Okay. So we retested the GI Effects Stool test four weeks after she completed the protocol. As you can see here, things don't always miraculously clear up after the initial protocol. So I really wanted to show this as a good example of what we can see in practice. In her case, the reference variance stayed about the same, and her pancreatic elastase levels did improve, as you'll see on the next slide, but she did have a little bit of an uptick in secretory [immunoglobulin A] (IgA) levels.



2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC-FID, Automated Chemistry, EIA	Result	QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	220	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	5.0		1.8-9.9 micromol/g
Fecal Fat (Total*)	10.2		3.2-38.6 mg/g
Triglycerides	<DL L		0.3-2.8 mg/g
Long-Chain Fatty Acids	6.9		1.2-29.1 mg/g
Cholesterol	1.0		0.4-4.8 mg/g
Phospholipids	2.3		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<17	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	2,700 H	680 2040	<=2,040 mcg/mL
Gut Microbiome Metabolites			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	53.0		>=23.3 micromol/g
n-Butyrate Concentration	11.2		>=3.6 micromol/g
n-Butyrate %	21.1		11.8-33.3 %
Acetate %	52.7		48.1-69.2 %
Propionate %	26.3		<=29.3 %
Beta-glucuronidase	3,664		368-6,266 U/g

Gastrointestinal Microbiome (Culture)

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathogenic significance should be based upon clinical symptoms.

Microbiology Legend: NG No Growth; NP Non-Pathogen; PP Potential Pathogen; P Pathogen

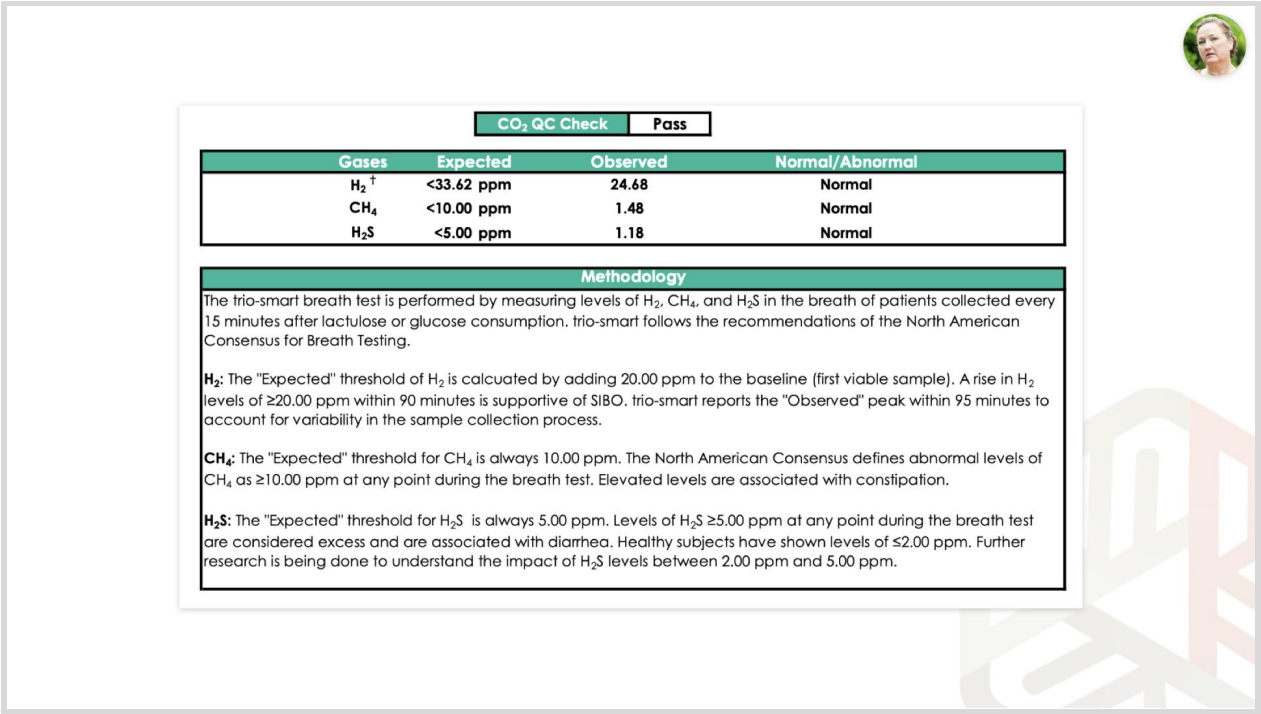
Additional Bacteria

Non-Pathogen: Organisms that fall under this category are those that constitute normal, commensal flora, or have not been recognized as etiological agents of disease.
Potential Pathogen: Organisms that fall under this category are considered potential or opportunistic pathogens when present in heavy growth.
Pathogen: The organisms that fall under this category have a well-recognized mechanism of pathogenicity in clinical literature and are considered significant regardless of the quantity that appears in the culture.

Bacteriology (Culture)

		1+ 2+ 3+ 4+
Lactobacillus spp.	NG	
Escherichia coli	4+ NP	
Bifidobacterium	2+ NP	
Additional Bacteria		
alpha haemolytic Streptococcus	4+ NP	
Enterococcus faecalis	4+ NP	
Enterobacter cloacae	4+ PP	
Mycology (Culture)		
Saccharomyces cerevisiae	2+ NP	
Rhodotorula species	1+ NP	

Pancreatic elastase came up a tiny bit from 197 to 220. So [it's] moving in the right direction, but still lower than optimal. Her fecal secretory IgA, as I mentioned, shot way up. This could be a result of aggravating infection, increasing immune response to treatment, or the continued presence of other pathogens. There was a new potential pathogen seen on the follow-up test for *Enterobacter cloacae*. I often see this happen after a protocol where I'll get an uptick of some of these potential pathogens. So I do pay attention to them and make sure to check in on them with the patient and figure out what the overall plan is before getting too worked up over one organism that has shifted in quantity just slightly after a protocol. There [are] just a lot of changes and [shifts] that we're doing by doing these long protocols.



CO_2 QC Check	Pass

Gases	Expected	Observed	Normal/Abnormal
H_2 †	<33.62 ppm	24.68	Normal
CH_4	<10.00 ppm	1.48	Normal
H_2S	<5.00 ppm	1.18	Normal

Methodology

The trio-smart breath test is performed by measuring levels of H_2, CH_4, and H_2S in the breath of patients collected every 15 minutes after lactulose or glucose consumption. trio-smart follows the recommendations of the North American Consensus for Breath Testing.

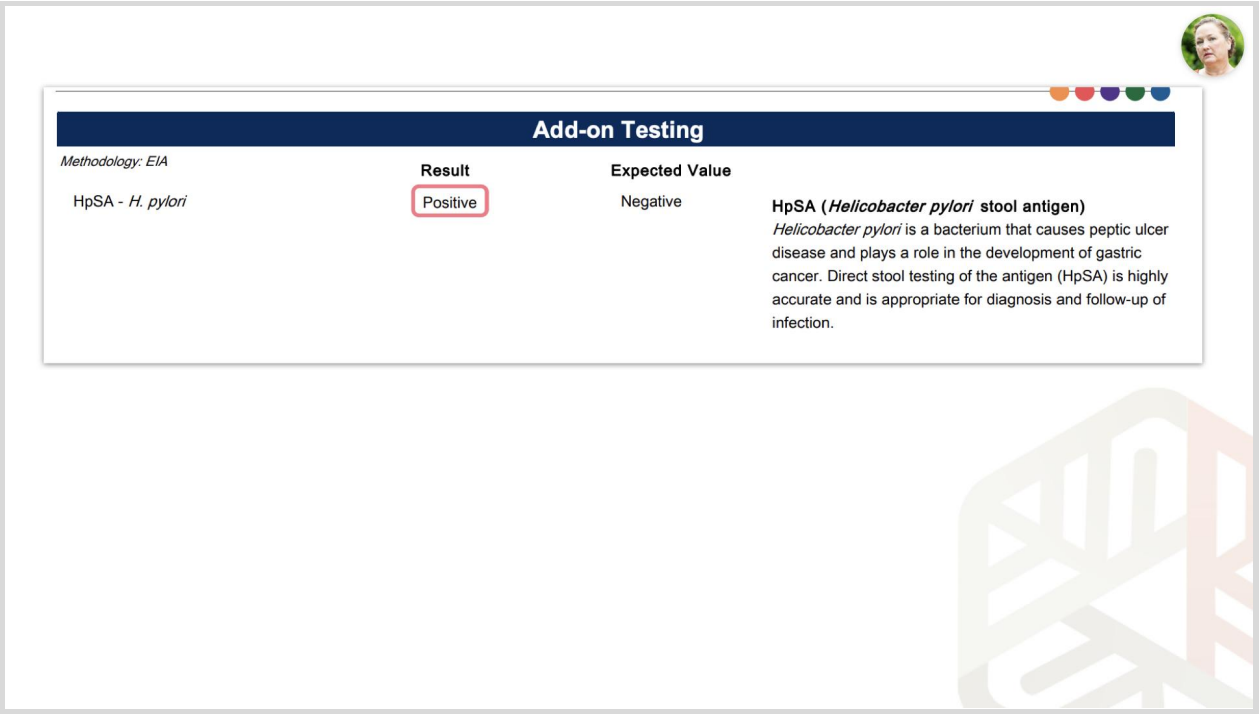
H_2: The "Expected" threshold of H_2 is calcuated by adding 20.00 ppm to the baseline (first viable sample). A rise in H_2 levels of ≥20.00 ppm within 90 minutes is supportive of SIBO. trio-smart reports the "Observed" peak within 95 minutes to account for variability in the sample collection process.

CH_4: The "Expected" threshold for CH_4 is always 10.00 ppm. The North American Consensus defines abnormal levels of CH_4 as ≥10.00 ppm at any point during the breath test. Elevated levels are associated with constipation.

H_2S: The "Expected" threshold for H_2S is always 5.00 ppm. Levels of H_2S ≥5.00 ppm at any point during the breath test are considered excess and are associated with diarrhea. Healthy subjects have shown levels of ≤2.00 ppm. Further research is being done to understand the impact of H_2S levels between 2.00 ppm and 5.00 ppm.

The most remarkable improvement here was the SIBO breath test. So it's not always easy to get improvement in the SIBO test [in] the first round, but here you can see negative methane and then negative hydrogen sulfide levels. A little bit of [an] uptick on the hydrogen overall, even though it's still negative. And that may just be because the methane, the methanogens, and hydrogen sulfide producers were no longer consuming hydrogen. So that's possibly what we're seeing here.

Overall, she did report improvements in bloating, abdominal pain, and constipation and had about a four-pound weight loss. So [she's] still dealing with some mild indigestion and thyroid concerns and would like to continue losing more weight.



Add-on Testing

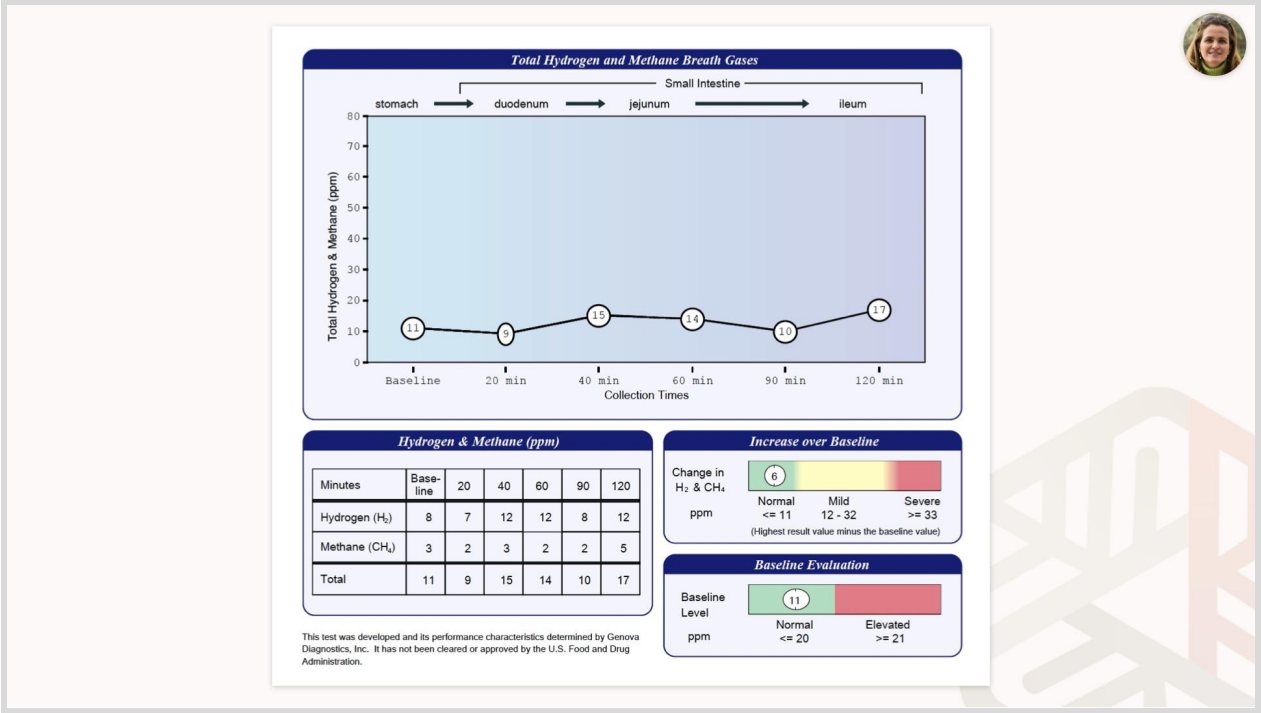
	Result	Expected Value	
Methodology: EIA			
HpSA - *H. pylori*	Positive	Negative	**HpSA (*Helicobacter pylori* stool antigen)** *Helicobacter pylori* is a bacterium that causes peptic ulcer disease and plays a role in the development of gastric cancer. Direct stool testing of the antigen (HpSA) is highly accurate and is appropriate for diagnosis and follow-up of infection.

We ended up adding the repeat *H. pylori* test to the Genova panel since it was easier for her with retesting. So you can see here how her Genova reports their stool antigen test. Her *H. pylori* tests remain positive. So we plan to shift focus over to *H. pylori*. And [I] gave her the option of repeating an antimicrobial protocol that's a little more focused on *H. pylori* or consider[ing] prescription options. She [decided] to try an antimicrobial protocol again since she felt a lot better on the previous protocol.

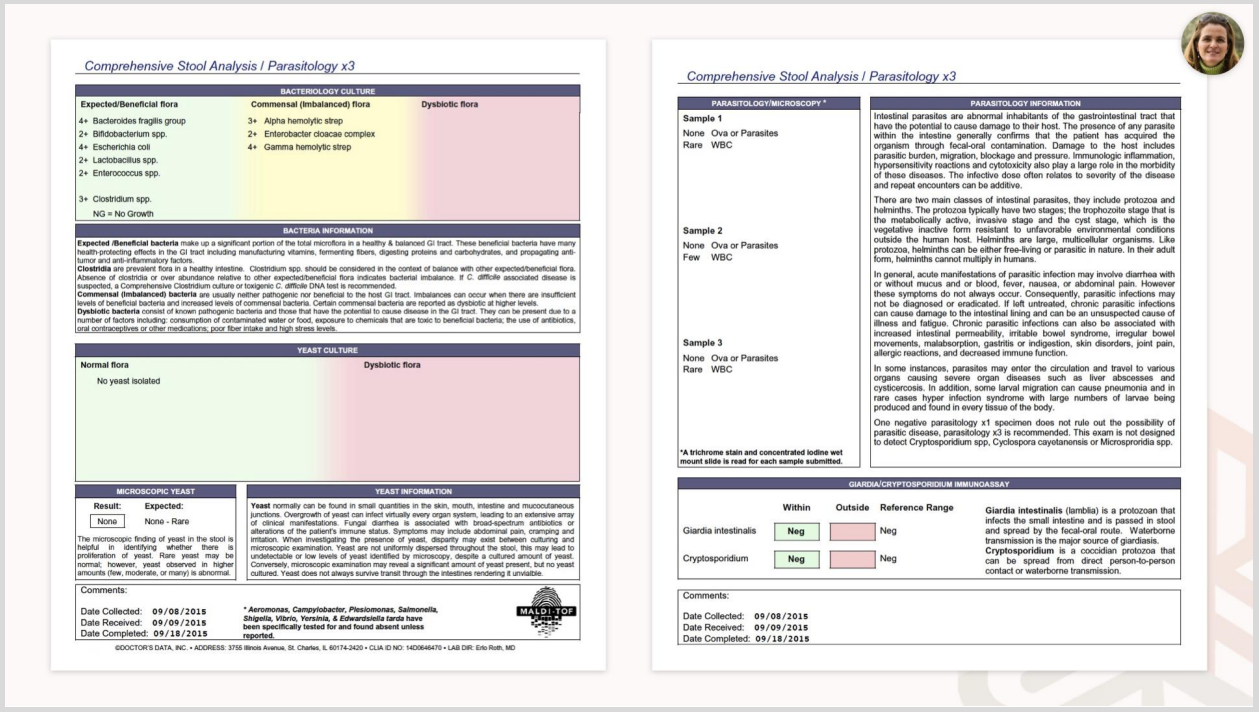
CASE #2: 38-YEAR-OLD FEMALE

Our next case is a 38-year-old female who Chris and I saw a handful of years ago. [Her] chief complaints [were] of Hashimoto's [disease], insomnia, gas, bloating, constipation, [and] this adrenal fatigue that she had been labeled previously. You'll often see patients write that on their forms. We're going to be talking a lot more about the [hypothalamic–pituitary–adrenal] (HPA) axis unit to come. And then histamine [intolerance] symptoms. So she had self-diagnosed with SIBO based on some internet research. [She] took some herbs for it on her own. We also find this happens with some of our patients. They'll come in [and] tell you they have SIBO even though they haven't had a test for it just on the basis of what they read. And that makes sense. Everyone's trying to feel better. Hashimoto's onset was just after her first child was born, which is the most common time for that to happen in women. And she was also progressively

needing more and more thyroid medication in order to feel well. She was also on amitriptyline for sleep.



We'll start with the SIBO result. As you can see, this is the 120 minutes Genova SIBO breath test because this is what was available at the time. [It's] pretty normal for hydrogen and methane.



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	3+ Alpha hemolytic strep	
2+ Bifidobacterium spp.	2+ Enterobacter cloacae complex	
4+ Escherichia coli	4+ Gamma hemolytic strep	
2+ Lactobacillus spp.		
2+ Enterococcus spp.		
3+ 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
No yeast isolated	

MICROSCOPIC YEAST

Result:	Expected:
None	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.

Comments:

Date Collected: 09/08/2015
Date Received: 09/09/2015
Date Completed: 09/18/2015

** Aeromonas, Campylobacter, Plesiomonas, Salmonella, Shigella, Vibrio, Yersinia, & Edwardsiella tarda have been specifically tested for and found absent unless reported.*

MALDI-TOF

Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *

Sample 1
None Ova or Parasites
Rare WBC

Sample 2
None Ova or Parasites
Few WBC

Sample 3
None Ova or Parasites
Rare WBC

***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 Microsporidia spp.

GIARDIA/CRYPTOSPORIDIUM IMMUNOASSAY

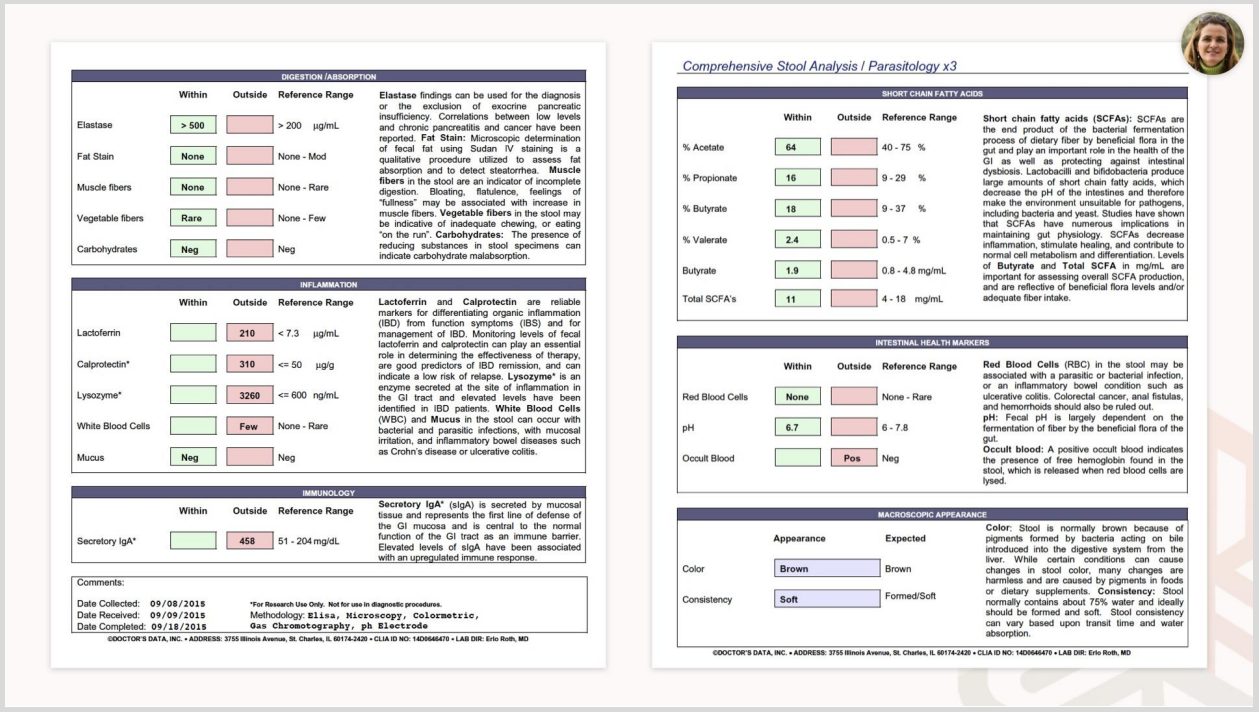
	Within	Outside	Reference Range
Giardia intestinalis	Neg		Neg
Cryptosporidium	Neg		Neg

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.

Comments:

Date Collected: 09/08/2015
Date Received: 09/09/2015
Date Completed: 09/18/2015

This is the old [Comprehensive Stool Analysis/Parasitology] times three-day sample from Doctor's Data. The main thing I'm looking for here are parasites, yeast, red blood cells, etc., which were all negative with the exception of a few to rare white blood cells. [There are] pretty good levels of beneficial bacteria in the Doctor's Data stool test. Some commensal imbalance flora with *Bifidobacterium* and *Lactobacillus*, which are arguably two of the most important species. [They] should comprise about 30 trillion of the 100 trillion microorganisms in our colon. A reminder that this was done via culture and is no longer really the preferred methodology for assessing microbiome diversity and abundance, but it is what we had at the time.



DIGESTION /ABSORPTION

	Within	Outside	Reference Range
Elastase	> 500		> 200 µg/mL
Fat Stain	None		None - Mod
Muscle fibers	None		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		210	< 7.3 µg/mL
Calprotectin*		310	<= 50 µg/g
Lysozyme*		3260	<= 600 ng/mL
White Blood Cells		Few	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*		458	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.

Comments:

Date Collected: 09/08/2015
Date Received: 09/09/2015
Date Completed: 09/18/2015

*For Research Use Only. Not for use in diagnostic procedures.
Methodology: Elisa, Microscopy, Colormetric, Gas Chromotography, ph Electrode

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Comprehensive Stool Analysis / Parasitology x3

SHORT CHAIN FATTY ACIDS

	Within	Outside	Reference Range
% Acetate	64		40 - 75 %
% Propionate	16		9 - 29 %
% Butyrate	18		9 - 37 %
% Valerate	2.4		0.5 - 7 %
Butyrate	1.9		0.8 - 4.8 mg/mL
Total SCFA's	11		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	None		None - Rare
pH	6.7		6 - 7.8
Occult Blood		Pos	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.

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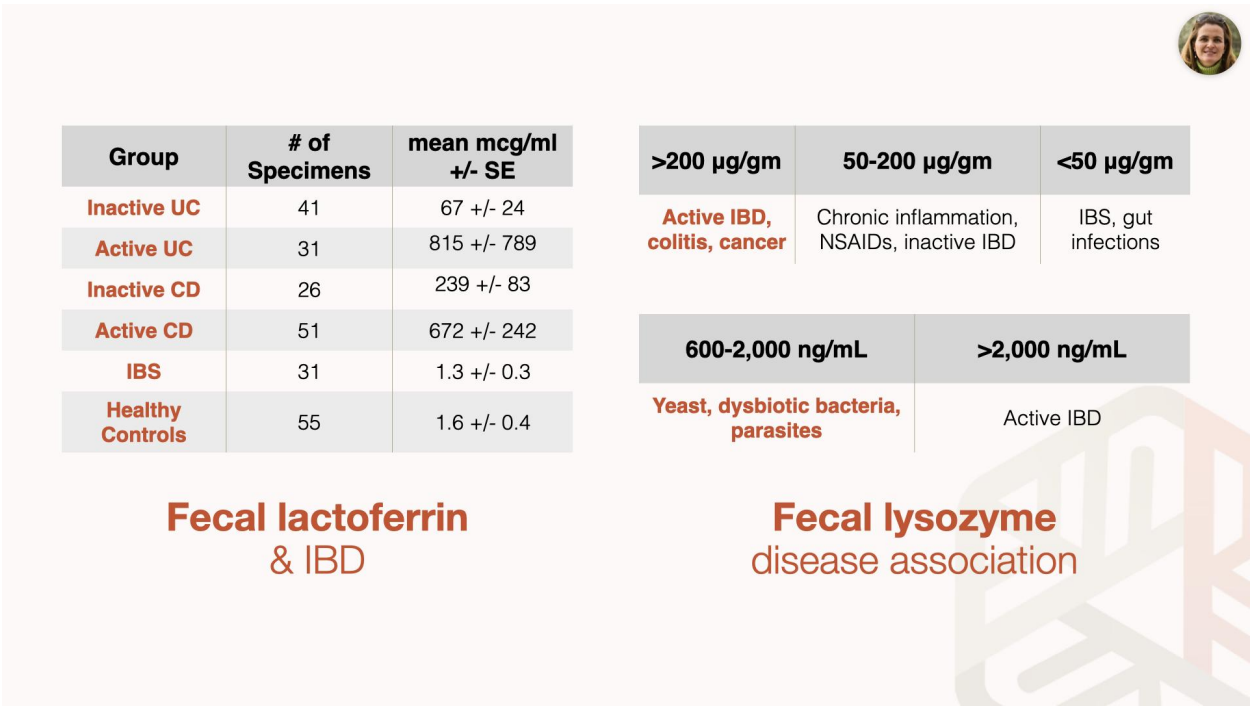
But check this out. Her fecal lactoferrin, calprotectin, and lysozyme were very high, particularly, and her secretory IgA was high. And she was positive for blood in the stool. Occult blood. So right away, when you see these numbers, you should be thinking about inflammatory bowel disease [(IBD)] because they're above the range that you would expect with just dysbiosis or gut infections.



Group	# of Specimens	mean mcg/ml +/- SE
Inactive UC	41	67 +/- 24
Active UC	31	815 +/- 789
Inactive CD	26	239 +/- 83
Active CD	51	672 +/- 242
IBS	31	1.3 +/- 0.3
Healthy Controls	55	1.6 +/- 0.4

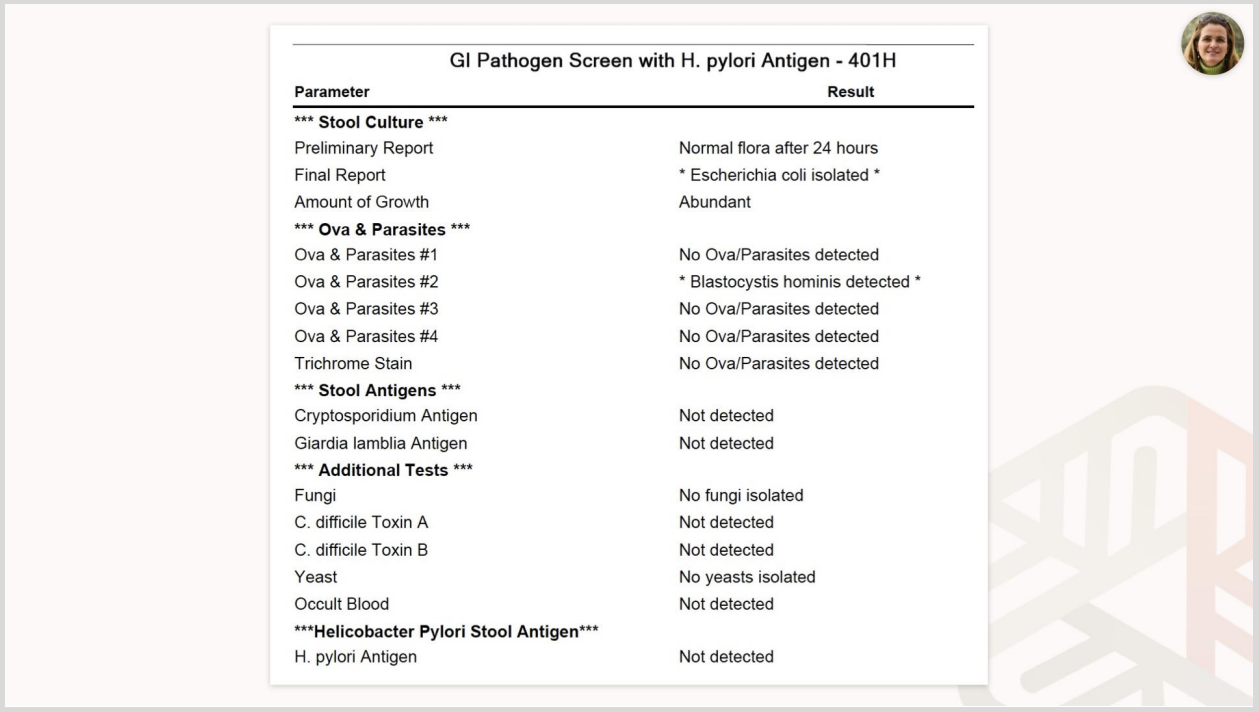
Fecal lactoferrin
& IBD

>200 µg/gm	50-200 µg/gm	<50 µg/gm
Active IBD, colitis, cancer	Chronic inflammation, NSAIDs, inactive IBD	IBS, gut infections

600-2,000 ng/mL	>2,000 ng/mL
Yeast, dysbiotic bacteria, parasites	Active IBD

Fecal lysozyme
disease association

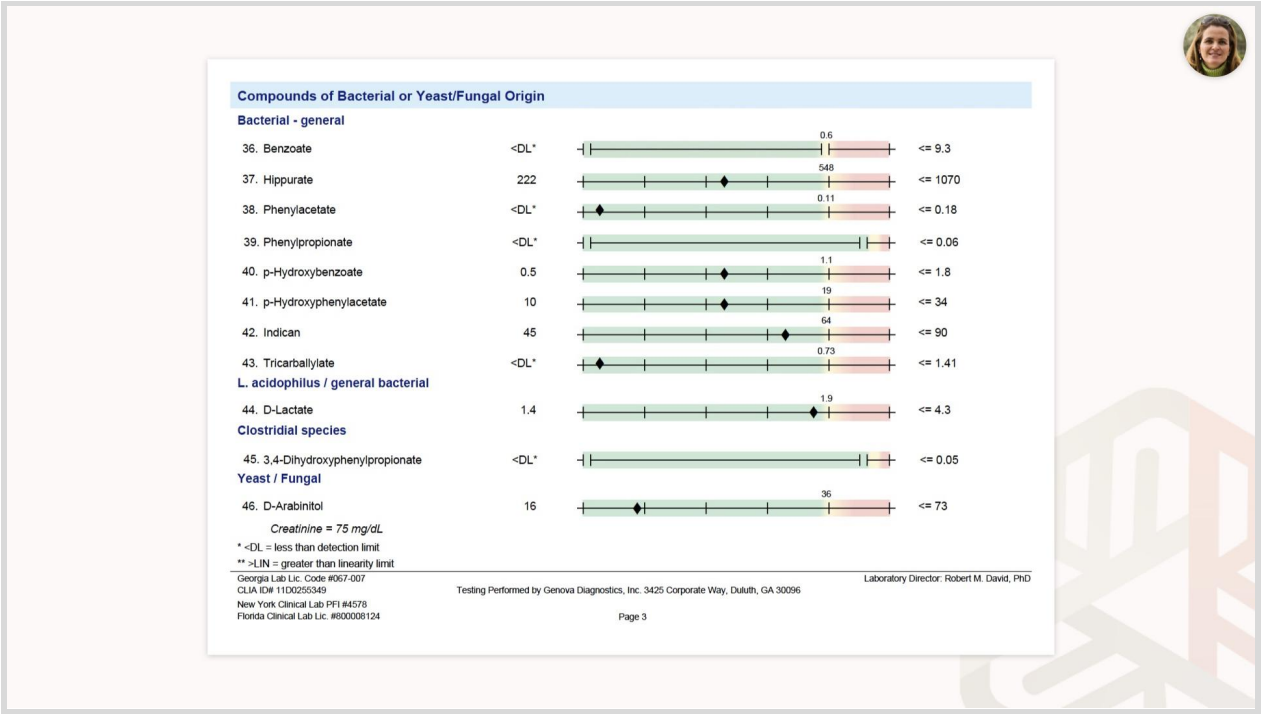
Here's the remainder of this chart. So lactoferrin of 210 puts her in the inactive ulcerative colitis or inactive Crohn's disease range. And remember, these are just loose guidelines. You can't really make any diagnosis based on these ranges. It's just meant to be some guidance for you. And calprotectin of 310, though, does put her firmly in that active IBD range. And then, a lysozyme of 3,260 also put her in the active IBD range. So you've got two of the three markers that are suggesting [an] active IBD flare.



GI Pathogen Screen with H. pylori Antigen - 401H

Parameter	Result
***** Stool Culture *****	
Preliminary Report	Normal flora after 24 hours
Final Report	* Escherichia coli isolated *
Amount of Growth	Abundant
***** Ova & Parasites *****	
Ova & Parasites #1	No Ova/Parasites detected
Ova & Parasites #2	* Blastocystis hominis detected *
Ova & Parasites #3	No Ova/Parasites detected
Ova & Parasites #4	No Ova/Parasites detected
Trichrome Stain	No Ova/Parasites detected
***** Stool Antigens *****	
Cryptosporidium Antigen	Not detected
Giardia lamblia Antigen	Not detected
***** Additional Tests *****	
Fungi	No fungi isolated
C. difficile Toxin A	Not detected
C. difficile Toxin B	Not detected
Yeast	No yeasts isolated
Occult Blood	Not detected
*****Helicobacter Pylori Stool Antigen*****	
H. pylori Antigen	Not detected

She also had *Blastocystis hominis* on the BioHealth Stool Test. A reminder that BioHealth is now out of business. But this is again what we were using at the time. So it's unclear how much of a problem this is, especially given the really elevated markers of gut inflammation, but it's notable and worth paying attention to.



Compounds of Bacterial or Yeast/Fungal Origin

Bacterial - general			
36. Benzoate	<DL*	0.6	<= 9.3
37. Hippurate	222	548	<= 1070
38. Phenylacetate	<DL*	0.11	<= 0.18
39. Phenylpropionate	<DL*		<= 0.06
40. p-Hydroxybenzoate	0.5	1.1	<= 1.8
41. p-Hydroxyphenylacetate	10	19	<= 34
42. Indican	45	64	<= 90
43. Tricarballylate	<DL*	0.73	<= 1.41
L. acidophilus / general bacterial			
44. D-Lactate	1.4	1.9	<= 4.3
Clostridial species			
45. 3,4-Dihydroxyphenylpropionate	<DL*		<= 0.05
Yeast / Fungal			
46. D-Arabinitol	16	36	<= 73

Creatinine = 75 mg/dL

* <DL = less than detection limit
** >LIN = greater than linearity limit

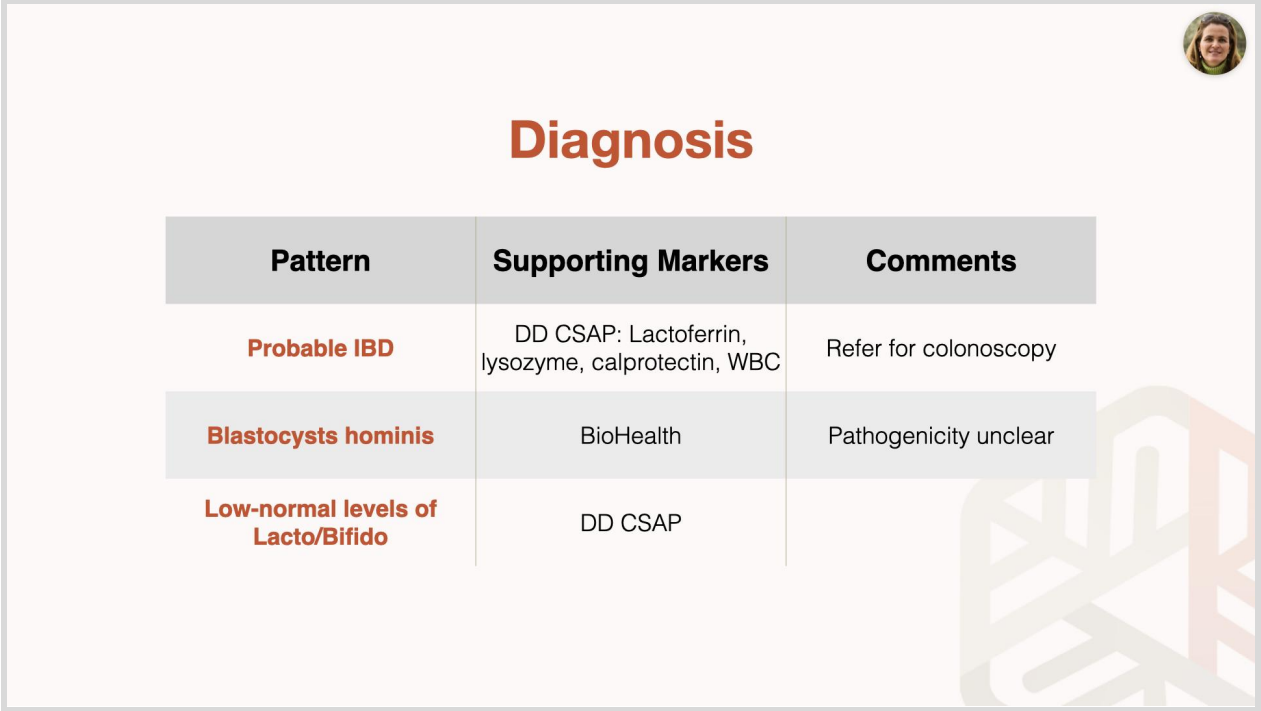
Georgia Lab Lic. Code #067-007
CLIA ID# 11D0255349
New York Clinical Lab PFI #4578
Florida Clinical Lab Lic. #800008124

Testing Performed by Genova Diagnostics, Inc. 3425 Corporate Way, Duluth, GA 30096

Laboratory Director: Robert M. David, PhD

Page 3

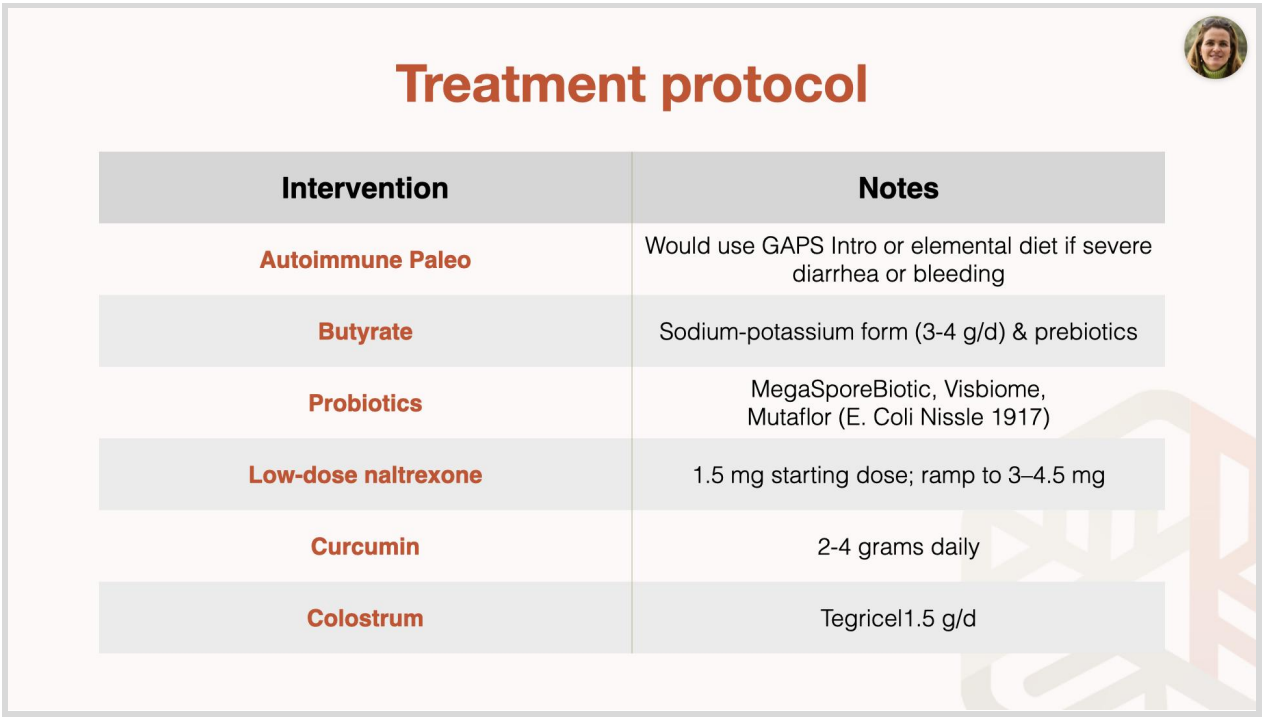
And then [there's] nothing to speak about on the organic acids test. All pretty normal.



Diagnosis

Pattern	Supporting Markers	Comments
Probable IBD	DD CSAP: Lactoferrin, lysozyme, calprotectin, WBC	Refer for colonoscopy
Blastocysts hominis	BioHealth	Pathogenicity unclear
Low-normal levels of Lacto/Bifido	DD CSAP	

We referred her to a gastroenterologist for a colonoscopy. And I skipped the blood panel in this case because the numbers were so high that we're relatively certain that she had IBD. And sure enough, she did have terminal ileitis with Crohn's disease. So there's an important thing to pay attention to here. She didn't have the typical Crohn's disease symptoms that most people think about. So bloody diarrhea, multiple bowel movements throughout the day, [and] mucus in the stool. And in fact, she even had a tendency toward constipation. And that's not super uncommon, actually, when the disease is primarily in the small intestine, as it was for her. So don't let lack of bloody diarrhea or frequent loose stools turn you off to the idea of IBD because it can definitely be present even without that. So just the pattern here that we see probable IBD with those markers on the Doctor's Data test, *Blastocystis hominis* from BioHealth. [However], the pathogenicity of that's a little unclear given her other issues. And [she had] low normal levels of *Lactobacillus* and *Bifidobacterium*.



Treatment protocol

Intervention	Notes
Autoimmune Paleo	Would use GAPS Intro or elemental diet if severe diarrhea or bleeding
Butyrate	Sodium-potassium form (3-4 g/d) & prebiotics
Probiotics	MegaSporeBiotic, Visbiome, Mutaflor (E. Coli Nissle 1917)
Low-dose naltrexone	1.5 mg starting dose; ramp to 3–4.5 mg
Curcumin	2-4 grams daily
Colostrum	Tegricel1.5 g/d

So in this case, the focus of the treatment became IBD and regulating the immune system. She also had Hashimoto's [disease], and no one had really addressed the autoimmune component. You'll find, and the research shows this, that unfortunately, when someone has one autoimmune condition, they're much more likely to have another. So we're seeing this with Crohn's [disease] and Hashimoto['s disease] in this particular patient. Her physicians in the past just gave her a thyroid medication, which explains why she continued to need more and more thyroid hormone because the autoimmune dysfunction was progressing and making her

thyroid gland function more and more poorly. We treated her as if she was in an active flare of IBD, which two of the three fecal markers, as well as the colonoscopy, did suggest. And she did have significant symptomatology. So we used autoimmune Paleo. If she had severe diarrhea or bleeding, I probably would have used more of like a [gut and psychology syndrome] (GAPS) or elemental diet. But with constipation, those can actually make that a little worse in some cases.

For supplements and medications, I should note that I got back in and updated the brand and dosing on this so that it's current with what we're recommending currently. So there may be some variation in actual recommendations that were made a few years ago, but these are the most accurate of what we [are] doing now. We use butyrate, sodium potassium form, three to four grams per day. [We generally prefer] the product ProButyrate by Tesseract, three capsules twice daily. Particular probiotics, which can be helpful for IBD, like Mutaflor [*Escherichia*] *coli* Nissle, Visbiome, [and] MegaSporeBiotic. Low-dose naltrexone, starting at 1.5 milligrams and slowly ramping up. I think she ended up [at] 3 milligrams here, although 4.5 is the upper end. And even then, some practitioners are pushing that up a little bit more. For traditional immune regulation, we had her take higher-dose curcumin. Generally, about three to four grams per day. So she did curcumin. I believe at the time, we were using Novasol. But you can check the preferred supplement page for our current preferred brand dose. We've also added colostrum, the Tegricel variety, 1.5 grams per day.

Comprehensive Stool Analysis / Parasitology x3

DIGESTION /ABSORPTION

	Within	Outside	Reference Range
Elastase	> 500		> 200 µg/mL
Fat Stain	Few		None - Mod
Muscle fibers	None		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	< 0.5		< 7.3 µg/mL
Calprotectin*	< 10		<= 50 µg/g
Lysozyme*	122		<= 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*		295	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.

Comments:

Date Collected: 09/27/2015
Date Received: 09/30/2015
Date Completed: 10/08/2015

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Methodology: Elisa, Microscopy, Colormetric, Gas Chromotography, ph Electrode

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At the six-month follow-up, lactoferrin, calprotectin, and lysozyme had normalized. Now keep in mind that in some cases, you'll never see them go completely normal. They can sometimes fall into that inactive range and still be a little elevated, which isn't totally unexpected for people with IBD. But in her case, they did go back into that normal range, which was nice to see. Secretory IgA is still elevated. I think I have found this is often the last marker to improve and can take a long time to normalize. The patient had really big improvements in [gastrointestinal] function. Also, [we] had to reduce the dose of her thyroxine because she [started] to feel a little hyperthyroid. And this can happen as you begin to improve immune function. The dose they were on before when their immune system was really overactive and suppressing thyroid function really becomes too much when their immune system starts to become balanced and isn't attacking the thyroid gland as much, so the thyroid starts to restore some ability to produce thyroid hormone, and then her histamine tolerance symptoms decreased and energy levels improved. We didn't end up treating [*Blastocystis hominis*] in her case because we really suspected the IBD was the primary contributor, and most of her symptoms had resolved, but we would certainly consider doing this if she continues to have problems in the future.