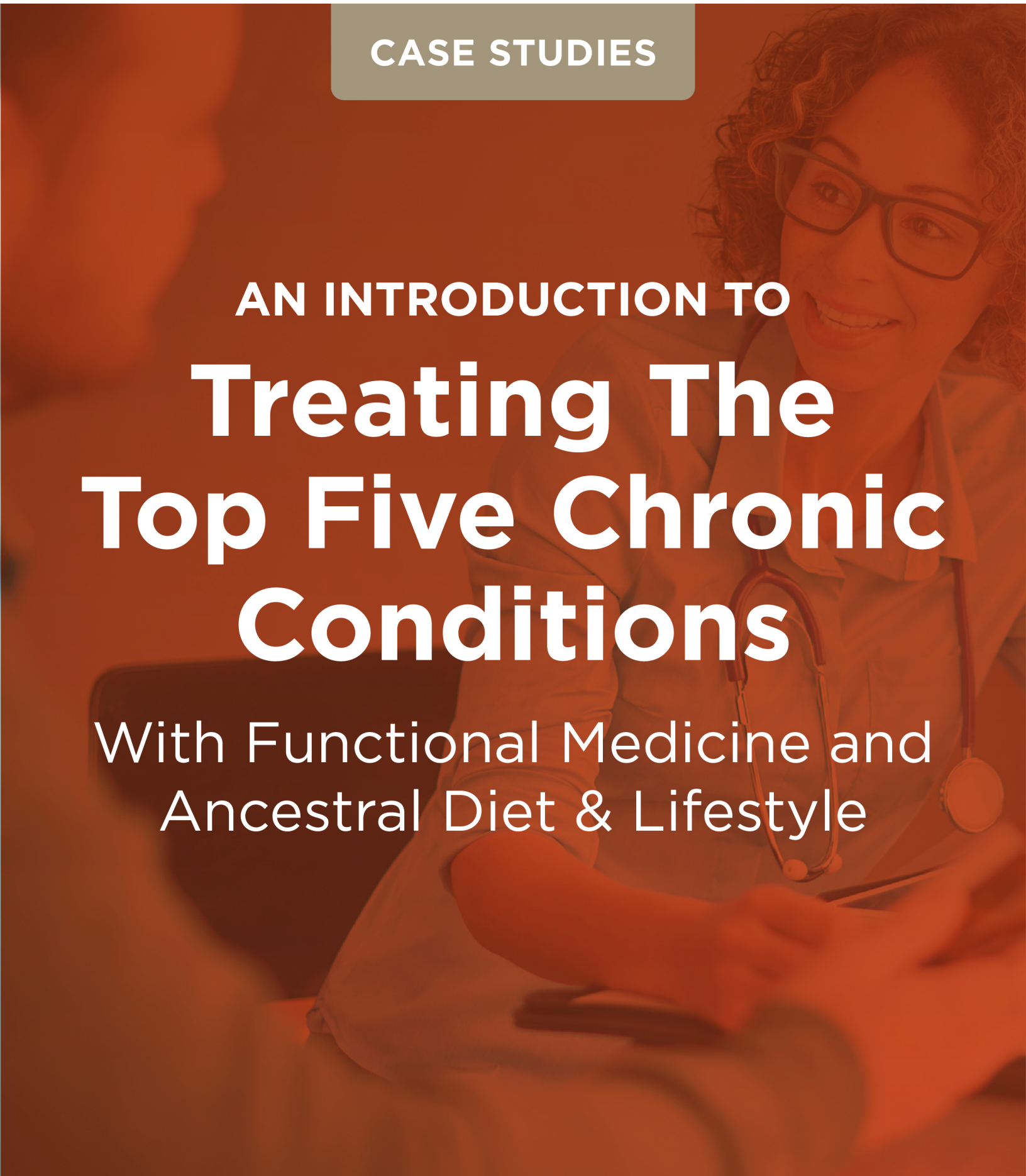
KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

CASE STUDIES



AN INTRODUCTION TO

Treating The Top Five Chronic Conditions

With Functional Medicine and Ancestral Diet & Lifestyle

KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Introduction

Dear Reader,

Thank you for downloading these case studies. You may be new to Functional Medicine or have had Functional Medicine training before but still feel like you need more direction. You're not alone. In order to be a successful and effective Functional Medicine practitioner, you will need more than just theory and concepts.

We strongly believe that the ability to leverage a Functional Medicine approach to change the future of healthcare goes beyond just concepts, theory, and passive lecture—to hard evidence and practical approaches grounded in the real world, with real patients and real results. These case studies are a great way for you to see what Functional Medicine looks like in action.

In the following five case studies, you'll see just how powerful Functional Medicine and ancestral health can be when applied to real-life patients:

- How blood sugar control was restored in a 66-year-old patient with diabetes
- How rheumatoid arthritis in a 46-year-old patient was resolved by treating the gut
- How hypothyroidism was resolved in a 26-year-old patient by restoring iodine levels
- How mental and physical performance were optimized in a 41-year-old CEO
- How HPA axis dysregulation was resolved in a 42-year-old with fatigue, anxiety and weight gain

We hope these case studies give you a greater insight into how digging deeper and resolving the root cause of chronic illness can result in true healing rather than symptom suppression.

In health,
Kresser Institute

Inflammatory Joint Pain and Hormone Imbalance Resolved by Treating the Gut

CASE SUMMARY

A 46-year-old female experienced a downward spiral after the death of a loved one and the loss of her job. She complained of joint pain, gastrointestinal symptoms, cold hands and feet, problems thinking, anxiety, and insomnia. She had been given a diagnosis of rheumatoid arthritis but did not want to take immunosuppressive drugs. Routine lab tests, HLA-B27, a stool test, SIBO, and hormone panels showed thyroid dysfunction and genetic predisposition to autoimmunity. She also had high iron levels and gut dysbiosis. Especially noteworthy was an overgrowth of Klebsiella, a bacteria known to contribute to inflammatory joint disease. Treating Michelle's dysbiosis resolved her joint pain, improved her cognitive function, and normalized her thyroid markers and cortisol levels.

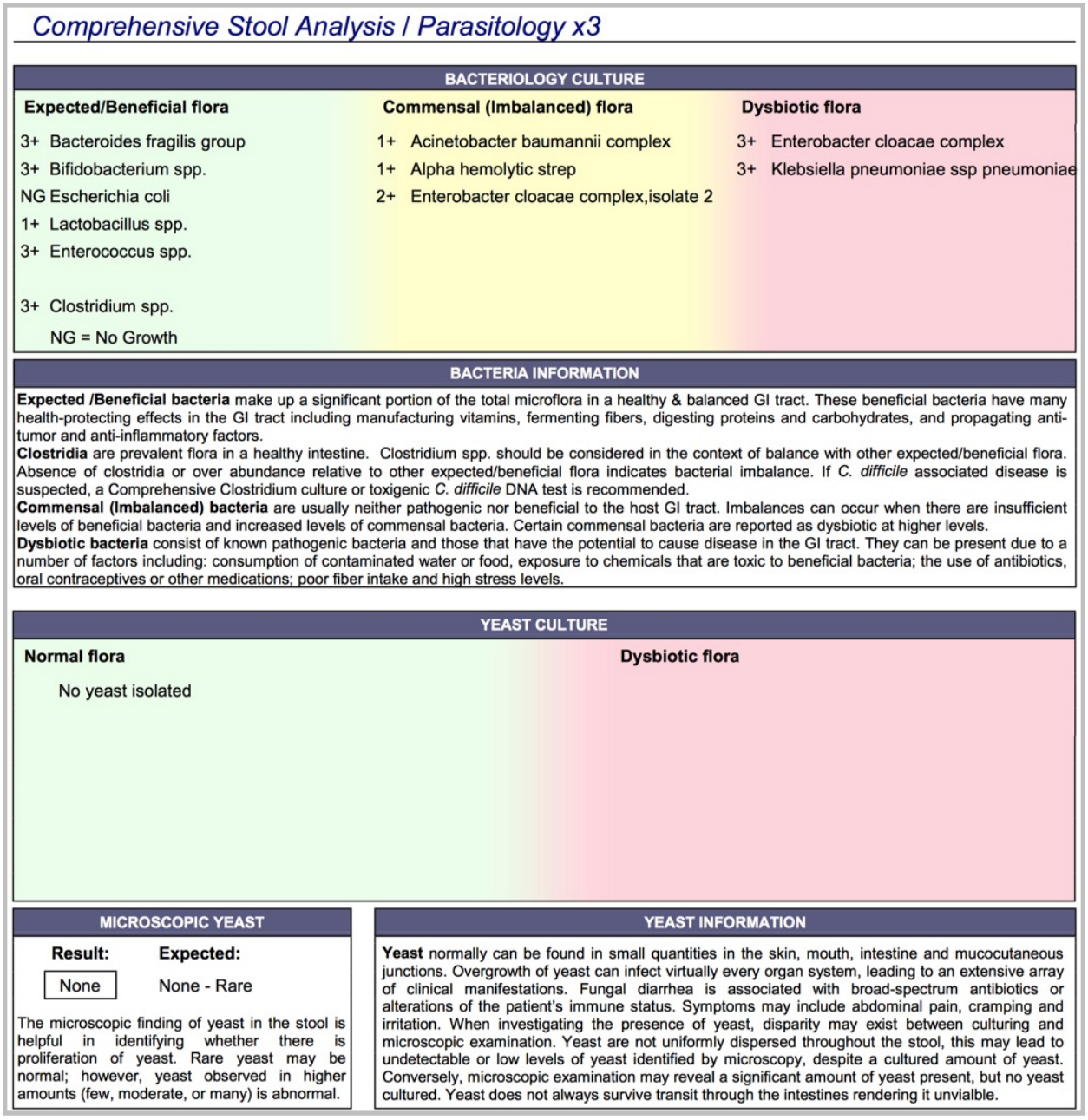
Michelle, a 46-year-old female, presented with bilateral joint pain in the hands and feet, digestive symptoms (gas, bloating, constipation), cold hands and feet, brain fog, anxiety, and sleep disturbance. Her symptoms had worsened in the last three-month period, after she lost her job and her mother passed away.

She had been given a provisional diagnosis of rheumatoid arthritis by another clinician. She was prescribed immunosuppressive drugs, which she refused. She occasionally took ibuprofen to manage the joint pain, but she was concerned about its long-term effects. She had a family history of autoimmune disease (her mother had Hashimoto's thyroiditis and her sister had Crohn's disease). She believed that she might also have some form of autoimmunity.

I ran a full panel of lab tests on Michelle: a stool test, HLA-B27 blood test, small intestinal bacterial overgrowth breath test, urinary organic acids, routine lab tests with a thyroid panel, and a urine hormone profile. I found several pathologies that were contributing to her symptoms.

Initial Testing

FIGURE 1: *Comprehensive Stool Analysis. Dysbiotic flora are highlighted in red. Commensal flora, which may be imbalanced, are highlighted in yellow.*



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
3+ Bacteroides fragilis group	1+ Acinetobacter baumannii complex	3+ Enterobacter cloacae complex
3+ Bifidobacterium spp.	1+ Alpha hemolytic strep	3+ Klebsiella pneumoniae ssp pneumoniae
NG Escherichia coli	2+ Enterobacter cloacae complex,isolate 2	
1+ Lactobacillus spp.		
3+ 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

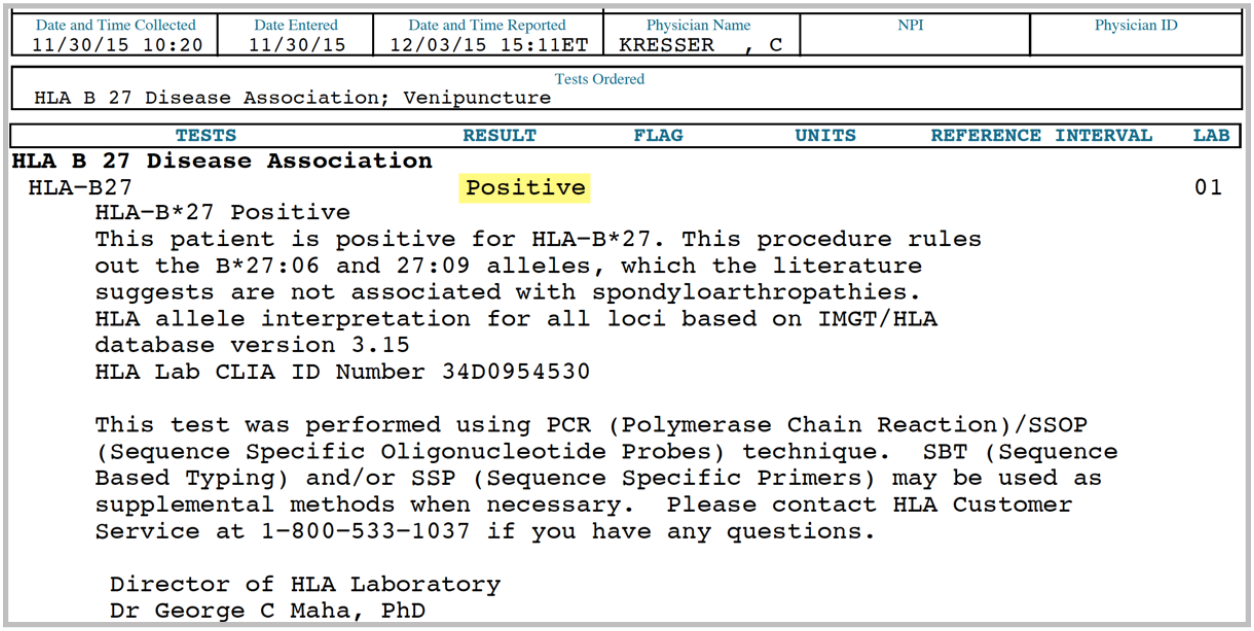
Yeast normally can be found in small quantities in the skin, mouth, intestine and mucocutaneous junctions. Overgrowth of yeast can infect virtually every organ system, leading to an extensive array of clinical manifestations. Fungal diarrhea is associated with broad-spectrum antibiotics or alterations 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 unvialble.

Michelle's stool test found low levels of Lactobacillus and E. coli, both important species of beneficial bacteria. In addition, it found a 3+ for two species of pathogenic bacteria, *Enterobacter cloacae* and *Klebsiella pneumoniae*. She was negative for yeast.

The *Klebsiella* is of particular concern given her symptoms. *Klebsiella* species are associated with conditions that are characterized by joint pain, including ankylosing spondylitis, reactive arthritis, and rheumatoid arthritis. It has also been reported in irritable bowel syndrome (which this patient would likely meet the diagnostic criteria for) and other digestive conditions such as Crohn's disease. The association between *Klebsiella* and autoimmune disease appears to be mediated—at least in some cases—by the HLA-B27 protein,[1] which is found on the surface of white blood cells.

I tested Michelle for HLA-B27 and she was positive. This finding suggests that she may be more susceptible to autoimmune conditions, and a *Klebsiella* infection might be more problematic for her than for others who are HLA-B27 negative.

FIGURE 2: *HLA-B27 Blood Test.*



Date and Time Collected	Date Entered	Date and Time Reported	Physician Name	NPI	Physician ID
11/30/15 10:20	11/30/15	12/03/15 15:11ET	KRESSER , C		

Tests Ordered
HLA B 27 Disease Association; Venipuncture

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
HLA B 27 Disease Association					
HLA-B27	Positive				01

HLA-B*27 Positive
This patient is positive for HLA-B*27. This procedure rules out the B*27:06 and 27:09 alleles, which the literature suggests are not associated with spondyloarthropathies.
HLA allele interpretation for all loci based on IMGT/HLA database version 3.15
HLA Lab CLIA ID Number 34D0954530

This test was performed using PCR (Polymerase Chain Reaction)/SSOP (Sequence Specific Oligonucleotide Probes) technique. SBT (Sequence Based Typing) and/or SSP (Sequence Specific Primers) may be used as supplemental methods when necessary. Please contact HLA Customer Service at 1-800-533-1037 if you have any questions.

Director of HLA Laboratory
Dr George C Maha, PhD

FIGURE 3: *Small Intestinal Bacterial Overgrowth Test Results.*

SIBO
CENTER FOR DIGESTIVE HEALTH
NCNM CLINIC

Test Results

NCNM Clinic Lab
3025 SW Corbett Ave.
Portland, OR 97201
Phone (503) 552-1931
Fax (503) 444-6709

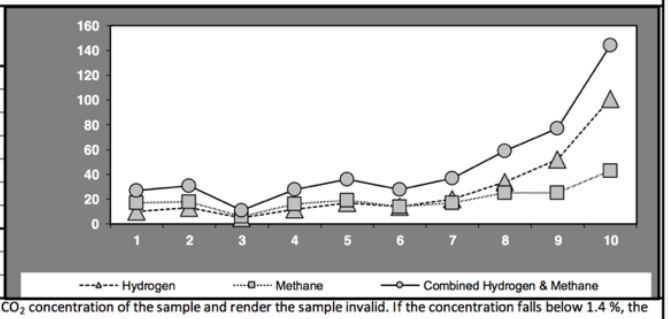
CLIA CERTIFICATION: 38D0624258

[redacted]

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	10	17	27	OK
2	20 min	13	18	31	OK
3	40 min	5	6	11	OK
4	60 min	12	16	28	OK
5	**85 min****	17	19	36	OK
6	**105 min****	14	14	28	OK
7	**125 min****	20	17	37	OK
8	**145 min****	34	25	59	OK
9	**165 min****	52	25	77	OK
10	**185 min****	101	43	144	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 =	27	H	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	15	-	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	13	H	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	26	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.	**NEGATIVE**
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**POSITIVE**
SIBO Suspected - Elevated Combined Hydrogen & Methane Gasses	Increases in combined hydrogen and methane gas values greater than 15ppm over the lowest preceding value are indicative of bacterial overgrowth.	**POSITIVE**

Notes

The following symptoms were reported during collection: none reported.

Note: The actual collection times were shifted 5 minutes later than the standard collection times, starting with Sample #5. Note that the 120 minute sample was collected at 125 minutes. See **bold times****

Her SIBO breath test results indicated methane overproduction. This suggested bacterial overgrowth in the small intestine, which was likely contributing to her constipation.

FIGURE 4: *Urinary Organix (Organic Acids) from Genova Diagnostics.*

Organix
Urine Organic Acids
U.S. patent pending 2008

0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

Summary of Abnormal Findings

	Findings	Intervention Options	Common Metabolic Association
Fatty Acid Metabolism			
Adipate	High	Carnitine, B2	Fatty acid oxidation
Carbohydrate Metabolism			
L-Lactate	High	CoQ10, Lipoic Acid, B1, B2, B3, B5	Glucose oxidation
ß-Hydroxybutyrate	High	Cr, V, Lipoic Acid, Mg, Mn	Ketosis
Energy Production Markers			
No Abnormality Found			
B-Complex Vitamin Markers			
Xanthurenate	Very High	B6	Impaired Tryptophan metabolism
ß-Hydroxyisovalerate	Very High	Biotin, B2	Impaired Isoleucine metabolism
Methylation Cofactor Markers			
Formiminoglutamate	High	Folic acid	Tetrahydrofolate insufficiency
Neurotransmitter Metabolism Markers			
Kynurenate	Very High	B6	Receptor antagonist
Oxidative Damage and Antioxidant Markers			
p-Hydroxyphenyllactate	High	Vitamin C, Vitamin E	Increased cell turn over
Detoxification Indicators			
2-Methylhippurate	High	Glycine	Xylene exposure
Sulfate	High	Antioxidants and removal of toxicant or oxidant stress source	Acute detox or oxidant stress
Bacterial - General			
Benzoate	High	Glycine	Hepatic Phase II conjugation

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

Her urine organic acids test confirmed the microbial overgrowth and imbalance in her gut, and revealed several other issues including:

- B vitamin deficiency. SIBO and a microbial imbalance decrease the absorption of several nutrients, including B vitamins.
- Oxidative stress
- Impaired carbohydrate metabolism
- Impaired fatty acid metabolism

- Impaired detoxification capacity

Her routine blood test was mostly unremarkable, with the following exceptions. She had several markers of iron overload, including ferritin and UIBC that were out of the reference range, and iron saturation that was out of the functional/optimal range (<45%). Michelle had excessive iron storage but not frank hemochromatosis. Many people don't meet the diagnostic criteria for hemochromatosis. The iron elevation also wasn't an artifact of inflammation (inflammation alone can cause high ferritin levels) because her iron saturation and UIBC were abnormal in addition to ferritin. High iron levels have been shown to contribute to joint pain, cognitive dysfunction, and many other symptoms.

Her TSH and thyroid antibodies were normal, but her free T3 (triiodothyronine, free) was low at 1.7 (range: 2.0–4.4 pg/mL). This was likely contributing to her cold hands and feet, constipation, and brain fog. She also had a low white blood cell count, which is often observed in autoimmune conditions.

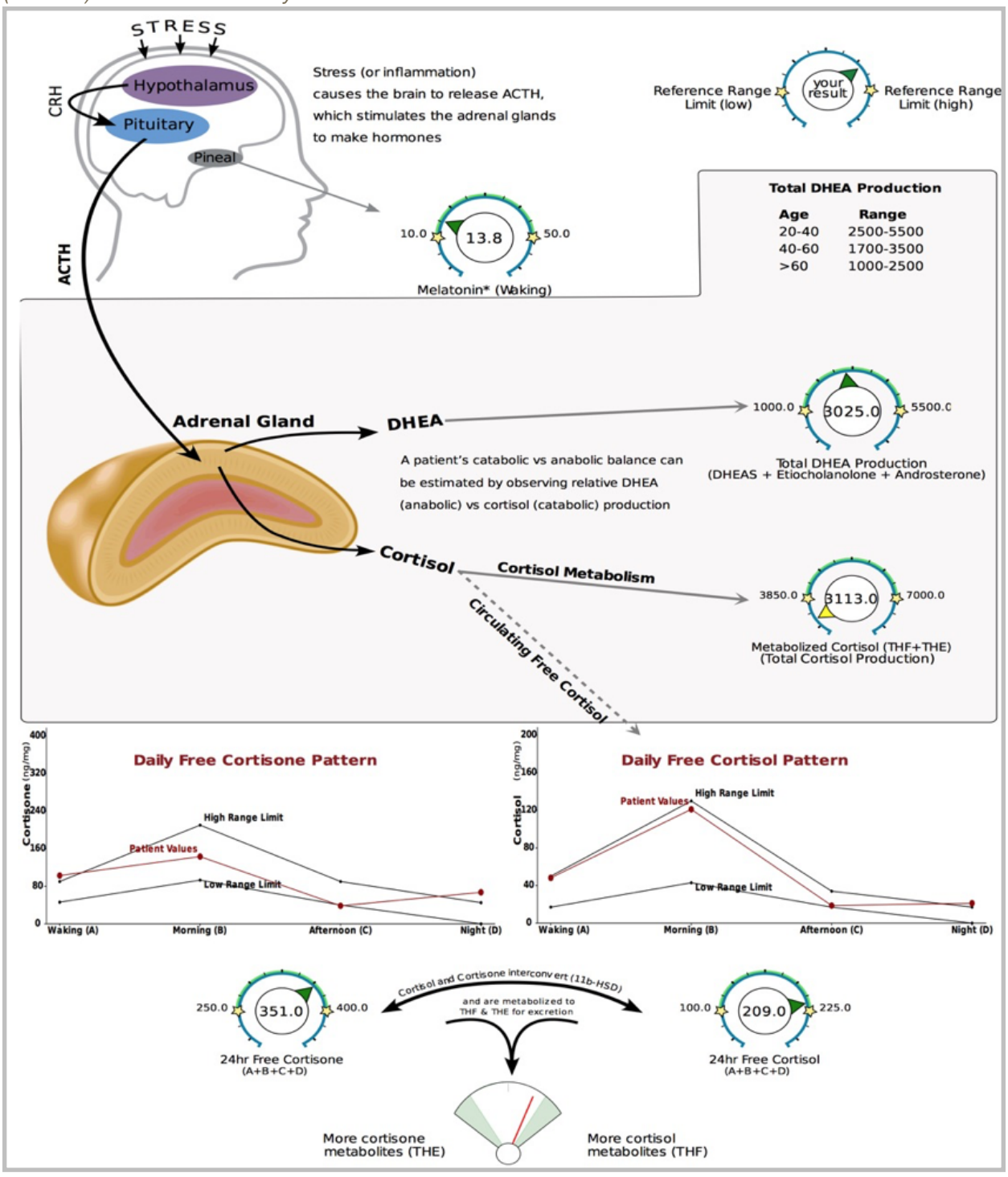
FIGURE 5: *Routine Laboratory Tests Including Thyroid Function Markers, Iron, and Vitamin D.*

Thyroid					01
TSH	1.700		uIU/mL	0.450 - 4.500	01
Thyroxine (T4)	6.4		ug/dL	4.5 - 12.0	01
T3 Uptake	36		%	24 - 39	01
Free Thyroxine Index	2.3			1.2 - 4.9	
Triiodothyronine (T3)	75		ng/dL	71 - 180	01
.					01
Immunoassay					01
Vitamin D, 25-Hydroxy	44.2		ng/mL	32.0 - 100.0	01
Effective November 21, 2011 Vitamin D, 25-Hydroxy reference intervals will be changing to 30-100.					
Recent studies consider the lower limit of 32.0 ng/mL to be a threshold for optimal health. Hollis BW. J Nutr. 2005 Feb;135(2):317-22.					
.					01
CBC, Platelet Ct, and Diff					01
WBC	**3.9**	**Low**	x10E3/uL	4.0 - 10.5	01
RBC	4.17		x10E6/uL	3.80 - 5.10	01
Hemoglobin	13.2		g/dL	11.5 - 15.0	01

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Fe+TIBC+Fer					
Iron Bind.Cap.(TIBC)	271		ug/dL	250 - 450	
UIBC	**139**	**Low**	ug/dL	150 - 375	01
Iron, Serum	132		ug/dL	35 - 155	01
Iron Saturation	49		%	15 - 55	
Ferritin, Serum	**237**	**High**	ng/mL	13 - 150	01
Thyroid Antibodies					
Thyroid Peroxidase (TPO) Ab	8		IU/mL	0 - 34	01
Antithyroglobulin Ab	<20		IU/mL	0 - 40	01
Siemens (DPC) ICMA Methodology					
Thyroxine (T4) Free, Direct, S					
T4,Free(Direct)	1.01		ng/dL	0.82 - 1.77	01
Copper, Serum	109		ug/dL	70 - 155	02
			Detection Limit = 5		
Zinc, Plasma or Serum	99		ug/dL	70 - 150	02
			Detection Limit = 5		
Triiodothyronine,Free,Serum	**1.7**	**Low**	pg/mL	2.0 - 4.4	01

In this case, her low free T3 may be secondary to her gut dysfunction. Approximately 20 percent of T4 is converted into T3 in the gut. Inflammation—which she is clearly experiencing—also reduces the conversion of T4 to T3.

FIGURE 6: *Analysis of HPA-axis Function Using the Dried Urine Test Comprehensive Hormones (DUTCH) from Precision Analytical.*



Finally, Michelle's urine hormones revealed high-normal free cortisol but low metabolized cortisol during a 24-hour period. In addition, her diurnal free cortisol production was disrupted, with high levels at night, high-normal levels upon rising and in the morning, and low levels in the

afternoon. Elevated cortisol levels might have reflected her stress response, consistent with her history of job loss and the death of her mother. Hypothyroidism impairs the body's ability to metabolize cortisol, so this pattern of high free cortisol but low total metabolized cortisol suggested that Michelle had poor thyroid function, which was consistent with her low free T3.

Treatment

One of the core principles in functional medicine is to address the underlying cause of illness, rather than just suppressing symptoms. I chose to address her GI issues (the SIBO, dysbiosis, and Klebsiella/HLA-B27) and then re-test her thyroid markers before taking any specific action for the thyroid dysfunction, because I believed that it would resolve on its own once her gut function improved and inflammation decreased.

The primary goals of the treatment protocol were:

- Reduce overgrowth of *Klebsiella* and prevent further immune attack against HLA-B27 proteins
- Reduce levels of methanogenic microbes in the small intestine by treating SIBO
- Restore nutrient balance and metabolic function by improving digestive absorption of nutrients
- Increase levels of beneficial bacteria and restore a healthy microbial balance in her intestine
- Bring her iron levels back into a normal range
- Increase her free T3 levels and improve her thyroid function indirectly by addressing her GI health
- Normalize her free and total cortisol levels indirectly by addressing her GI health

For *Klebsiella*, SIBO, and microbial overgrowth, I used a protocol of antimicrobial botanicals, soil-based and transient commensal probiotics with specific antimicrobial effects, a biofilm disruptor, and a potent extract of lauric acid (an antimicrobial fatty acid). For iron reduction, I suggested a course of phlebotomy (via blood donation) until her ferritin was <100 ng/mL and her iron saturation was <40 percent. To help with her inflammatory symptoms and balance and regulate her immune function, I prescribed a liposomal form of curcumin.

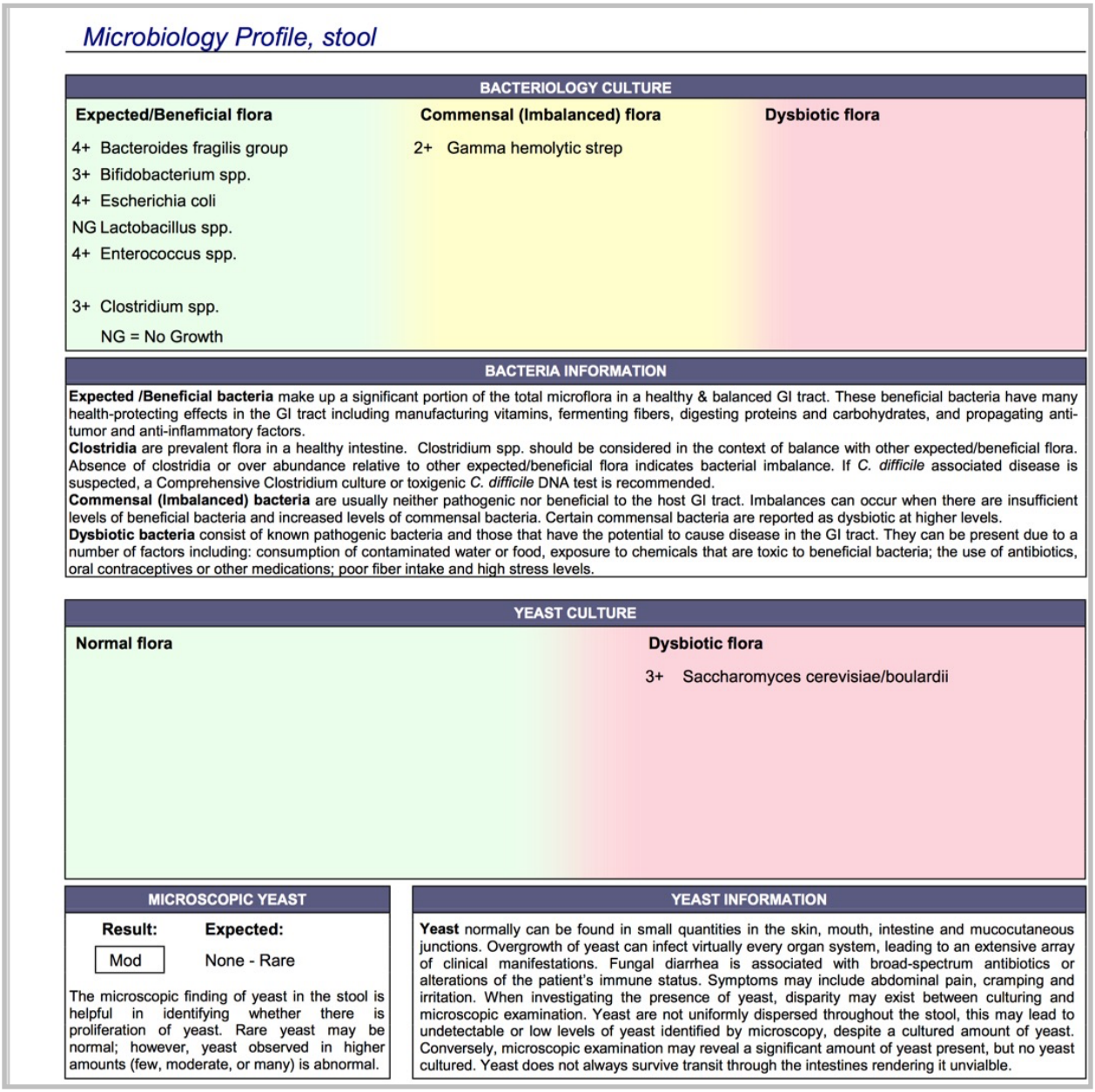
TABLE 1: *Michelle's Treatment Protocol with Dosages.*

TREATMENT	NUTRACEUTICAL	BRAND	DOSAGE
Antimicrobial	GI Synergy	Apex Energetics	1 packet BID (with breakfast and dinner)
Antimicrobial	Interfase Plus	Klaire Labs	3-4 capsules BID on an empty stomach
Probiotic	Prescript-Assist	Prescript-Assist	One BID upon rising and before bed
Probiotic/anti-microbial	MegaSporeBiotic	MegaSporeBiotic	One capsule with lunch
Probiotic	Ideal Bowel Support	Jarrow Formulas	*L. plantarum* for methanogens
Antimicrobial	Lauricidin	Med-Chem Laboratories	1 scoop three times daily with meals
Probiotic	Saccharomycin DF	Xymogen	3 billion CFU twice daily at lunch and before bed
Anti-inflammatory	Optimized Curcumin	ProHealth	One capsule three times a day on an empty stomach for seven days, then decrease to one capsule

After the antimicrobial protocol was completed, I prescribed a combination of fermented foods, fermentable dietary fibers, probiotics, and prebiotics to restore a healthy gut ecosystem.

Follow-up Testing and Clinical Outcome

FIGURE 7: *Comprehensive Stool Analysis Follow-Up.*



Microbiology Profile, stool

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	2+ Gamma hemolytic strep	
3+ Bifidobacterium spp.		
4+ Escherichia coli		
NG Lactobacillus spp.		
4+ 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
	3+ Saccharomyces cerevisiae/boulardii

MICROSCOPIC YEAST

Result:	Expected:
Mod	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 unvialble.

Michelle received treatment for 60 days and then I ran another set of tests to check on her progress. Michelle's follow-up test results indicated a significant improvement. As you can see from her stool test, the *Klebsiella* and *Enterobacter* (dysbiotic flora) were gone. Her beneficial bacteria improved, with the exception of *Lactobacillus,* which still needed attention.

She had a 3+ for *Saccharomyces boulardii*, which is marked as “dysbiotic flora” and a moderate (Mod) level of yeast in the microscopic section. At first glance this might suggest fungal overgrowth. However, one of the probiotics I treated her with was *Saccharomyces boulardii*, so this result is simply showing the presence of that in her stool. It is not a pathological finding.

FIGURE 8: *Follow-up Test Results for SIBO.*

SIBO CENTER FOR DIGESTIVE HEALTH NCNM CLINIC

Test Results

NCNM Clinic Lab
3025 SW Corbett Ave.
Portland, OR 97201
Phone (503) 552-1931
Fax (503) 444-6709

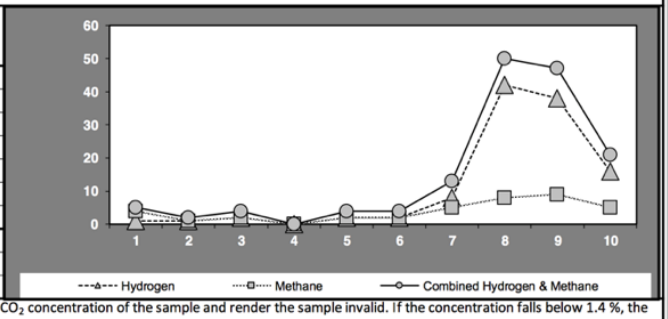
CLIA CERTIFICATION: 38D0624258

[redacted]

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	1	4	5	OK
2	20 min	1	1	2	OK
3	40 min	2	2	4	OK
4	60 min	0	0	0	OK
5	80 min	2	2	4	OK
6	100 min	2	2	4	OK
7	120 min	8	5	13	OK
8	140 min	42	8	50	OK
9	160 min	38	9	47	OK
10	180 min	16	5	21	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 =	5	-	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	8	-	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	5	-	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	13	-	≤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.	**NEGATIVE**
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.	**NEGATIVE**

Notes

The following symptoms were reported during collection:
at 32 minutes - "slight stomach cramping"
at 112 minutes - "diarrhea, intermittent gurgling"

Her follow-up SIBO results were normal.

Her organic acids urine test also improved significantly, with only two markers in the low-normal range. This shows that treating the gut effectively supplied Michelle with critical nutrients (especially B vitamins) that improved her metabolism.

FIGURE 9: *Urinary Organic Acids Follow-up Test.*

Organix
Urine Organic Acids
U.S. patent pending 2008

0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

Summary of Abnormal Findings

	Findings	Intervention Options	Common Metabolic Association
Fatty Acid Metabolism			
No Abnormality Found			
Carbohydrate Metabolism			
No Abnormality Found			
Energy Production Markers			
No Abnormality Found			
B-Complex Vitamin Markers			
No Abnormality Found			
Methylation Cofactor Markers			
No Abnormality Found			
Neurotransmitter Metabolism Markers			
Vanilmandelate	Low	Tyrosine, Phenylalanine	Epi- & Norepinephrine turnover inhibition
Homovanillate	Low	Tyrosine	Dopamine turnover inhibition
Oxidative Damage and Antioxidant Markers			
No Abnormality Found			
Detoxification Indicators			
No Abnormality Found			
Bacterial - General			
No Abnormality Found			
L. acidophilus / general bacteria			
No Abnormality Found			
Clostridial Species			
No Abnormality Found			
Yeast/Fungal			
No Abnormality Found			

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

Her iron saturation dropped to 28 percent after two blood donations. Her ferritin returned to the reference range, but it remained high normal. Further blood donations would be indicated provided that hemoglobin and iron saturation do not drop too low.

FIGURE 10: *Follow-up Results for Routine Laboratory Testing, Including Thyroid and Iron Markers.*

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Fe+TIBC+Fer					
Iron Bind.Cap.(TIBC)	265		ug/dL	250 - 450	
UIBC	192		ug/dL	150 - 375	01
Iron, Serum	73		ug/dL	35 - 155	01
Iron Saturation	28		%	15 - 55	
Ferritin, Serum	149		ng/mL	13 - 150	01
Comp. Metabolic Panel (14)					
Glucose, Serum	74		mg/dL	65 - 99	01
BUN	18		mg/dL	6 - 24	01
Creatinine, Serum	0.82		mg/dL	0.57 - 1.00	01
eGFR If NonAfricn Am	89		mL/min/1.73	>59	
eGFR If Africn Am	102		mL/min/1.73	>59	
Note: A persistent eGFR <60 mL/min/1.73 m2 (3 months or more) may indicate chronic kidney disease. An eGFR >59 mL/min/1.73 m2 with an elevated urine protein also may indicate chronic kidney disease. Calculated using CKD-EPI formula.					
BUN/Creatinine Ratio	22			9 - 23	
Sodium, Serum	140		mmol/L	134 - 144	01
Please note reference interval change					
Potassium, Serum	3.7		mmol/L	3.5 - 5.2	01
Chloride, Serum	100		mmol/L	97 - 108	01
Carbon Dioxide, Total	28		mmol/L	20 - 32	01
Calcium, Serum	9.1		mg/dL	8.7 - 10.2	01
Protein, Total, Serum	6.4		g/dL	6.0 - 8.5	01
Albumin, Serum	4.2		g/dL	3.5 - 5.5	01
Globulin, Total	2.2		g/dL	1.5 - 4.5	
A/G Ratio	1.9			1.1 - 2.5	
Bilirubin, Total	0.4		mg/dL	0.0 - 1.2	01
Alkaline Phosphatase, S	64		IU/L	25 - 150	01
AST (SGOT)	29		IU/L	0 - 40	01
ALT (SGPT)	27		IU/L	0 - 40	01

Tests Ordered

TSH; Reverse T3, Serum; Triiodothyronine (T3); Triiodothyronine,Free,Serum; Venipuncture

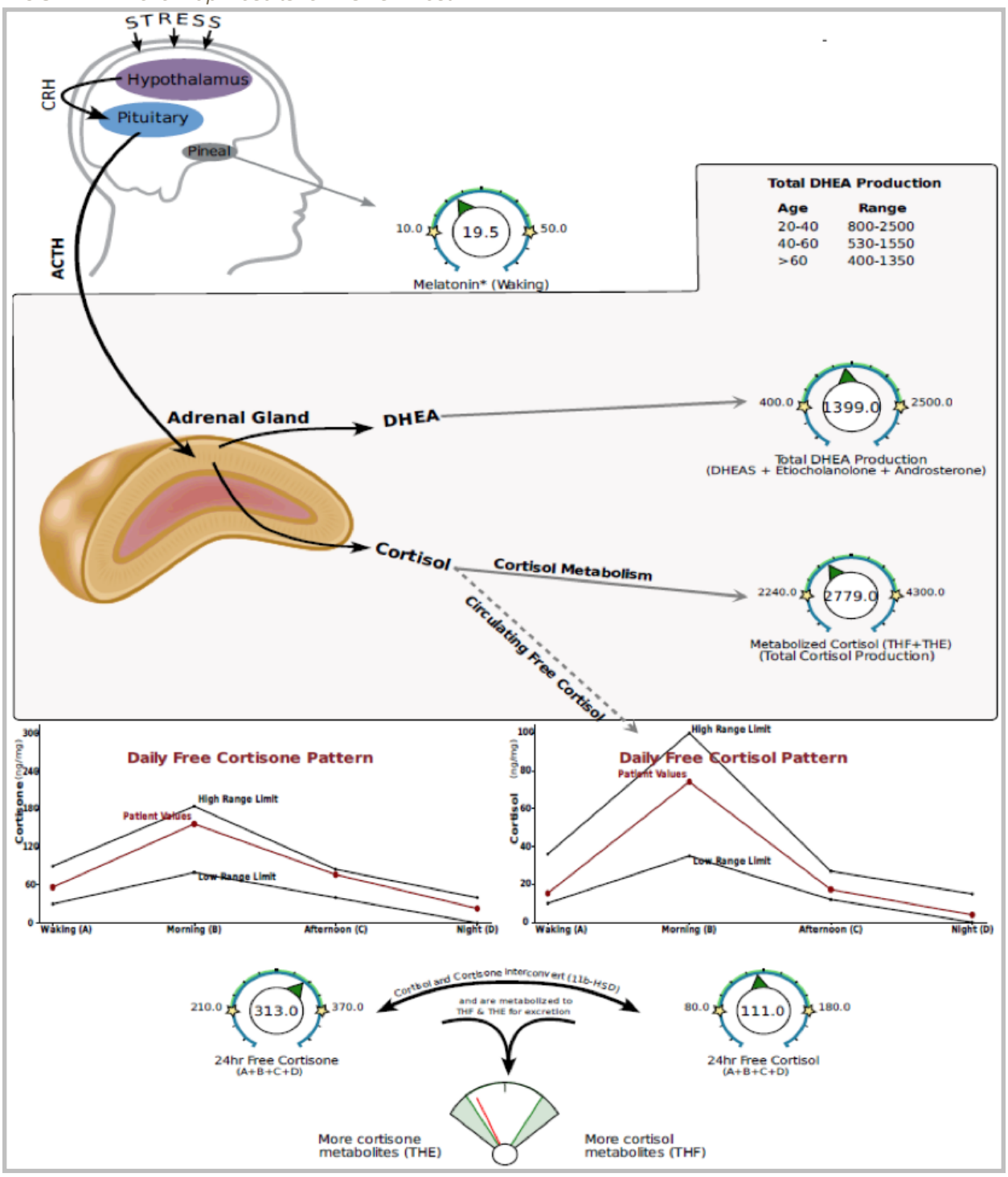
TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
TSH	2.770		uIU/mL	0.450 - 4.500	01
Reverse T3, Serum	29.6		ng/dL	13.5 - 34.2	02
Triiodothyronine (T3)	108		ng/dL	71 - 180	01
Triiodothyronine,Free,Serum	2.6		pg/mL	2.0 - 4.4	01

01 SO LabCorp San Diego Dir: Kelli Chase, MD
13112 Evening Creek Dr So Ste 200, San Diego, CA 92128-4108
02 BN LabCorp Burlington Dir: William F Hancock, MD
1447 York Court, Burlington, NC 27215-3361
For inquiries, the physician may contact **Branch: 800-762-4344 Lab: 858-668-3700**

Her free T3 improved dramatically without any specific focus on her thyroid, supporting the functional medicine principle of addressing the underlying cause. That said, both her TSH and reverse T3 are high-normal, which may suggest an ongoing thyroid issue or chronic stressor that is not influenced by her GI function. This would not be surprising given her family history of thyroid disease and her recent stressful experiences.

Finally, her DUTCH test results normalized. Her free cortisol decreased to 111 (range: 80–180) her metabolized cortisol increased to 2,779 (range: 2240–4300), and her diurnal cortisol rhythm improved. This also illustrates the importance of addressing the deepest cause(s) of the signs and symptoms you observe first in the treatment process.

FIGURE 11: *Follow-up Results for DUTCH Test*



Most importantly, Michelle's symptoms improved dramatically. Her joint pain was reduced by 80 to 90 percent, and she no longer needed ibuprofen or any other OTC pain medication to manage it.

Her body temperature normalized and she no longer had cold hands and feet. Her constipation, which had been present for over a decade, resolved—as did her gas and bloating. She was able to think more clearly and concentrate for longer periods, and she no longer felt anxious. For the first time in many years she was sleeping deeply through the night and waking up in the mornings feeling refreshed and energized.

Discussion

Michelle presented with joint pain, gut dysfunction, and cognitive and thyroid symptoms. Gastrointestinal testing revealed a *Klebsiella pneumoniae* overgrowth, and genetic testing showed that she was positive for HLA-B27, indicating susceptibility to autoimmunity.

The association between *Klebsiella* and autoimmune disease appears to be mediated—at least in some cases—by the HLA-B27 protein,[1] which is found on the surface of white blood cells. HLA-B27 is encoded by the B locus in the major histocompatibility complex (MHC) on chromosome 6 and presents antigenic peptides (derived from self and non-self antigens) to T cells.

The genetic prevalence of HLA-B27 varies significantly according to ethnicity, ranging from as low as 0.1 percent in people of Japanese descent to 24 percent of people in Northern Scandanavia.

Ninety-two percent of Caucasian people with ankylosing spondylitis (AS) have HLA-B27, but only a small percentage of people with HLA-B27 will go on to develop AS, rheumatoid arthritis, Crohn's disease, or other autoimmune conditions.[1] This suggests that an environmental factor must be driving the connection observed between HLA-B27 and these diseases.

Recent research suggests that *Klebsiella* may be this factor. Dr. Alan Ebringer at Middlesex Hospital in London found that *Klebsiella* has molecules resembling the HLA-B27 blood group.[2,3] Although *Klebsiella* is a normal resident of the digestive tract, it can overgrow when the gut microbiota is disrupted or out of balance.

Elevated levels of antibodies to *Klebsiella* have been found in AS patients, especially during flare-ups. Researchers speculate that the body produces antibodies to attack the *Klebsiella* bacteria, but these antibodies also act upon HLA-B27 proteins in a phenomenon known as "molecular mimicry."[1] The destruction of the HLA-B27 proteins is what causes the joint pain[3] and

inflammation that characterizes rheumatic diseases like AS and rheumatoid arthritis, as well as Crohn's disease.

Michelle's urine hormone test results showed that she had trouble metabolizing cortisol, which is a sign of hypothyroidism. Again, cortisol and thyroid markers were not addressed directly in this case. Instead, restoring gut function normalized cortisol patterns and thyroid function.

Michelle's case illustrates why I prefer DUTCH testing to saliva testing for cortisol and HPA axis assessment. Thyroid hormone is required for the metabolic clearance of cortisol. Patients with hypothyroidism or low T3 levels will have trouble metabolizing cortisol. They often present with high free cortisol but low cortisol metabolites in the urine. In fact, the ratios between free and metabolized cortisol as well as cortisol and cortisone are being investigated as markers of subclinical thyroid hypofunction.[4]

If you only did a saliva test on this patient for cortisol, you'd assume that her cortisol was high (because of the high free cortisol). However, metabolized cortisol is a better marker for overall production. Less than 5 percent of the cortisol in the body is in the free (unbound) form; the rest is cleared by several metabolic pathways and excreted in the urine.

If you gave this patient supplements to lower cortisol levels, as indicated by the saliva test results, she would probably get worse. Her metabolized cortisol was low. Cortisol is a potent anti-inflammatory hormone, and her low levels could be one of the driving factors behind her joint pain and other inflammatory symptoms.

At the same time, giving her supplements to increase cortisol might also have an adverse effect. She already had high free cortisol levels, and free cortisol is the most potent form of that hormone. In this case, the best strategy was once again to address the underlying cause of the dysfunction, which was the poor thyroid function. But as mentioned earlier, the poor thyroid function was itself likely a "symptom" of a deeper problem: the disrupted gut microbiota and microbial overgrowth. A successful and focused functional medicine diagnosis and treatment is sometimes like peeling an onion!

Metabolic testing (organic acids) showed that she had widespread nutrient insufficiencies. By treating the gut alone, her nutrient status improved. It is safe to assume that she was able to digest and assimilate nutrients better once we resolved her gut dysbiosis.

Michelle showed high iron markers, suggesting iron overload, even though she did not meet the strict diagnostic criteria for hemochromatosis.[5] There are many potential causes of iron overload, many of which are still poorly understood. Also, studies have shown that even people who are heterozygous for HFE (human hemochromatosis protein) gene mutations can have higher than normal levels of iron. Because high iron levels can cause symptoms, phlebotomy treatments to lower her iron likely contributed to her improved sense of wellbeing.

Addressing Michelle's GI health had far-reaching consequences: it reduced joint inflammation, improved nutrient status, and normalized cortisol and thyroid markers. Clinically, her improvement was dramatic. She no longer complained of joint pain, hypothyroid symptoms, gut symptoms, or cognitive problems.

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Diabetes and Other Blood Sugar Disorders Case Study

Restored Blood Sugar Control in a Diabetic Woman with Gastrointestinal Complaints and Nutritional Deficiencies

CASE SUMMARY

Chandra, a 66-year-old woman with type 2 diabetes and gastrointestinal complaints, experienced a wake-up call when her mother died of diabetes-related complications. Chandra had a poor diet and a sedentary lifestyle and complained of abdominal pain, nausea, vomiting, bloating, decreased appetite, and heartburn. Testing confirmed her high blood sugar and hemoglobin A1c (HbA1c). It also revealed systemic inflammation, low vitamin D and vitamin B12, and disrupted cortisol patterns. There was evidence of autoimmune attack of thyroid proteins and intrinsic factor. Her stool test showed bacterial and fungal overgrowth, Helicobacter pylori, and a significant inflammatory and immune response in the gut. The treatment protocol included a Paleo diet, physical activity, supplementation to increase vitamin B12 and vitamin D, and treatment for gastrointestinal (GI) dysbiosis. Finally, there were supplement and lifestyle interventions to balance thyroid function, HPA axis, and blood sugar. Over the course of treatment, Chandra had an 80 percent improvement in her GI symptoms; she lost 19 pounds; and she reported much better energy. Her fasting blood glucose went from 156 mg/dL to 90 mg/dL and hemoglobin A1c went from 8.0% to 5.8%. This case demonstrates that the progression of diabetes can be prevented with careful attention to diet, physical activity, hormonal balance, gut health,

Initial Presentation and Lab Testing

Chandra, a 66-year old female, came to see me with the following concerns: abdominal pain with nausea and vomiting at night, bloating, decreased appetite, heartburn, and type 2 diabetes.

She worked as a software engineer and spent about eight to 10 hours a day sitting in front of a computer. She did not exercise other than an occasional walk with friends on the weekend. Her diet was poor and she rarely cooked her own food. Breakfast was usually coffee and a muffin in the car on the way to work. For lunch, she grabbed something quick from the company cafeteria or a local restaurant and ate quickly at her desk. For dinner she would get take-out from a local restaurant most nights during the week and go out to eat on the weekends.

Chandra had a family history of type 2 diabetes and had been diagnosed herself nearly 10 years before she came to see me. However, she had a strong mistrust of conventional Western medicine and chose not to take the medications that were prescribed by her primary care physician. She intermittently took Ayurvedic herbs, which she was more comfortable with, but they failed to bring her blood sugar down to normal levels.

Although she was not following a diet when she came to see me, she had previously made several attempts to follow the low-fat, high-carbohydrate diet recommended by organizations like the American Diabetes Association (ADA). She reported difficulty sticking with this approach: She always felt hungry, gained weight, and experienced a worsening of her blood sugar.

Chandra's mother had passed away six months prior to our appointment, largely from complications related to type 2 diabetes. This served as a wake-up call for Chandra, and she felt more motivated to address the root causes of her condition, including making the necessary dietary and lifestyle changes.

Chandra's poor diet and sedentary lifestyle were obviously contributing to her high blood sugar. I ran a full panel of laboratory tests to identify any other underlying conditions that may have been provoking metabolic dysfunction, as well as digestive distress.

TABLE 1A: *Routine Laboratory Test Results. Includes standard laboratory ranges and functional (or optimum) ranges. Results highlighted in yellow are outside of the functional ranges. Results highlighted in red are outside of the standard lab ranges. Results in orange are outside of the functional range and the laboratory range.*

Marker	Value	Functional Range	Lab Range
Glucose	156	75 - 90	65 - 99
Hemoglobin A1c	8.0	4.4 – 5.4	4.8 - 5.6
Uric Acid	5.0	3.2 - 5.5	3.7 - 8.6
BUN	8	13 – 18	8 - 27
Creatinine	1.03	0.85 – 1.1	0.57 - 1
BUN/Creatinine Ratio	8	9 – 23	10 - 22
Sodium	140	135 – 140	134 - 144
Potassium	5.1	4.0 – 4.5	3.5 - 5.2
Chloride	101	100 – 106	97 - 108
C02	23	25 – 30	18 - 29
Calcium	9.4	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.7	3.5 – 4.0	2.5 - 4.5
Magnesium	2.0	2.0 – 2.6	1.6 - 2.3
Protein, total	6.6	6.9 – 7.4	6.0 - 8.5
Albumin	4.3	4.0 – 5.0	3.6 - 4.8
Globulin	2.3	2.4 – 2.8	1.5 - 4.5
A/G ratio	1.9	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	0.4	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	92	42 – 107	39 - 117
LDH	220	140 - 180	121 - 224
AST	20	10 - 30	0 - 40
ALT	17	10 - 22	0 - 44
GGT	13	< 15	0 - 65
TIBC	270	275 – 425	250 - 450
UIBC	197	175 - 350	150 - 375
Iron	73	40 – 135	40 - 155
Iron saturation	27	17 – 45	15 - 55
Ferritin	77	30 - 100	30 - 400
Vitamin B-12	179	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	8.3	35 - 60	30.0 - 100.0
Cholesterol, total	219	150 - 250	100 - 199
Triglycerides	102	50 – 100	0 - 149
HDL	47	55 – 85	> 39
LDL	152	0 - 175	0 - 99
T. Chol / HDL Ratio	4.7	< 3	0 - 5.0
Triglycerides / HDL Ratio	2.17	< 2	< 3.8
CRP-hs	2.16	< 1.0	0.00 - 3.00
Homocysteine	19.9	< 7.0	0.0 - 15.0

TABLE 1B: *Routine Laboratory Test Results, continued.*

Marker	Value	Functional Range	Lab Range
TSH	5.160	0.5 – 2.5	0.45 - 4.50
T4, total	5.8	6.0 – 12	4.5 - 12.0
T3 Uptake	32	28 - 35	24 - 39
T3, Total	92	100 – 180	71 - 180
Copper	96		72 - 166
Zinc	80		56 - 134
Zinc / Copper Ratio	0.83	> 0.85	
Serum Methylmalonic Acid (MMA)	202	< 300	0 - 378
WBC	5.1	5.0 – 8.0	3.4 - 10.8
RBC	4.49	4.4 – 4.9	4.14 - 5.8
Hemoglobin	13.8	13.5 - 14.5	12.6 - 17.7
Hematocrit	39.7	37 - 44	37.5 - 51.0
MCV	88	85 – 92	79 - 97
MCH	30.7	27.7 – 32.0	26.6 - 33.0
MCHC	34.8	32 – 35	31.5 - 35.7
RDW	13.5	11.5 – 15.0	12.3 - 15.4
Platelets	281	150 – 415	150 - 379
Neutrophils	62	40 – 60	
Lymphocytes	29	25 – 40	
Monocytes	6	4.0 – 7.0	
Eosinophils	2	0.0 – 3.0	
Basophils	1	0.0 – 3.0	

As expected, Chandra's fasting glucose (156 mg/dL) and hemoglobin A1c (8.0%) were in the diabetic range. Surprisingly, her triglycerides and HDL were within the laboratory reference range, although they were slightly outside of the functional (optimal) range. Other notable findings included:

- Depressed BUN/creatinine ratio. This is often caused by low muscle mass, which in Chandra's case was a result of her sedentary lifestyle.
- Borderline high LDH. Lactate dehydrogenase (LDH) is an enzyme that is elevated in a variety of conditions, including liver disease, kidney disease, and pernicious anemia (which was the likely cause in Chandra's case, as you'll see below).
- Low serum B12. This is more common in people following vegetarian or vegan diets, but does still occur in omnivores—especially those with gastrointestinal issues or pernicious anemia.
- Extremely low 25(OH)D. Chandra had one of the lowest vitamin D levels I have ever observed.

- Moderately elevated total and LDL cholesterol. Chandra's slightly elevated total and LDL cholesterol would not concern me on their own, but given her multiple markers of metabolic dysfunction, further investigation was warranted.
- Borderline high hs-CRP. High-sensitivity C-reactive protein is a marker of systemic inflammation that is consistently associated with type 2 diabetes and other metabolic diseases.[1]
- Elevated homocysteine. Homocysteine is a sticky, inflammatory protein associated with metabolic and cardiovascular disease.
- Elevated TSH, with borderline low T4 and T3. A high thyroid-stimulating hormone (TSH) level is the most sensitive indicator of hypothyroidism. Chandra's T4 and T3 levels were within the lab reference range, but below the functional range.
- Borderline low zinc-copper ratio. The zinc-copper ratio is best understood as a marker of inflammation, rather than as a marker of nutritional status of either element.[2]
- Borderline low hemoglobin and hematocrit. This likely signals the early stages of megaloblastic anemia caused by B12 deficiency.

Based on these initial findings, I ordered additional blood tests, including a more complete thyroid panel with free T4, free T3, and thyroid antibodies (to determine if Chandra had Hashimoto's), post-meal blood sugar testing with a glucometer, and a comprehensive metabolic panel.

FIGURE 1: *Thyroid Function Markers and Thyroid Antibodies.*

Triiodothyronine,Free,Serum	**1.6**	**Low**	pg/mL	2.0 - 4.4	01
T4,Free(Direct)	0.94		ng/dL	0.82 - 1.77	01
Thyroid Antibodies					
Thyroid Peroxidase (TPO) Ab	<6		IU/mL	0 - 34	01
Thyroglobulin, Antibody	**1.1**	**High**	IU/mL	0.0 - 0.9	01
Please Note:					01
Low positive Thyroglobulin antibodies are seen in a portion of the asymptomatic populations.					
Antithyroglobulin antibodies measured by Beckman Coulter Methodology					

The thyroid panel revealed low levels of free T3, the most active form of thyroid hormone. They also found elevated thyroglobulin antibodies, which are indicative of Hashimoto's thyroiditis.

FIGURE 2A: *The MetSyn Profile from Genova Diagnostics measures glucose, HbA1c, lipids, inflammation, and metabolism.*

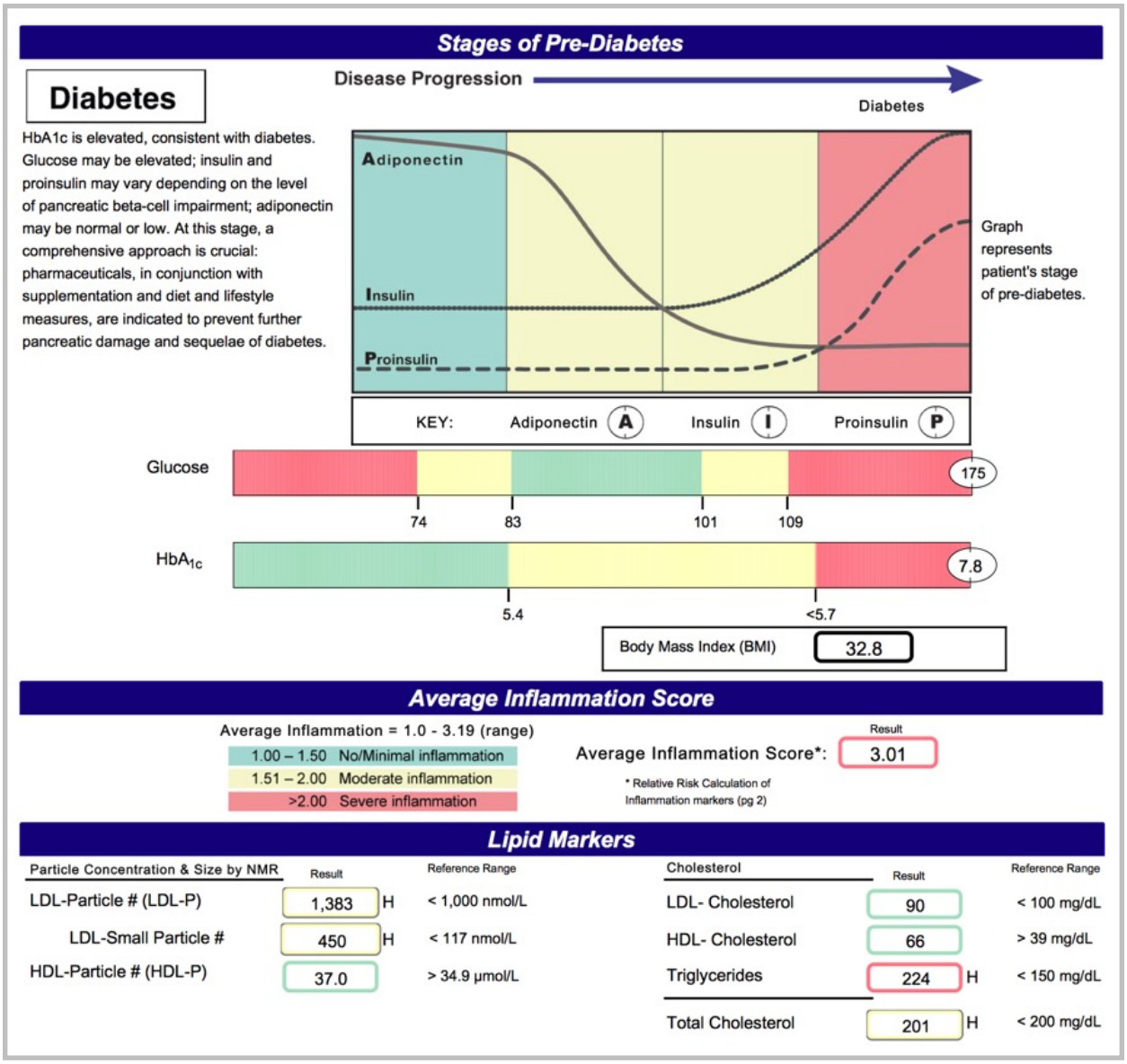
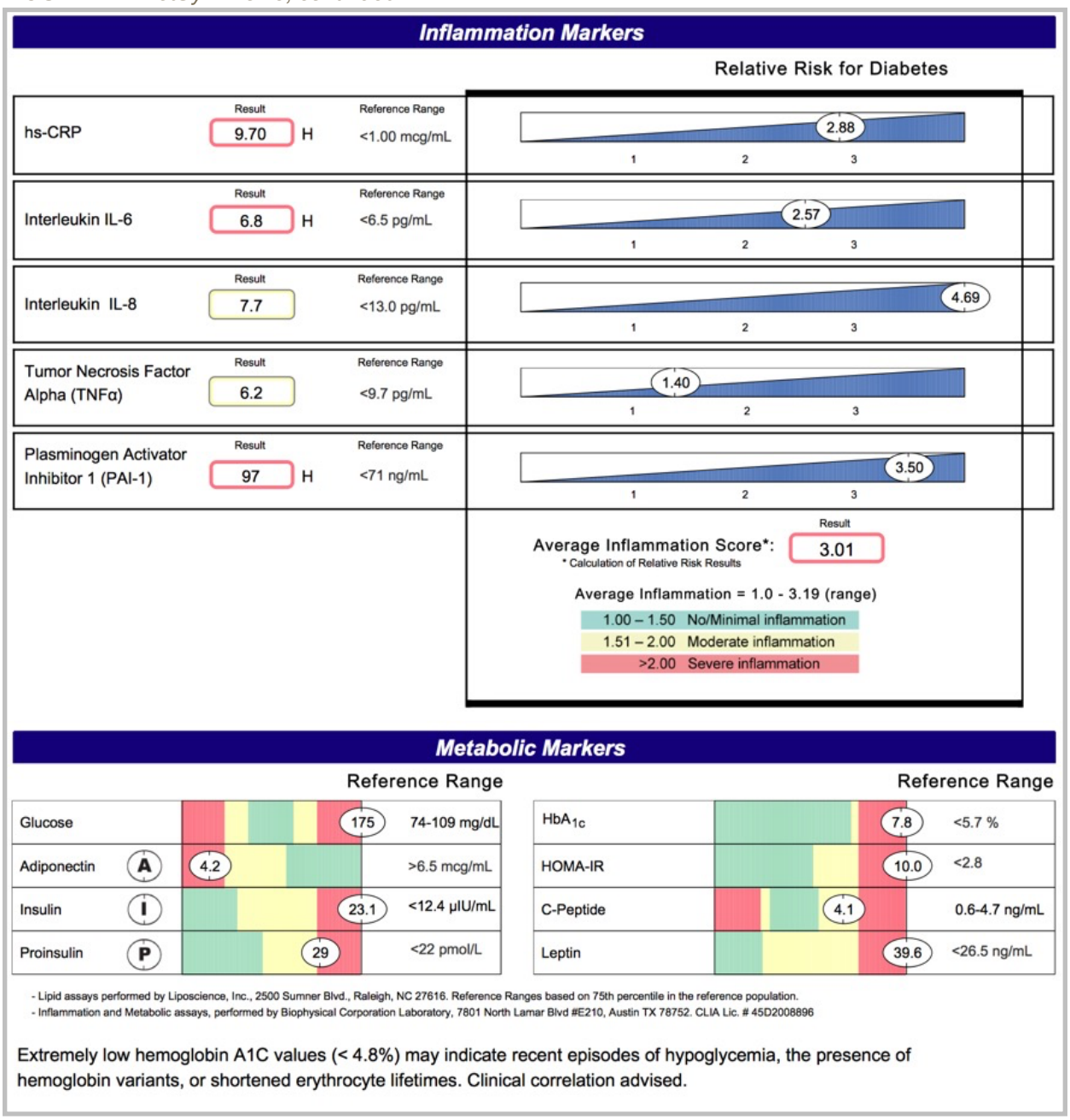


FIGURE 2B: *MetSyn Profile, continued.*



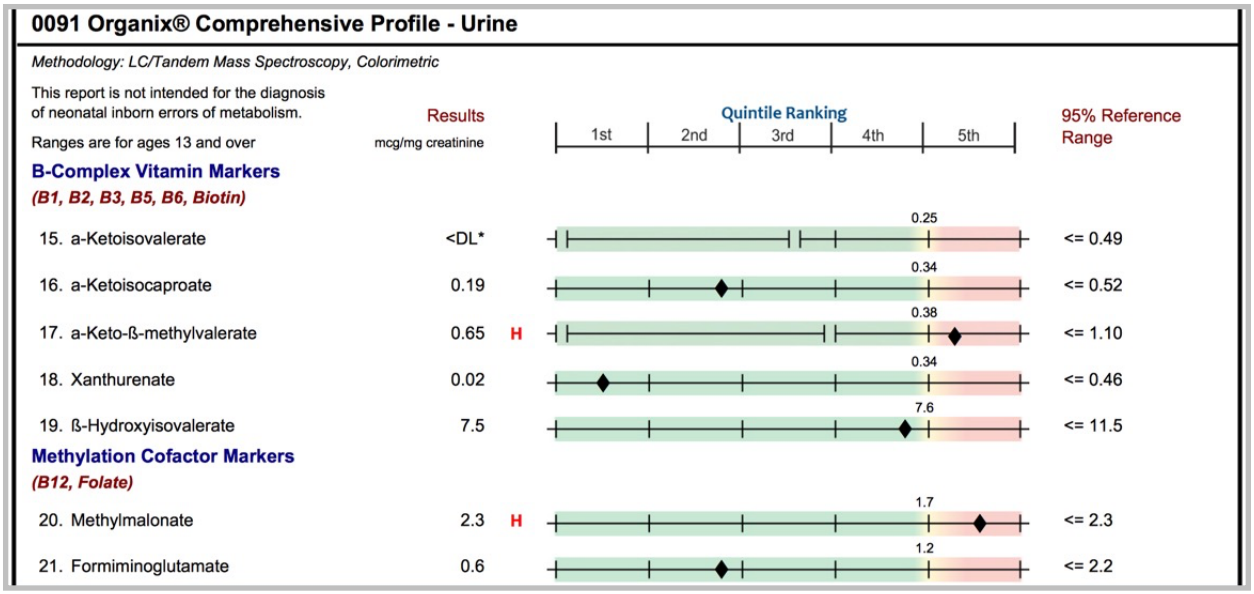
The MetSyn profile from Genova Diagnostics has a number of markers for diabetes and metabolic dysfunction. Chandra had elevated LDL particle number, small LDL particle number, insulin, pro-insulin, homeostasis model assessment-estimated insulin resistance (HOMA-IR), C-peptide, and leptin levels. She also had elevated inflammatory markers, such as hs-CRP, interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-a), and plasminogen activator inhibitor-1 (PAI-1).

TABLE 2: *Glucometer Readings Taken at Home. Blood sugar was measured under fasting conditions, one hour after eating, or two hours after eating. The suggested ranges are <99 mg/dL fasting, <140 mg/dL one hour after a meal, and <120 mg/dL two hours after a meal. Colors separate days with multiple readings.*

Date	Time	Type	BG reading	
5/4/2015	7:49	Fasting	163	Colors separate days with multiple readings
5/19/2015	6:47	Fasting	152	HIGH
5/23/2015	7:24	Fasting	143	HIGH
5/24/2015	7:51	Fasting	150	HIGH
5/25/2015	7:26	Fasting	152	HIGH
5/25/2015	12:40	Just before lunch	147	
5/25/2015	14:29	1.5 h after lunch	146	
5/25/2015	16:15	3.25 h after lunch	131	
5/26/2015	5:57	Fasting	157	
5/27/2015	6:36	Fasting	161	
5/27/2015	14:20	Just before lunch	106	NORMAL/BORDERLINE HIGH
5/28/2015	5:30	Fasting	160	
5/29/2015	8:04	Fasting	145	
5/30/2015	6:27	Fasting	152	
5/30/2015	11:24	Just before lunch	115	NORMAL/BORDERLINE HIGH
5/31/2015	7:20	Fasting	142	
5/31/2015	12:02	Just before lunch	147	
5/31/2015	15:39	2.25 h after lunch	114	
6/1/2015	6:23	Fasting	152	
6/1/2015	15:01	2 h after lunch	143	
6/2/2015	5:32	Fasting	164	
6/2/2015	11:57	Just before lunch	114	NORMAL/BORDERLINE HIGH
6/2/2015	16:21	4 h after lunch	102	NORMAL
6/3/2015	7:14	Fasting	152	
6/4/2015	6:17	Fasting	171	
6/5/2015	6:32	Fasting	154	
6/6/2015	6:37	Fasting	151	
6/6/2015	14:49		179	
6/7/2015	6:18	Fasting	151	
6/15/2015	6:47	Fasting	153	
6/15/2015	11:28	Just before lunch	108	NORMAL/BORDERLINE HIGH
6/15/2015	14:07	2 h after lunch	110	NORMAL
6/16/2015	6:08	Fasting	145	
6/18/2015	7:16	Fasting	152	
6/19/2015	7:45	Fasting	150	

I asked Chandra to use a glucometer to test her blood sugar over several weeks, both before and after meals. Post-meal blood sugar is considered to be a more sensitive predictor of type 2 diabetes progression. The suggested cutoffs are <99 mg/dL fasting, <140 mg/dL one hour after a meal, and <120 mg/dL two hours after a meal. As you can see, both her fasting and post-meal glucose readings were consistently elevated, though on a relative basis, her fasting glucose is higher than her post-meal glucose.

FIGURE 3: *Organix Comprehensive Profile from Genova Diagnostics measures urinary markers of B vitamins.*



0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

This report is not intended for the diagnosis of neonatal inborn errors of metabolism.

Ranges are for ages 13 and over

	Results (mcg/mg creatinine)		Quintile Ranking (1st–5th)	95% Reference Range
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*				
15. a-Ketoisovalerate	<DL*		0.25	<= 0.49
16. a-Ketoisocaproate	0.19		0.34	<= 0.52
17. a-Keto-ß-methylvalerate	0.65	H	0.38	<= 1.10
18. Xanthurenate	0.02		0.34	<= 0.46
19. ß-Hydroxyisovalerate	7.5		7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*				
20. Methylmalonate	2.3	H	1.7	<= 2.3
21. Formiminoglutamate	0.6		1.2	<= 2.2

Chandra's urine organic acids test revealed elevated levels of methylmalonic acid (MMA). The conversion of succinic acid to methylmalonic acid requires methylcobalamin, an active form of B12. High levels of MMA suggest active B12 deficiency, which supports the finding of low B12 in Chandra's blood work.

FIGURE 4: *Intrinsic Factor Antibody Test.*

	RESULT		REFERENCE RANGE	
Intrinsic Factor Abs, Serum	**Positive**	**Abnormal**	Negative	02

Given that Chandra ate meat regularly but still had low B12 levels, I decided to screen her for pernicious anemia. Pernicious anemia is an autoimmune condition in which the body attacks either the parietal cells, which produce intrinsic factor; intrinsic factor itself; or both. Intrinsic factor is required to absorb B12 from diet or oral supplements, so patients with pernicious anemia will

become B12 deficient even if they are eating sufficient amounts of B12 or taking typical oral forms of B12. Chandra was positive for antibodies to intrinsic factor.

FIGURE 5A: *Comprehensive Stool Analysis from Doctor's Data. Dysbiotic flora are highlighted in red. Commensal flora, which may be imbalanced, are highlighted in yellow.*

Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	4+ Alpha hemolytic strep	4+ Citrobacter freundii complex
3+ Bifidobacterium spp.	2+ Citrobacter freundii complex,isolate 2	
NG Escherichia coli	4+ Gamma hemolytic strep	
1+ Lactobacillus spp.		
NG Enterococcus spp.		
2+ 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:
Many	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 unvialble.

FIGURE 5B: *Comprehensive Stool Analysis with* Helicobacter pylori *stool antigen.*

Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *	PARASITOLOGY INFORMATION
Sample 1 None Ova or Parasites Rare RBC Many Yeast **Sample 2** None Ova or Parasites Rare RBC Mod Yeast **Sample 3** None Ova or Parasites Many Yeast ***A trichrome stain and concentrated iodine wet mount slide is read for each sample submitted.**	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.

Helicobacter Pylori Stool Antigen

	Normal	Abnormal	Reference
H. pylori		Pos	Neg

The HpSA enzyme immunoassay (EIA) is an in vitro qualitative procedure for the detection of H. Pylori antigens in the stool. Test results are intended to aid the diagnosis of H. Pylori infection, and to monitor response during and post therapy.

FIGURE 5C: *Comprehensive Stool Analysis, continued.*

Comprehensive Stool Analysis / Parasitology x3

DIGESTION /ABSORPTION

	Within	Outside	Reference Range
Elastase		197	> 200 µg/mL
Fat Stain	Few		None - Mod
Muscle fibers	None		None - Rare
Vegetable fibers	Rare		None - Few
Carbohydrates		Int	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
Lysozyme*		3800	<= 600 ng/mL
Lactoferrin	1.3		< 7.3 µg/mL
White Blood Cells	None		None - Rare
Mucus	Neg		Neg

Lysozyme* is an enzyme secreted at the site of inflammation in the GI tract and elevated levels have been identified in IBD patients. **Lactoferrin** is a quantitative GI specific marker of inflammation used to diagnose and differentiate IBD from IBS and to monitor patient inflammation levels during active and remission phases of IBD. **White Blood Cells** (WBC): in the stool are an indication of an inflammatory process resulting in the infiltration of leukocytes within the intestinal lumen. WBCs are often accompanied by mucus and blood in the stool. **Mucus** in the stool may result from prolonged mucosal irritation or in a response to parasympathetic excitability such as spastic constipation or mucous colitis.

IMMUNOLOGY

	Within	Outside	Reference Range
Secretory IgA*		436	51 - 204mg/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.

Chandra's stool test revealed low levels of beneficial *E. coli*, *Enterococcus*, and *Lactobacillus*, high levels of imbalanced flora such as alpha- and gamma-hemolytic streptococcus. Chandra had dysbiosis. She showed high levels of the pathogenic bacterium *Citrobacter freundii* (Figure 5a). She also had significant fungal overgrowth (as seen under the microscope) in all three stool samples and tested positive for *H. pylori* (Figure 5b).

Chandra wasn't digesting or absorbing her food properly. Chandra's fecal elastase level was low, and she tested positive for carbohydrate malabsorption (Figure 5c).

Finally, Chandra's lysozyme and secretory IgA levels were elevated, indicating inflammation and immune activation in the gut. This was most likely due to her significant dysbiosis and fungal overgrowth.

FIGURE 6: *Small Intestinal Bacterial Overgrowth Breath Test Results.*

SIBO CENTER FOR DIGESTIVE HEALTH NCNM CLINIC

Test Results

NCNM Clinic Lab
3025 SW Corbett Ave.
Portland, OR 97201
Phone (503) 552-1931
Fax (503) 444-6709

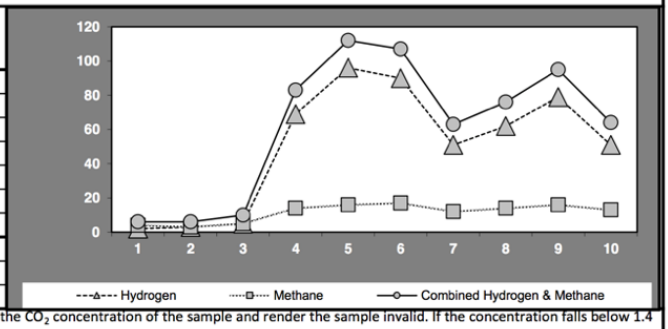
CLIA CERTIFICATION: 38D0624258

[redacted]

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

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



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

Analysis

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

Interpretation

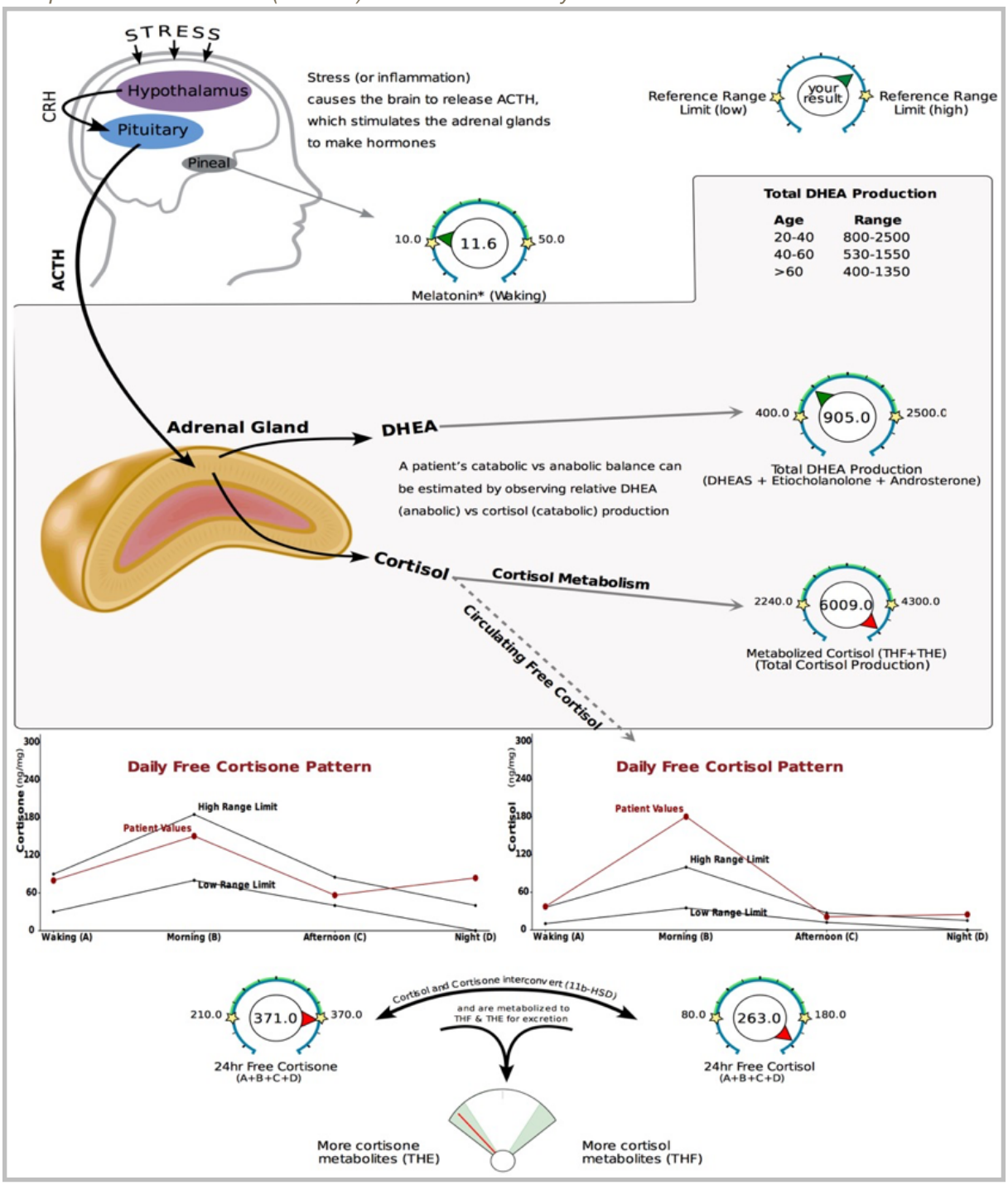
SIBO Suspected - Elevated Hydrogen	Increases of hydrogen greater than 20ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**POSITIVE**
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest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

Notes

The following symptoms were reported during collection:
at 60 min: mild belching
at 120 min: headache

Chandra's breath test results showed a classic "double peak" of both hydrogen and methane, which strongly suggested small intestine bacterial overgrowth (SIBO).

FIGURE 6: *Analysis of Hypothalamic–Pituitary–Adrenal Axis Function Using the Dried Urine Test Comprehensive Hormones (DUTCH) from Precision Analytical*



Chandra's DUTCH hormone profile revealed high levels of metabolized cortisol, free cortisone, and free cortisol. Her daily free cortisol and cortisone patterns were abnormal, suggesting a disrupted diurnal cortisol rhythm. She had an elevated cortisone-to-cortisol ratio. All of these findings are consistent with type 2 diabetes and metabolic dysfunction (see Discussion).

Initial Treatment Plan

Given all of these findings, we had a lot of work to do after the initial appointment! In a situation like this, starting with diet and lifestyle change is the most important intervention you can do, since it is likely the root cause of many if not most of the patient's pathologies.

I suggested that Chandra follow a Paleo Reset Diet for 60 days, without lowering her carbohydrate intake (see Discussion). I also suggested that Chandra increase her physical activity. Since she was almost completely sedentary, I recommended a gentle ramp-up including walking 5,000 steps a day (which she used a FitBit to track) and two to three days of strength training at the gym to increase her muscle mass and fat-burning capacity. Later, as her exercise tolerance improved, I would suggest adding some high-intensity interval training to further increase her fat-burning capacity.

In addition to the diet and lifestyle changes, we needed to address Chandra's pernicious anemia, Hashimoto's hypothyroidism, dysbiosis and fungal overgrowth, *H. pylori*, gut inflammation, SIBO, and disrupted HPA axis. If we tried to do this all at once, Chandra would have been taking 20-plus supplements and almost certainly would have been overwhelmed. Part of the "art" of functional medicine is figuring out how to layer and structure a treatment with complex, multifactorial presentations like this.

We began by addressing her gut, B12 and vitamin D deficiency, and HPA axis. Digestive symptoms were her primary reason for coming to see me, and it's important to address the patient's chief complaint or they will not stick around for long! Moreover, a large body of evidence suggests a strong association between a disrupted gut microbiome and both metabolic and thyroid dysfunction. B12 deficiency can have potentially irreversible neurological consequences if not addressed, and given that Chandra was already 66 years old, I wanted to restore normal B12 levels as soon as possible. I also knew that B12 deficiency causes fatigue, so she'd be more likely to follow through on her physical activity prescription once I corrected her B12 deficiency. Finally, high cortisol can contribute to hyperglycemia, poor thyroid function, and gut imbalances, so I felt it was important to address this in the initial phase of the treatment plan.

For her gut, I used a botanical antimicrobial protocol that included GI Synergy, Lauricidin, InterFase Plus, Prescript-Assist, *Saccharomyces boulardii*, and A-FNG to treat the SIBO, dysbiosis, and fungal overgrowth. For the *H. pylori*, I added Jarrow BroccoMax (one capsule three times a day with meals) and 500 mL per day of 100% cranberry juice, unsweetened.[3,4]

TABLE 3: *Chandra's Treatment Protocol with Dosages.*

TREATMENT	NUTRACEUTICAL	BRAND	DOSAGE
Probiotic	Prescript-Assist	Prescript-Assist	One BID upon rising and before bed
Probiotic	Saccharomycin DF	Xymogen	3 billion CFU twice daily at lunch and before bed
Antimicrobial	GI Synergy	Apex Energetics	1 packet BID (with breakfast and dinner)
Antimicrobial	Lauricidin	Med-Chem Laboratories	1 scoop three times daily with meals
Antimicrobial	A-FNG	Byron White Formulas	Slowly build to 20-30 drops BID with meals
Antimicrobial	InterFase Plus	Klaire Labs	3-4 capsules BID on an empty stomach
Microbial balance	BroccoMax	Jarrow Formulas	1 capsule TID with meals
Microbial balance	Cranberry juice, unsweetened		500 mL/day
Nutrition	Extra Virgin Cod Liver Oil	Rosita Real Foods	1 tsp/day
Nutrition	Trifolamin	Designs for Health	1 lozenge (5 mg)/day
Nutrition	Micellized Vitamin D3	Klaire Labs	10,000 IU/day
HPA-axis support	HPA Balance	Vital Plan	2 caps twice daily with food
HPA-axis support	Acetyl-CH	Apex Energetics	1 cap three times daily with food

For B12 deficiency, I used Trifolamin from Designs for Health. Trifolamin provides a synergistic combination of the three bioavailable forms of B12: methylcobalamin, adenosylcobalamin, and hydroxycobalamin, in a five mg sublingual lozenge. Sublingual delivery is crucial for patients with pernicious anemia because their intestinal absorption of B12 from diet or oral supplements is limited. I had Chandra take one lozenge per day and instructed her to continue this indefinitely.

For vitamin D, I prescribed one tsp/d of Extra Virgin Cod Liver Oil (to provide whole-food forms of both vitamin D and vitamin A, which work synergistically together), along with 10,000 IU of Micellized Vitamin D3 from Klaire Labs. I did not think that cod liver oil alone would be sufficient to raise her vitamin D quickly, and I prescribed a micellized form of D3 because Chandra had several gut conditions that could lead to malabsorption.

For her HPA axis, I prescribed a number of behavioral and lifestyle modifications, including restricting exposure to artificial light at night and ensuring at least 20 to 30 minutes of bright light exposure during the day (which she accomplished by taking a walk for half of her lunch hour), getting at least eight hours of sleep a night, and practicing mindfulness-based stress reduction at least three times a week. I also prescribed supplements to regulate her diurnal cortisol rhythm and reduce her cortisol, including HPA Balance from Vital Plan (two capsules twice a day, with breakfast and dinner) and Acetyl-CH Active from Apex Energetics (one capsule three times a day, with meals).

Sixty-Day Follow-up: Clinical Outcome and Additional Testing

After 60 days of this protocol, Chandra's digestive symptoms were 80 percent resolved, her energy levels improved significantly, she lost 19 pounds, and her blood sugar had dropped from the diabetic range to the pre-diabetic range. Her follow-up tests results also showed significant improvements across the board.

FIGURE 8: *Follow-up Thyroid Function Markers, Iron, and Vitamins D and B12.*

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
TSH+T4F+T3Free					
TSH	**4.540**	**High**	uIU/mL	0.450 - 4.500	01
Triiodothyronine,Free,Serum	3.0		pg/mL	2.0 - 4.4	01
T4,Free(Direct)	1.20		ng/dL	0.82 - 1.77	01

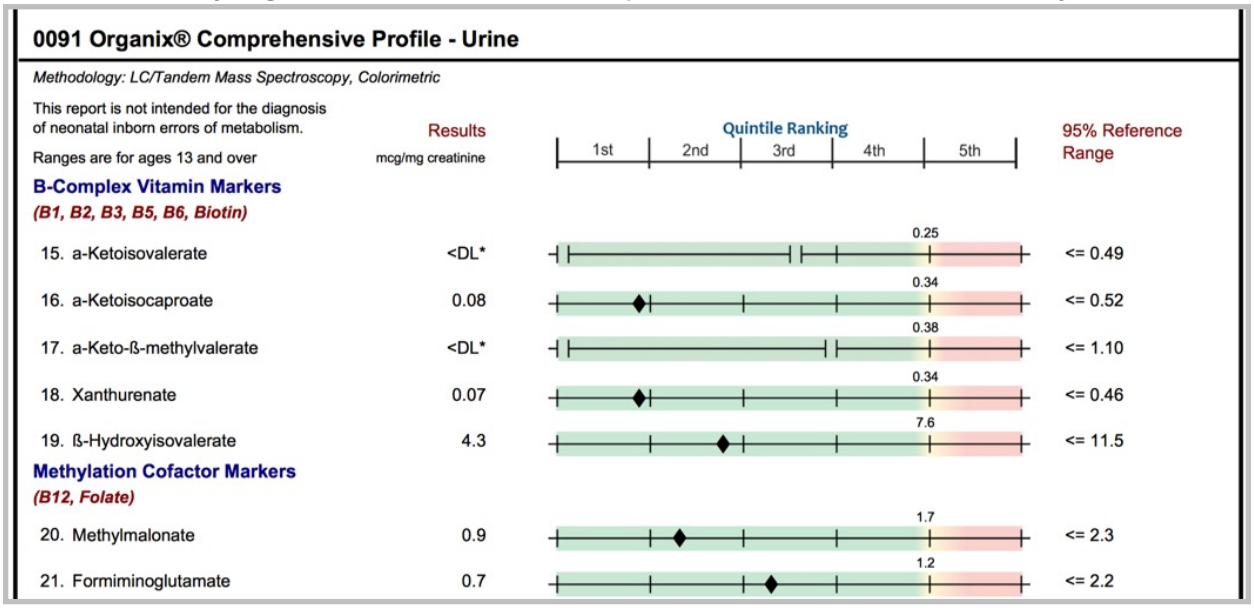
TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Iron Saturation	32		%	15 - 55	
Ferritin, Serum	131		ng/mL	30 - 400	01
Vitamin B12	744		pg/mL	211 - 946	01
Vitamin D, 25-Hydroxy	44.5		ng/mL	30.0 - 100.0	01

Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/mL (2).

1. IOM (Institute of Medicine). 2010. Dietary reference intakes for calcium and D. Washington DC: The National Academies Press.
2. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. JCEM. 2011 Jul; 96(7):1911-30.

Her free T3 levels were now well within the normal range. Inflammation and poor gut health reduce the conversion of T4 to T3, so it is likely that the dietary and lifestyle changes Chandra made improved her thyroid function. This is why I often do not address thyroid directly in the first step of the treatment in situations like this. Her vitamin D upon follow-up was firmly within the normal range, as was her serum vitamin B12.

FIGURE 9: *Urinary Organic Acid Markers Show Adequate Vitamin B12 Levels after 60 Days of Treatment.*



0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

This report is not intended for the diagnosis of neonatal inborn errors of metabolism.

Ranges are for ages 13 and over

	Results (mcg/mg creatinine)	Quintile Ranking (1st / 2nd / 3rd / 4th / 5th)	95% Reference Range
B-Complex Vitamin Markers *(B1, B2, B3, B5, B6, Biotin)*			
15. a-Ketoisovalerate	<DL*	0.25	<= 0.49
16. a-Ketoisocaproate	0.08	0.34	<= 0.52
17. a-Keto-ß-methylvalerate	<DL*	0.38	<= 1.10
18. Xanthurenate	0.07	0.34	<= 0.46
19. ß-Hydroxyisovalerate	4.3	7.6	<= 11.5
Methylation Cofactor Markers *(B12, Folate)*			
20. Methylmalonate	0.9	1.7	<= 2.3
21. Formiminoglutamate	0.7	1.2	<= 2.2

Her urine methylmalonate normalized, indicating that she had sufficient levels of active vitamin B12.

FIGURE 10A: *Comprehensive Stool Analysis Results after 60 Days of Treatment.*

Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	3+ Alpha hemolytic strep	
4+ Bifidobacterium spp.	3+ Gamma hemolytic strep	
4+ Escherichia coli		
4+ Lactobacillus spp.		
NG 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
1+ Candida parapsilosis	

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 unvialble.

FIGURE 10B: *Comprehensive Stool Analysis Results after 60 Days of Treatment, continued.*

Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *	PARASITOLOGY INFORMATION
Sample 1 None Ova or Parasites **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.**	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.

*****Helicobacter Pylori Stool Antigen*****

H. pylori Antigen	Not detected

FIGURE 10C: *Comprehensive Stool Analysis Results after 60 Days of Treatment, continued.*

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	3.9		< 7.3 µg/mL
Calprotectin*	39		<= 50 µg/g
Lysozyme*	82		<= 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*		33.0	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.

Chandra's follow-up stool test showed much-improved levels of beneficial bacteria and eradication of *Citrobacter freundii* and fungal overgrowth. Previously, her stool test showed many fungal cells under the microscope for all three stool samples. In this test, no fungal cells were seen for any of the samples. The *Candida parapsilosis* at 1+ growth did not strike me as a clinically relevant issue for her. Her follow-up stool antigen test for *H. pylori* was negative, indicating that the infection had been cleared.

Chandra's digestion improved. Her elastase and carbohydrate absorption markers normalized. Her gut inflammation decreased: Both lysozyme and sIgA decreased significantly. This suggests that her immune reactivity normalized, most likely because *Citrobacter*, fungus, and *H. pylori* had been removed. At the time of this writing, there were no follow-up results on Chandra's systemic inflammatory markers. But considering that dysbiosis and inflammation decreased in the gut, systemic markers of inflammation could have easily improved. Her sIgA was low on this test, whereas it was high on the initial test. This is not uncommon, in my experience, and sIgA is often one of the last markers to improve when addressing gut health.

FIGURE 11: *Follow-up SIBO Test Results*

SIBO CENTER FOR DIGESTIVE HEALTH NCNM CLINIC

Test Results

NCNM Clinic Lab
3025 SW Corbett Ave.
Portland, OR 97201
Phone (503) 552-1931
Fax (503) 444-6709

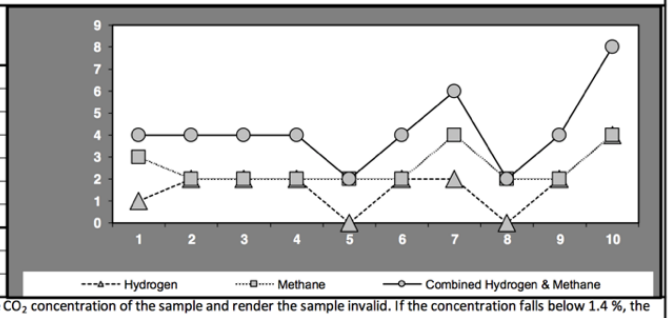
CLIA CERTIFICATION: 38D0624258

[redacted]

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	1	3	4	OK
2	20 min	2	2	4	OK
3	40 min	2	2	4	OK
4	60 min	2	2	4	OK
5	80 min	0	2	2	OK
6	100 min	2	2	4	OK
7	120 min	2	4	6	OK
8	140 min	0	2	2	OK
9	160 min	2	2	4	OK
10	180 min	4	4	8	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 =	4	-	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	2	-	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	2	-	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	4	-	≤15ppm

Interpretation

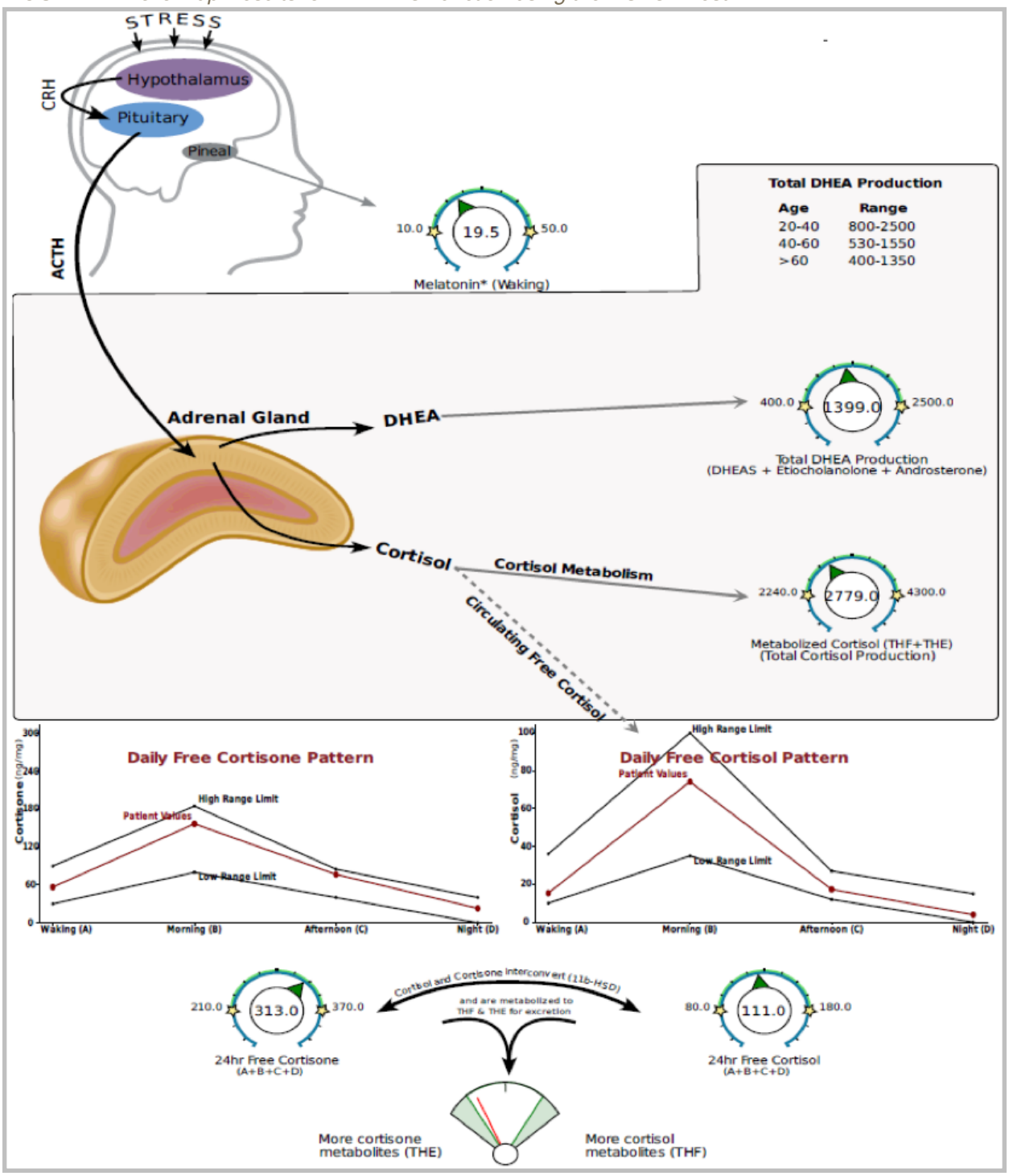
SIBO Suspected - Elevated Hydrogen	Increases of hydrogen greater than 20ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**NEGATIVE**
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest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

Notes

The following symptoms were reported during collection:
at 0 minutes - "slight sugar rush immediately after [sic] lactrose"
at 25 minutes - "feel fine"

Her SIBO breath test results were normal after 60 days of treatment. Her hydrogen and methane breath gases normalized, suggesting that bacterial overgrowth in the small intestine was no longer an issue for Chandra.

FIGURE 12: *Follow-up Results for HPA Axis Function using the DUTCH Test.*



Her DUTCH hormone profile revealed completely normal cortisol production. Frankly, I was quite surprised by this, as it often takes much longer to address HPA axis dysfunction, especially if it is a primary cause of symptoms. It is possible that Chandra's mother's death caused an unusual spike in her cortisol levels on her initial DUTCH test (Figure 7) that naturally normalized as time passed. It is also possible that interventions to normalize sleep patterns, remove gut infections, reduce body weight, and increase physical activity had a significant impact on Chandra's HPA axis function.

Treatment Plan Modifications Made after 60 Days

Even after 60 days of treatment, Chandra's TSH was still elevated. I felt that her thyroid needed additional support at that point. I prescribed a desiccated thyroid glandular supplement (from Nutri-Meds) because Chandra preferred not to take pharmaceuticals. Antimicrobials were discontinued at this time but other interventions continued, including HPA axis support and dietary changes.

120-Day Follow-up: Clinical Outcome and Additional Testing

After 60 days on the desiccated thyroid, we re-tested Chandra's thyroid numbers again, and they were normal. I also re-tested her blood sugar. After 120 days of overall treatment, Chandra's fasting glucose and HbA1c were still elevated, but they were significantly improved. Her results were toward the bottom of the pre-diabetic range, rather than well within the diabetic range.

FIGURE 13: *Follow-up Results for Thyroid Markers after 120 Days of Treatment.*

Tests Ordered

TSH+T4F+T3Free

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
TSH+T4F+T3Free					
TSH	2.290		uIU/mL	0.450 - 4.500	01
Triiodothyronine,Free,Serum	2.6		pg/mL	2.0 - 4.4	01
T4,Free(Direct)	1.24		ng/dL	0.82 - 1.77	01

FIGURE 14: *Chandra's Glucose and HbA1c after 120 Days of Treatment.*

Marker	Value	Functional Range	Lab Range
Glucose	108	75 - 90	65 - 99
Hemoglobin A1c	5.9	4.4 – 5.4	4.8 - 5.6
Uric Acid	4.1	3.2 - 5.5	2.5 - 7.1
BUN	21	13 – 18	6 - 24
Creatinine	0.78	0.85 – 1.1	0.57 - 1
Sodium	137	135 – 140	134 - 144
Potassium	4.7	4.0 – 4.5	3.5 - 5.2

Ideally, I'd like to get Chandra's blood sugar levels into the normal ranges. However, not all cases of diabetes can be reversed with natural interventions. In cases where type 2 diabetes has been present for many years and beta cell destruction may have occurred, it may not be completely reversible with diet and lifestyle changes and supplementation alone. This is particularly true if leptin and insulin are as elevated as they were for Chandra on her initial test (Figure 2b). The drug metformin may be a good option to further improve glucose control in cases like Chandra's, though the potential benefits of the small reduction in fasting glucose and A1c that we'd be likely to observe would have to be weighed against the side effects and risks of the medication.

Treatment Plan Modifications after 120 Days

Nutraceuticals are another option for further reduction of blood sugar in cases like this. I prescribed two supplements: Metabolic Synergy (two capsules three times a day with meals) and GlucoSupreme (two capsules twice a day with meals) from Designs for Health. These products contain a number of nutrients and botanicals that support blood sugar regulation. No other changes were made to the treatment protocol at this time.

FIGURE 15: *One Hundred Eighty-Day Follow-up Testing: Blood Glucose Regulation.*

Marker	Value	Functional Range	Lab Range
Glucose	90	75 - 90	65 - 99
Hemoglobin A1c	5.8	4.4 – 5.4	4.8 - 5.6
Uric Acid	6.1	3.2 - 5.5	2.5 - 7.1
BUN	9	13 – 18	6 - 20
Creatinine	0.71	0.85 – 1.1	0.57 - 1
BUN/Creatinine Ratio	13	9 – 23	9 - 23
Sodium	138	135 – 140	134 - 144
Potassium	4.2	4.0 – 4.5	3.5 - 5.2
Chloride	101	100 – 106	97 - 108

After an additional 60 days on these supplements (amounting to 180 days total of treatment), Chandra had a fasting glucose <100 mg/dL for the first time in 10 years. Her HbA1c was still elevated, as were some of her post-meal glucose levels. However, this is a remarkable improvement using only diet and lifestyle changes and supplements.

Discussion

Chandra was a 66-year-old untreated diabetic woman with significant gastrointestinal symptoms and poor dietary and lifestyle habits. Chandra had marked improvement of GI symptoms, energy, and blood sugar after six months of a Paleo diet, normalization of HPA axis function, nutritional supplementation for pernicious anemia and vitamin D, treatment for GI dysbiosis and inflammation, and supplements to support thyroid function and blood sugar regulation.

Dietary Recommendations

I suggested that Chandra follow a Paleo Reset Diet for 60 days. Numerous studies have shown that Paleo is effective for reducing blood sugar and improving inflammatory markers and that it is more satiating per calorie than Mediterranean or low-fat diets, which makes it easier for patients to follow.[5,6]

I did not specifically instruct Chandra to lower her carbohydrate intake for two reasons. First, the Paleo diet studies that showed significant improvement in metabolic function were not very-low-carb diets; they typically ranged between 20 and 30 percent of calories from carbohydrate. I believe that carbohydrate quality (e.g., eating whole-food, unrefined carbohydrates rather than highly refined carbohydrates) is more important than carbohydrate quantity in most cases, and if significant weight loss and metabolic improvement is possible without severely restricting an entire macronutrient category, that is preferable from a general health and compliance perspective. Second, most patients that follow a Paleo diet naturally eat fewer carbohydrates, since their choices of carbohydrate are limited to starchy plants like sweet potatoes and fruits.

Nutrition

VITAMIN D

Chandra had one of the lowest vitamin D levels I have ever observed—8.3 ng/mL (Table 1a). I recommend vitamin D serum levels of 25–50 ng/mL. Chandra spent very little time outdoors and did not take a vitamin D supplement. She was of East Indian descent and had relatively dark skin, which means she produced less 25(OH)D in response to sun exposure than people with lighter skin. Low levels of vitamin D are associated with metabolic dysfunction in numerous studies.[7]

VITAMIN B12 AND PERNICIOUS ANEMIA

Chandra had very low levels of vitamin B12, high urinary methylmalonate (Figure 3), very high homocysteine, low hemoglobin, and low hematocrit. Homocysteine is a sticky, inflammatory protein associated with metabolic and cardiovascular disease (Table 1a). Vitamin B12 and folate are required to convert homocysteine back into methionine in the methylation cycle; thus, Chandra's B12 deficiency was the likely cause of her high homocysteine level.

Given that Chandra ate meat regularly but still had low B12 levels, I decided to screen her for pernicious anemia. Pernicious anemia is an autoimmune condition in which the body attacks either the parietal cells, which produce intrinsic factor; intrinsic factor itself; or both. Intrinsic factor is required to absorb B12 from diet or oral supplements, so patients with pernicious anemia will become B12 deficient even if they are eating sufficient amounts of B12 or taking typical oral forms of B12. Chandra was positive for antibodies to intrinsic factor (Figure 4). This test approaches 100 percent specificity, which means that if it is positive, it is almost certain that the patient has pernicious anemia. (Note that although intrinsic factor antibodies are highly specific, they are only 50 to 70 percent sensitive. This means that 30 to 50 percent of patients with pernicious anemia will not have antibodies to intrinsic factor.)[8]

Borderline low hemoglobin and hematocrit (Table 1b) likely pointed to the early stages of pernicious anemia caused by B12 deficiency. B12 deficiency progresses in four stages, and it is only in the final stage that the patient becomes anemic. This is one of many reasons that it is important to test B12 levels on a routine blood panel. Unfortunately, this is rarely done in conventional medicine. Chandra had no idea that she was B12 deficient and had pernicious anemia prior to her appointment with me, and she was 66 years old![9]

HPA DYSFUNCTION AND DIABETES

Chandra had high levels of metabolized cortisol, free cortisone, and free cortisol. Her daily free cortisol and cortisone patterns were abnormal, suggesting a disrupted diurnal cortisol rhythm. She had an elevated cortisone-to-cortisol ratio. This was consistent with research showing an association between metabolic dysfunction, high cortisol levels, and excess weight and type 2 diabetes.[10,11]

Fat tissue can contribute to HPA axis dysfunction. Fat tissue itself releases cortisol.[12,13] The relationship between HPA axis function and obesity is bi-directional and most studies have not been able to show a causal relationship between high free cortisol (HPA axis dysfunction) and obesity. However, studies do show increased clearance of cortisol (and thus higher cortisol metabolites) with increasing weight.[14] There is a stepwise relationship between urinary cortisol metabolites and body BMI, even at levels that aren't obese.[15] In addition, the conversion of cortisone to cortisol is impaired in obesity, which leads to a high ratio of cortisone to cortisol in these patients.[16]

THYROID FUNCTION

Chandra had high TSH, low-normal T4 and T3 (Table 1b), and low levels of free T3, the most active form of thyroid hormone (Figure 1). She had elevated thyroglobulin antibodies, which are indicative of Hashimoto's thyroiditis. This suggested that Chandra's thyroid dysfunction was caused by autoimmunity. Some studies suggest that thyroid autoimmunity may contribute to endothelial dysfunction and other metabolic and cardiovascular abnormalities.[17]

GASTROINTESTINAL HEALTH AND DIABETES

Chandra had very low fecal pancreatic elastase, suggesting difficulty with digestion (Figure 5c). Studies have found a strong correlation between low fecal elastase and type 2 diabetes.[18] She also had SIBO (Figure 6). One study found an association between delayed orocecal transit time/SIBO and patients with type 2 diabetes, but it was unclear whether SIBO contributed to type 2 diabetes, or the other way around.[19] Nevertheless, I frequently see these conditions appear together in clinical practice, and the relationship is likely bi-directional.

Conclusions

Chandra had a strong family predisposition to diabetes that was compounded by a sedentary lifestyle and a poor diet. She was diabetic and headed down a path of diabetes-related complications and an increased risk of death. Chandra had significant gastrointestinal symptoms including abdominal pain with nausea and vomiting, bloating, decreased appetite, and heartburn.

Lab testing showed elevated blood glucose and HbA1c, extremely low vitamin D, inflammation, pernicious anemia, Hashimoto's thyroiditis and associated thyroid dysfunction. She had gut dysbiosis including bacterial and fungal overgrowth and colonization with *H. pylori*. She wasn't digesting or absorbing her food and showed signs of inflammation and immune upregulation in the GI tract. Finally, her cortisol diurnal rhythm and cortisol metabolism were disturbed.

Treatment primarily focused on diet and physical activity, gut dysbiosis, vitamins B12 and D, HPA axis function, and thyroid support. After 60 days, Chandra had an 80 percent reduction in her GI symptoms and had lost 19 pounds. She reported significant energy improvements. After 180 days of treatment, thyroid function markers had normalized, and her fasting glucose was < 100 mg/dL for the first time in 10 years. Laboratory markers confirmed that blood glucose was better regulated, vitamin levels improved, gut dysbiosis resolved, and HPA and thyroid function normalized. This case demonstrates that the course of diabetes and pre-diabetes can be halted, and even reversed, with careful attention to diet, physical activity, hormonal balance, gut health, and customized nutrition.

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Thyroid Disorders Case Study

Hypothyroidism Resolved by Restoring Iodine Levels

CASE SUMMARY

A 26-year-old woman complained of classic hypothyroid symptoms, had been given a hypothyroid diagnosis, and wanted to investigate natural alternatives to treatment with levothyroxine. Thyroid function tests, iron, and vitamin D were abnormal. Testing of gastrointestinal health suggested dysbiosis, especially bacterial overgrowth, and inflammation. She had difficulty metabolizing cortisol, a feature of hypothyroidism. Her diet was extremely low in iodine and she was eating goitrogenic foods, which pointed to iodine deficiency. Treatment included kelp tablets, selenium-rich foods, cod liver oil, an antimicrobial protocol, probiotics, and lifestyle changes and supplements to support HPA axis function. After three months on this program, her hypothyroid symptoms improved dramatically and her TSH and other thyroid markers normalized—without any medication at

Janel, 26, came to see me after being diagnosed with hypothyroidism. She was overweight, her hands and feet “felt like icicles,” her hair was falling out, and she was constipated.

Her doctor prescribed levothyroxine, a synthetic thyroid hormone, but Janel wanted to know why her thyroid wasn’t working properly and whether there was something she could do to address her condition without resorting to medication.

I ran a thyroid panel (TSH, T3, T4, free T3, free T4), complete blood count (CBC), comprehensive metabolic panel, and some other blood tests available through standard laboratories such as iron and vitamin D. Because of her constipation and hypothyroid symptoms, I also ran tests on her gastrointestinal function using a small intestinal bacterial overgrowth (SIBO) breath test, a stool analysis, and urinary organic acids to look for dysbiosis. I ordered a panel to look at her hypothalamic-pituitary-adrenal (HPA) axis function and a urine iodine test.

My panel of initial tests returned the following notable results.

FIGURE 1: *Thyroid Function Tests and Complete Blood Count.*

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
TSH	**23.770**	**High**	uIU/mL	0.450 - 4.500	01
Thyroxine (T4)	8.9		ug/dL	4.5 - 12.0	01
T3 Uptake	30		%	24 - 39	01
Free Thyroxine Index	2.7			1.2 - 4.9	
Triiodothyronine (T3)	77		ng/dL	71 - 180	01
Copper, Serum	110		ug/dL	72 - 166	02
			Detection Limit = 5		
Zinc, Plasma or Serum	116		ug/dL	56 - 134	02
			Detection Limit = 5		
Methylmalonic Acid, Serum	167		nmol/L	0 - 378	02
.					01
CBC, Platelet Ct, and Diff					01
WBC	4.5		x10E3/uL	3.4 - 10.8	01
RBC	4.57		x10E6/uL	3.77 - 5.28	01
Hemoglobin	13.8		g/dL	11.1 - 15.9	01
Hematocrit	40.7		%	34.0 - 46.6	01
MCV	89		fL	79 - 97	01
MCH	30.2		pg	26.6 - 33.0	01
MCHC	33.9		g/dL	31.5 - 35.7	01
RDW	12.8		%	12.3 - 15.4	01
Platelets	203		x10E3/uL	150 - 379	01
Neutrophils	50		%		01
Lymphs	40		%		01
Monocytes	9		%		01
Eos	1		%		01
Basos	0		%		01
Neutrophils (Absolute)	2.2		x10E3/uL	1.4 - 7.0	01
Lymphs (Absolute)	1.8		x10E3/uL	0.7 - 3.1	01
Monocytes(Absolute)	0.4		x10E3/uL	0.1 - 0.9	01
Eos (Absolute)	0.0		x10E3/uL	0.0 - 0.4	01
Baso (Absolute)	0.0		x10E3/uL	0.0 - 0.2	01
Immature Granulocytes	0		%		01
Immature Grans (Abs)	0.0		x10E3/uL	0.0 - 0.1	01
T4F+T3F					
Triiodothyronine,Free,Serum	2.3		pg/mL	2.0 - 4.4	01
T4,Free(Direct)	1.28		ng/dL	0.82 - 1.77	01
Thyroid Stim Immunoglobulin	32		%	0 - 139	02
Cardiovascular Report					
Interpretation	Note				03
Supplement report is available.					
PDF Image	.				03

Janel's thyroid-stimulating hormone (TSH) was significantly elevated at 23.77. Her total and free T4 were well within the normal reference range, but both her total T3 and free T3 were low-normal. Total T3 was 77 ng/dL (range: 71–180) and free T3 was 2.3 pg/mL (range: 2–4.4). These levels are below what I consider to be optimal (i.e., outside of the functional range). Janel also had low levels of vitamin D and high levels of iron, both of which are associated with poor thyroid function.

FIGURE 2: *Preliminary Testing Including Serum Iron, Vitamin D, Lipids, C-Reactive Protein, and Homocysteine.*

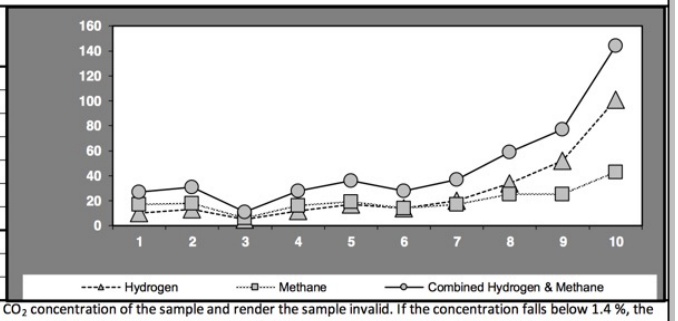
TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Iron, Serum	**173**	**High**	ug/dL	35 - 155	01
Iron Saturation	**58**	**High**	%	15 - 55	
Ferritin, Serum	33		ng/mL	15 - 150	01
Vitamin B12	688		pg/mL	211 - 946	01
Vitamin D, 25-Hydroxy	**28.6**	**Low**	ng/mL	30.0 - 100.0	01
Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/mL (2). 1. IOM (Institute of Medicine). 2010. Dietary reference intakes for calcium and D. Washington DC: The National Academies Press. 2. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. JCEM. 2011 Jul; 96(7):1911-30.					
Cholesterol, Total	160		mg/dL	100 - 199	01
Triglycerides	67		mg/dL	0 - 149	01
HDL Cholesterol	68		mg/dL	>39	01
Comment					01
According to ATP-III Guidelines, HDL-C >59 mg/dL is considered a negative risk factor for CHD.					
VLDL Cholesterol Cal	13		mg/dL	5 - 40	
LDL Cholesterol Calc	79		mg/dL	0 - 99	
T. Chol/HDL Ratio	2.4		ratio units	0.0 - 4.4	
Please Note:					01
T. Chol/HDL Ratio					
				Men / Women	
			1/2 Avg.Risk	3.4 / 3.3	
			Avg.Risk	5.0 / 4.4	
			2X Avg.Risk	9.6 / 7.1	
			3X Avg.Risk	23.4 / 11.0	
LDL/HDL Ratio	1.2		ratio units	0.0 - 3.2	
Please Note:					01
LDL/HDL Ratio					
				Men / Women	
			1/2 Avg.Risk	1.0 / 1.5	
			Avg.Risk	3.6 / 3.2	
			2X Avg.Risk	6.2 / 5.0	
			3X Avg.Risk	8.0 / 6.1	
C-Reactive Protein, Cardiac	0.50		mg/L	0.00 - 3.00	01
Relative Risk for Future Cardiovascular Event					
			Low	<1.00	
			Average	1.00 - 3.00	
			High	>3.00	
Homocyst(e)ine, Plasma	7.4		umol/L	0.0 - 15.0	01

FIGURE 3: *Small Intestinal Bacterial Overgrowth Breath Test Results.*

Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	10	17	27	OK
2	20 min	13	18	31	OK
3	40 min	5	6	11	OK
4	60 min	12	16	28	OK
5	**85 min****	17	19	36	OK
6	**105 min****	14	14	28	OK
7	**125 min****	20	17	37	OK
8	**145 min****	34	25	59	OK
9	**165 min****	52	25	77	OK
10	**185 min****	101	43	144	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 =	27	H	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	15	-	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	13	H	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	26	H	≤15ppm

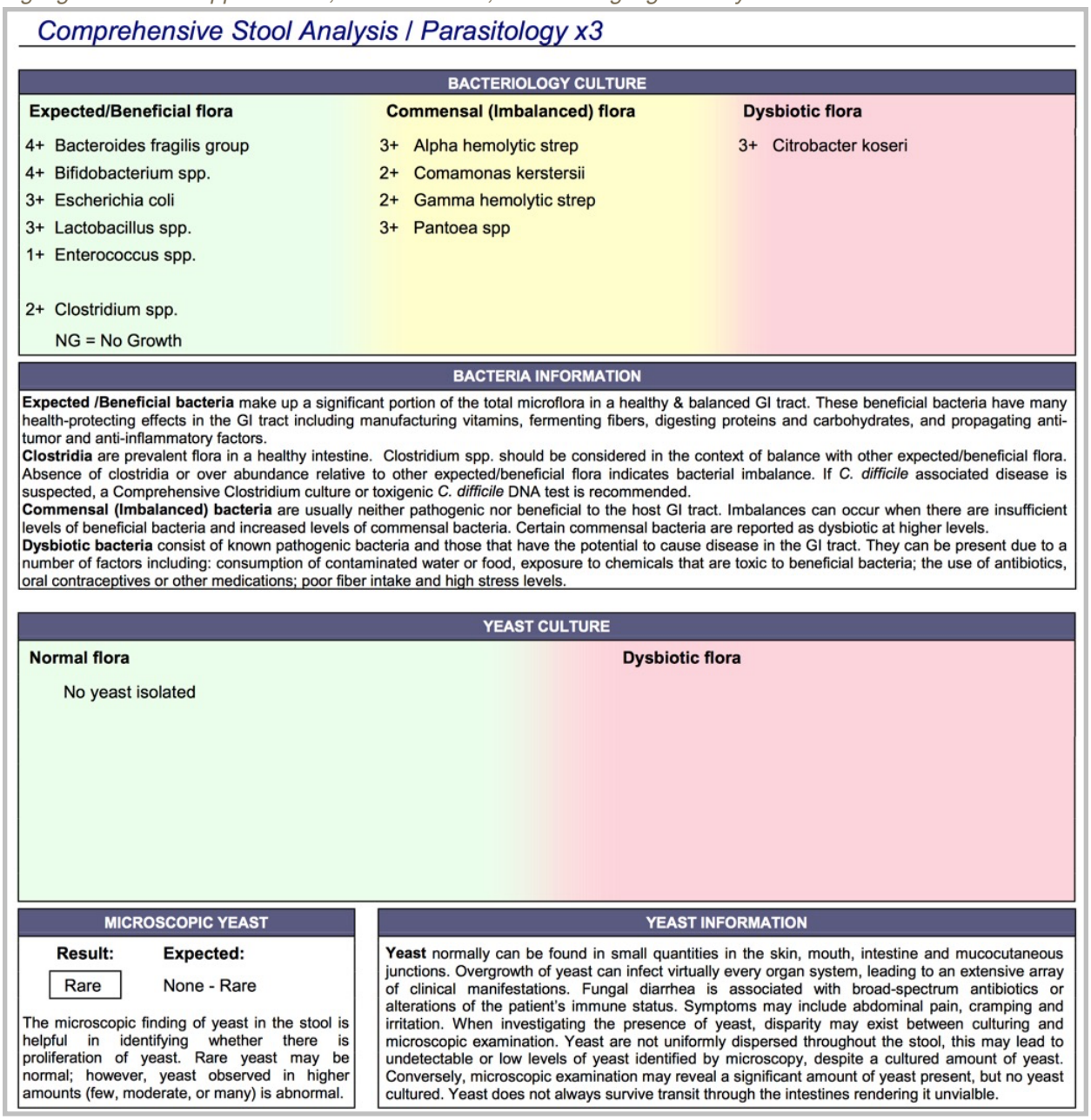
Interpretation

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

Breath testing revealed the presence of bacterial overgrowth in the small intestine. The SIBO test is based on this concept: an oral lactulose challenge will be fermented by small intestinal bacteria and excreted by the body in the form of hydrogen and methane breath gases. Janel's results showed high methane and hydrogen breath gases.

SIBO may impair the absorption of several nutrients that are important for thyroid health, such as zinc, selenium, and iodine. On the other hand, some studies have shown that hypothyroidism may contribute to SIBO by decreasing intestinal motility.[1] It is therefore difficult to know if SIBO caused Janel's hypothyroidism or if her hypothyroidism caused SIBO.

FIGURE 4A: *Comprehensive Stool Analysis & Parasitology from Doctor's Data. Dysbiotic flora are highlighted in red. Opportunistic, or imbalanced, flora are highlighted in yellow.*



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	3+ Alpha hemolytic strep	3+ Citrobacter koseri
4+ Bifidobacterium spp.	2+ Comamonas kerstersii	
3+ Escherichia coli	2+ Gamma hemolytic strep	
3+ Lactobacillus spp.	3+ Pantoea spp	
1+ Enterococcus spp.		
2+ 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:
Rare	None - Rare

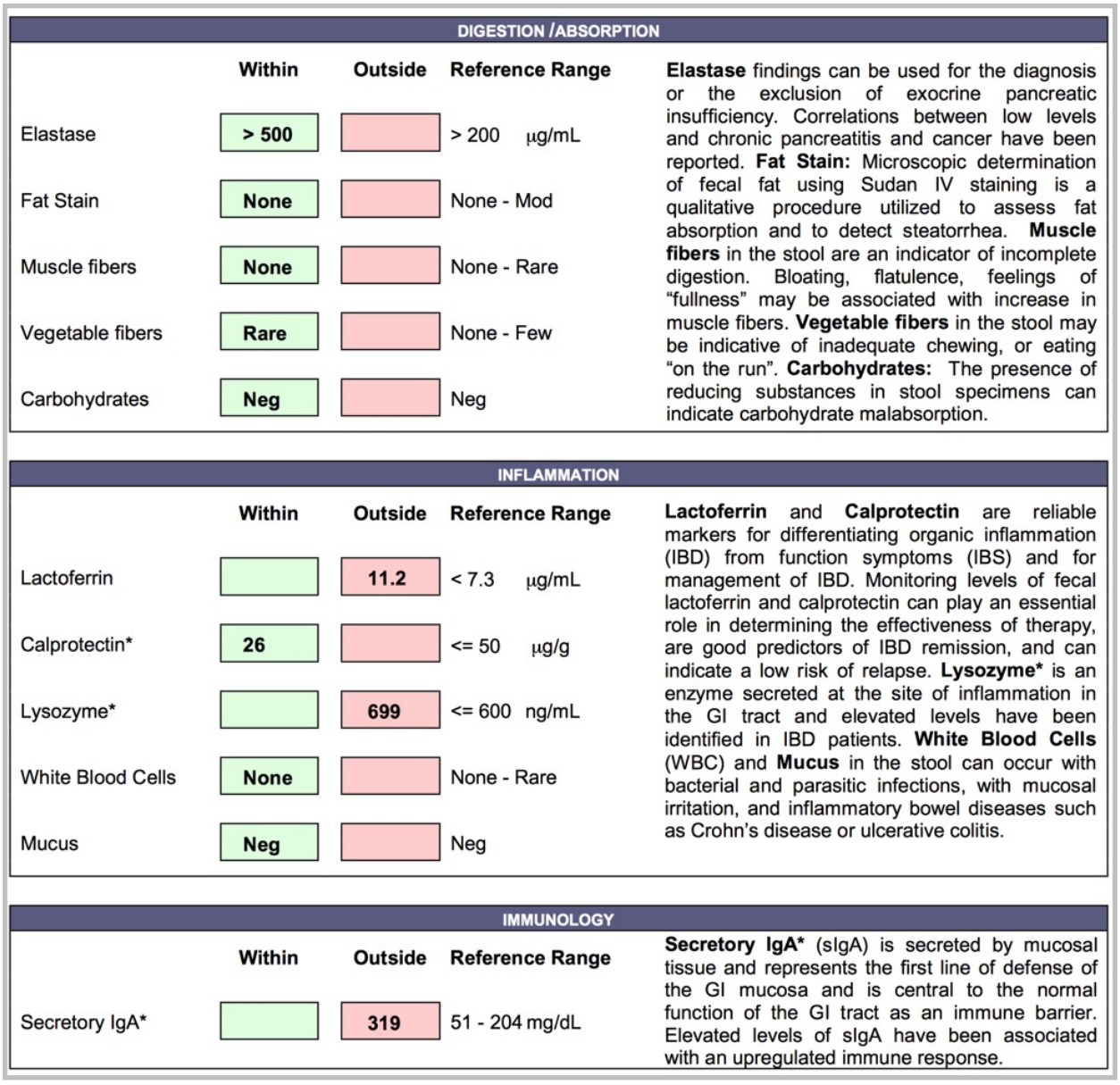
The microscopic finding of yeast in the stool is helpful in identifying whether there is proliferation of yeast. Rare yeast may be normal; however, yeast observed in higher amounts (few, moderate, or many) is abnormal.

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 unvialble.

Janel's stool test showed a 3+ growth for *Citrobacter koseri*, a species of bacteria that can be pathogenic when overrepresented in the GI tract. Janel had adequate levels of beneficial flora (*Bifidobacteria* and *Lactobacillus*, for example) but some imbalanced flora were accumulating (*Pantoea* species, *Comamonas kerstersii*, etc.). These may or may not have contributed to her symptoms. No fungi or parasites were detected on her test.

FIGURE 4B: *Comprehensive Stool Analysis & Parasitology (continued) Showing Markers of Digestion, Inflammation, and Immune Function.*



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		11.2	< 7.3 µg/mL
Calprotectin*	26		<= 50 µg/g
Lysozyme*		699	<= 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.

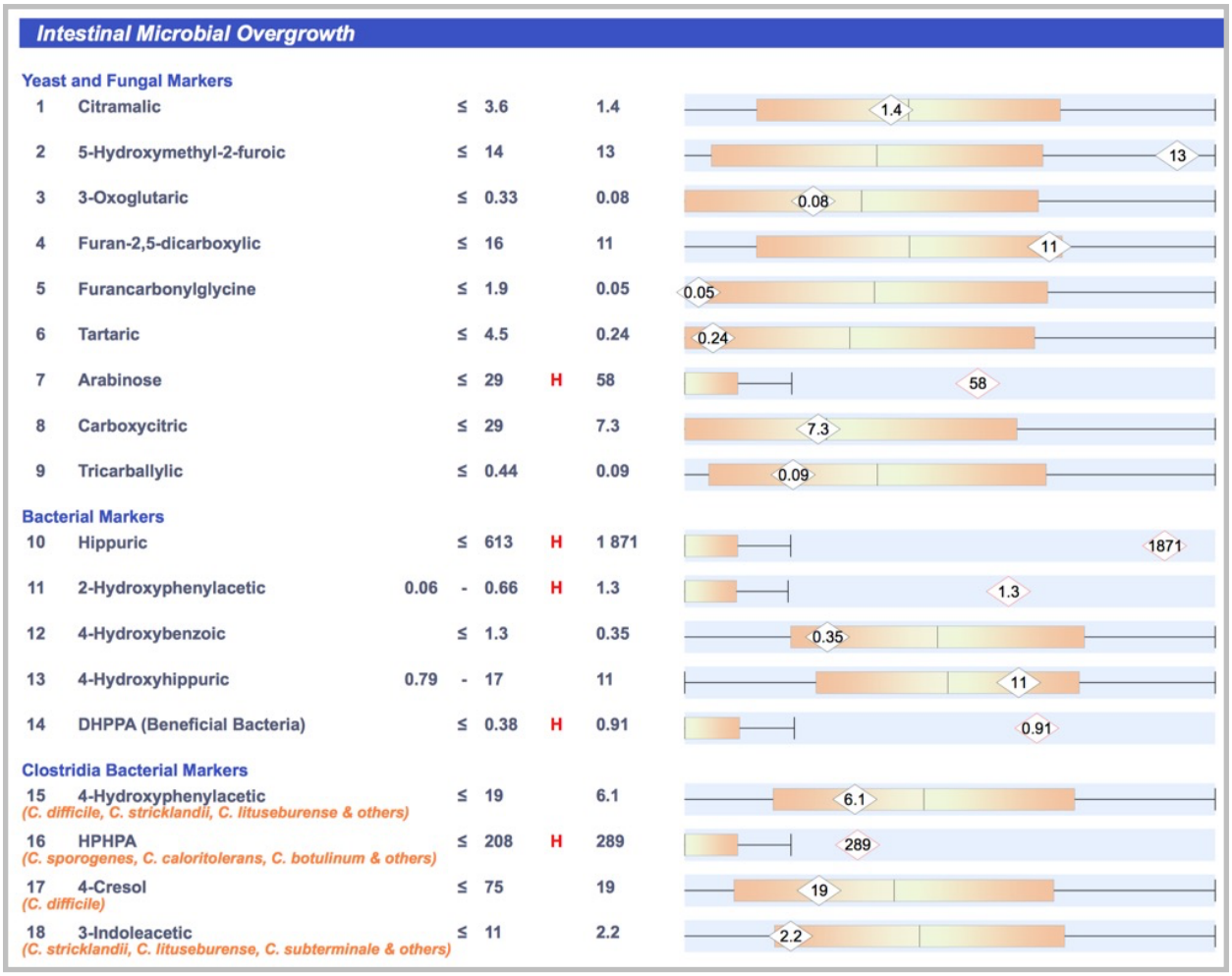
IMMUNOLOGY

	Within	Outside	Reference Range
Secretory IgA*		319	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.

Janel's stool test revealed elevations in lactoferrin and lysozyme. When significantly elevated, these markers are indicative of active inflammatory bowel disease (IBD). When only mildly elevated, however, they often represent inflammation secondary to pathogenic microbes or other causes. She had a very high secretory immunoglobulin A (sIgA), a marker of immune function in the GI tract. This high level suggested that her immune system was in overdrive, possibly due to bacterial overgrowth (*C. koseri*) or another underlying inflammatory pathology.

FIGURE 5: *Urine Organic Acids from Great Plains Laboratory, Showing Markers of Bacterial and Yeast Metabolism.*

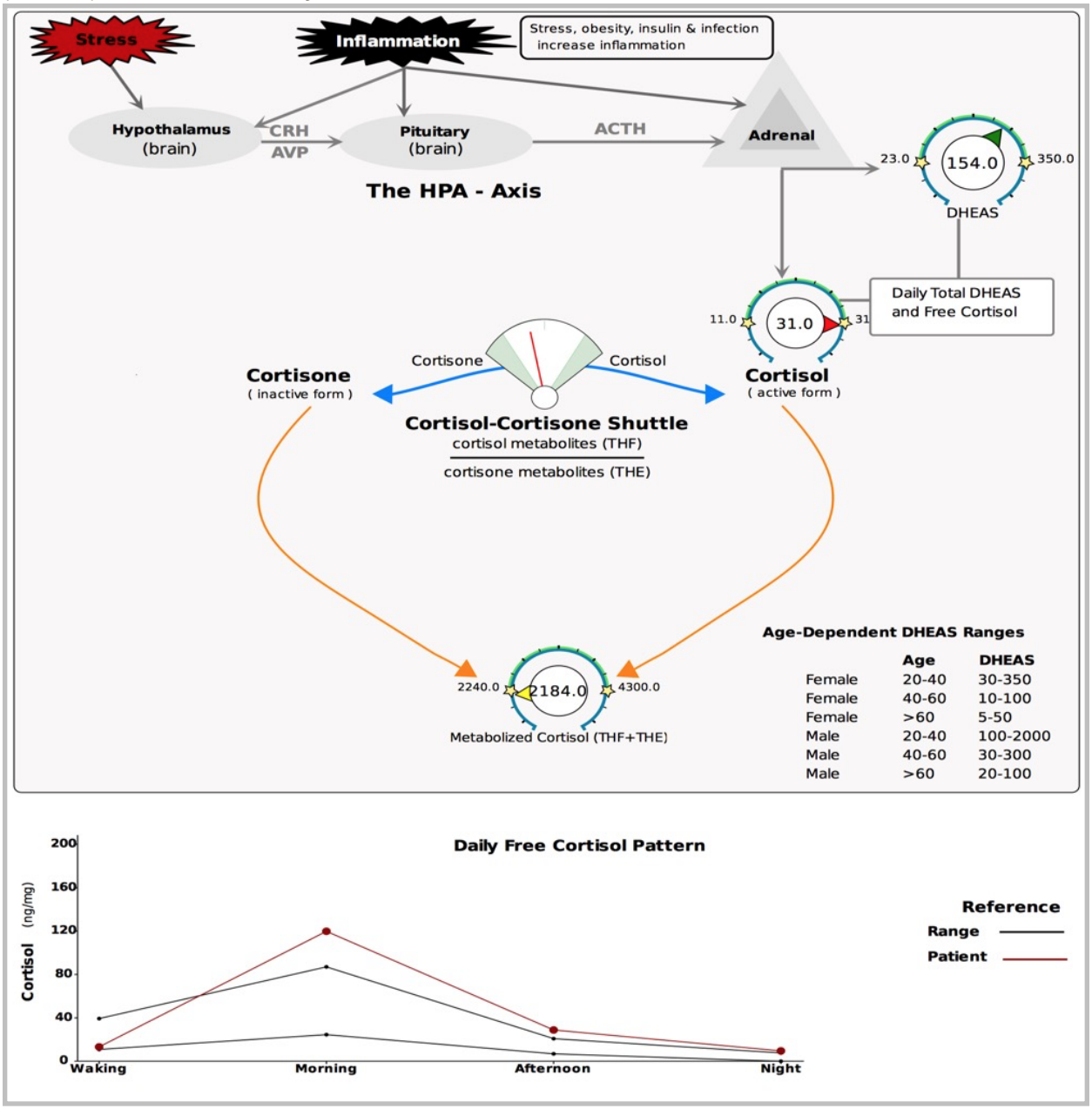


Intestinal Microbial Overgrowth

Yeast and Fungal Markers						
1	Citramalic		≤ 3.6		1.4	1.4
2	5-Hydroxymethyl-2-furoic		≤ 14		13	13
3	3-Oxoglutaric		≤ 0.33		0.08	0.08
4	Furan-2,5-dicarboxylic		≤ 16		11	11
5	Furancarbonylglycine		≤ 1.9		0.05	0.05
6	Tartaric		≤ 4.5		0.24	0.24
7	Arabinose		≤ 29	H	58	58
8	Carboxycitric		≤ 29		7.3	7.3
9	Tricarballylic		≤ 0.44		0.09	0.09
Bacterial Markers						
10	Hippuric		≤ 613	H	1 871	1871
11	2-Hydroxyphenylacetic	0.06 -	0.66	H	1.3	1.3
12	4-Hydroxybenzoic		≤ 1.3		0.35	0.35
13	4-Hydroxyhippuric	0.79 -	17		11	11
14	DHPPA (Beneficial Bacteria)		≤ 0.38	H	0.91	0.91
Clostridia Bacterial Markers						
15	4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*		≤ 19		6.1	6.1
16	HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*		≤ 208	H	289	289
17	4-Cresol *(C. difficile)*		≤ 75		19	19
18	3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*		≤ 11		2.2	2.2

Her urine organic acids test (OAT) had several markers for gut dysbiosis, particularly an overgrowth of Clostridia species (HPHPA) that produce known neurotoxins and a marker that may be associated with fungal overgrowth (5-hydroxymethyl-2-furoic acid). The SIBO, stool, and organic acids tests showed that Janel had moderate dysbiosis (primarily bacterial).

FIGURE 6: *Analysis of HPA-axis Function Using the Dried Urine Test Comprehensive Hormones (DUTCH) from Precision Analytical.*



A hormone test assessing her hypothalamic-pituitary-adrenal (HPA) axis function revealed high free cortisol, but low metabolized (total) cortisol. Janel's free cortisol was 31 (range: 11–31) and her metabolized cortisol was 2184 (range: 2240–4300). Hypothyroidism impairs the body's ability to metabolize cortisol, so this pattern of high free cortisol but low total metabolized cortisol suggested that Janel had poor thyroid function and could not metabolize cortisol properly. This test also showed a disrupted diurnal cortisol rhythm. The normal range is represented by the

two black lines on the bar graph. Janel's cortisol results, represented by the red line, showed high cortisol in the morning, afternoon, and night samples.

As I reviewed Janel's dietary survey, I noticed that she didn't eat seafood or seaweed (because of an allergy), and that she used sea salt rather than iodized salt. I also noted that she was consuming a green smoothie with large amounts of raw kale every morning. Kale is a goitrogen that can inhibit iodine uptake in the thyroid gland. Because of her low intake of iodine and high intake of raw kale, I suspected she was iodine deficient, which I confirmed with a 24-hour urine iodine test.

For treatment, I started Janel on an iodine protocol and asked her to eat more selenium-rich food, such as Brazil nuts. (She was already eating a "Paleo template" diet.) I told her to limit her goitrogenic foods to three to six servings a week and make sure to cook those foods to reduce their effects on thyroid function. I also prescribed a high-vitamin, extra-virgin cod liver oil to bring up her vitamin D levels (while also providing vitamin A and omega-3 fatty acids).

I treated her SIBO, bacterial overgrowth, and inflammatory markers by using a botanical antimicrobial protocol for 30 days. GI Synergy (Apex Energetics) and InterFase Plus (Klaire Labs) are designed to remove bacteria, fungi, and parasites in the gastrointestinal tract. MegaSporeBiotic is a probiotic and antioxidant formula that rebuilds beneficial gut bacteria but also has an antimicrobial effect (it contains *Bacillus* species probiotics, which some pharmaceutical antibiotics have been isolated from). Because Janel had elevated methane breath gases, I gave her Ideal Bowel Support (Jarrow Formulas), which is a beneficial bacteria (*Lactobacillus plantarum*) that degrades methane.

I addressed her HPA axis dysregulation with a comprehensive program including circadian regulation (controlling exposure to light during day and evening), stress management, adaptogens, and other nutrients to support HPA axis function and improve cortisol metabolism.

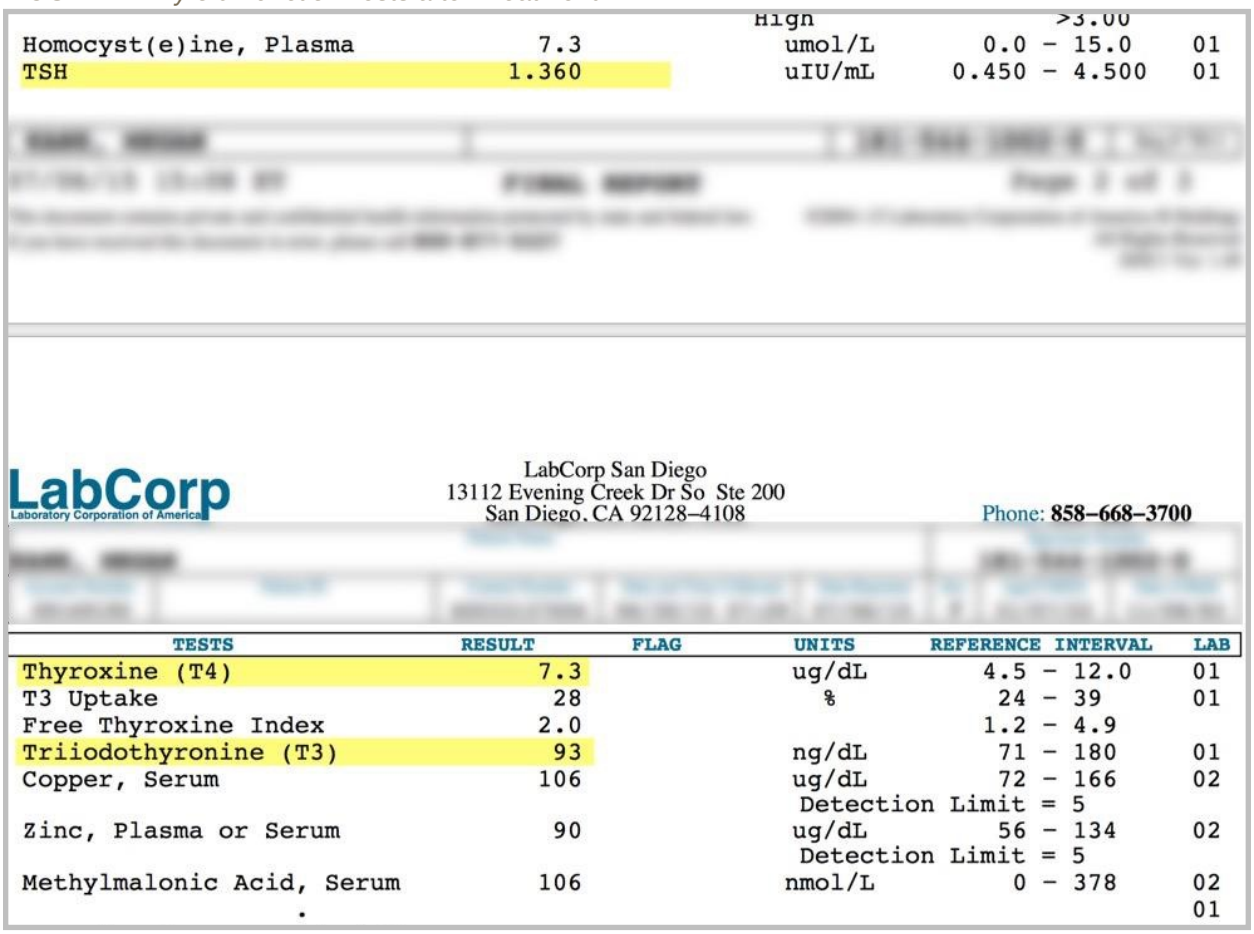
Finally, I had her donate blood to reduce her iron levels into an optimal range.

TABLE 1: *Janel's Treatment Protocol with Dosages.*

TREATMENT	NUTRACEUTICAL	BRAND	DOSAGE
Iodine	Kelp tablets	NOW	Two tablets, once a day. After three months, reduce to one tablet, once a day.
Antimicrobial	GI Synergy	Apex Energetics	1 packet BID (with breakfast and dinner)
Antimicrobial	InterFase Plus	Klaire Labs	3-4 capsules BID on an empty stomach
Probiotic	Prescript-Assist	Prescript-Assist	One BID upon rising and before bed
Probiotic/antimicrobial	MegaSporeBiotic	MegaSporeBiotic	One capsule with lunch
Probiotic	Ideal Bowel Support	Jarrow Formulas	L. plantarum for methanogens
HPA axis support	HPA Balance	Vital Plan	2 caps twice daily with food
HPA axis support	Kavinace	Neuroscience	2 caps one hour before bed
HPA axis support	Acetyl-CH	Apex Energetics	1 cap three times daily with food

After three months on this program, her hypothyroid symptoms had improved dramatically and her TSH and other thyroid markers had normalized—without any medication at all (Figure 7).

FIGURE 7: *Thyroid Function Tests after Treatment.*



	High		>3.00	
Homocyst(e)ine, Plasma	7.3	umol/L	0.0 - 15.0	01
TSH	1.360	uIU/mL	0.450 - 4.500	01

LabCorp
Laboratory Corporation of America

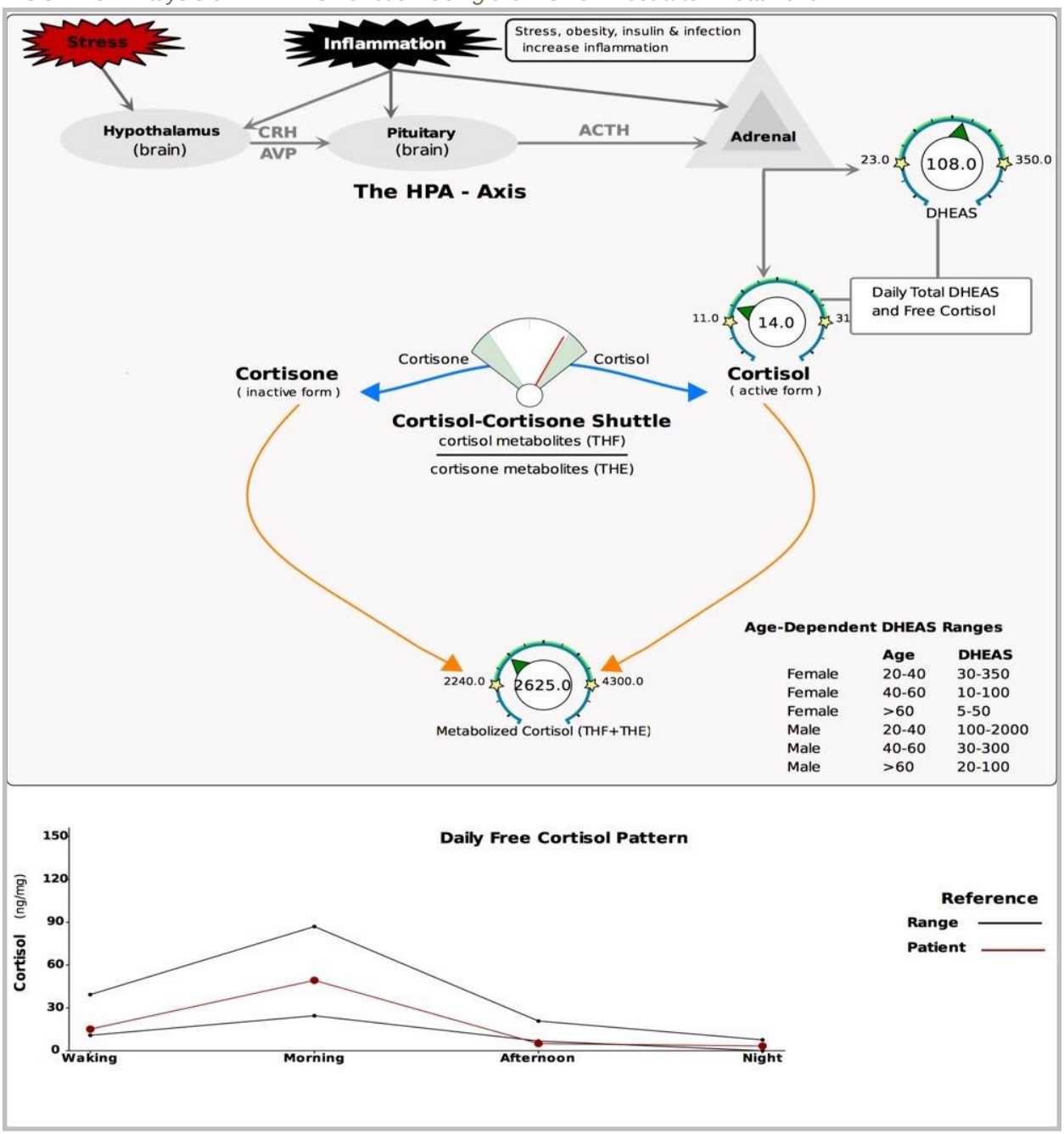
LabCorp San Diego
13112 Evening Creek Dr So Ste 200
San Diego, CA 92128-4108

Phone: **858-668-3700**

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Thyroxine (T4)	7.3		ug/dL	4.5 - 12.0	01
T3 Uptake	28		%	24 - 39	01
Free Thyroxine Index	2.0			1.2 - 4.9	
Triiodothyronine (T3)	93		ng/dL	71 - 180	01
Copper, Serum	106		ug/dL	72 - 166	02
			Detection Limit = 5		
Zinc, Plasma or Serum	90		ug/dL	56 - 134	02
			Detection Limit = 5		
Methylmalonic Acid, Serum	106		nmol/L	0 - 378	02
.					01

Her HPA axis function improved, with normalization of her total free cortisol production as well as the free cortisol diurnal rhythm. On her first test of HPA axis function, Janel had high free cortisol but low metabolized cortisol. Her follow-up test showed a decreased total free cortisol of 14.0 (range: 11–31) and an increased metabolized cortisol of 2625 (range: 2240–4300), placing her in the normal ranges for both results. On her initial test, she also had high cortisol in the morning, afternoon, and night. After treatment, her cortisol levels decreased and she had normal cortisol upon waking and in the morning, afternoon, and night.

FIGURE 8: *Analysis of HPA Axis Function Using the DUTCH Test after Treatment.*



Janel no longer complained of cold hands and feet and her hair loss slowed down dramatically until it wasn't an issue anymore. She started having regular bowel movements. She was pleased and empowered to resolve her thyroid condition without taking medications.

References

[1] Patil, A. (2014). Link between hypothyroidism and small intestinal bacterial overgrowth. *Indian Journal of Endocrinology and Metabolism*, 18(3), 307.

Digestive Disorders Case Study

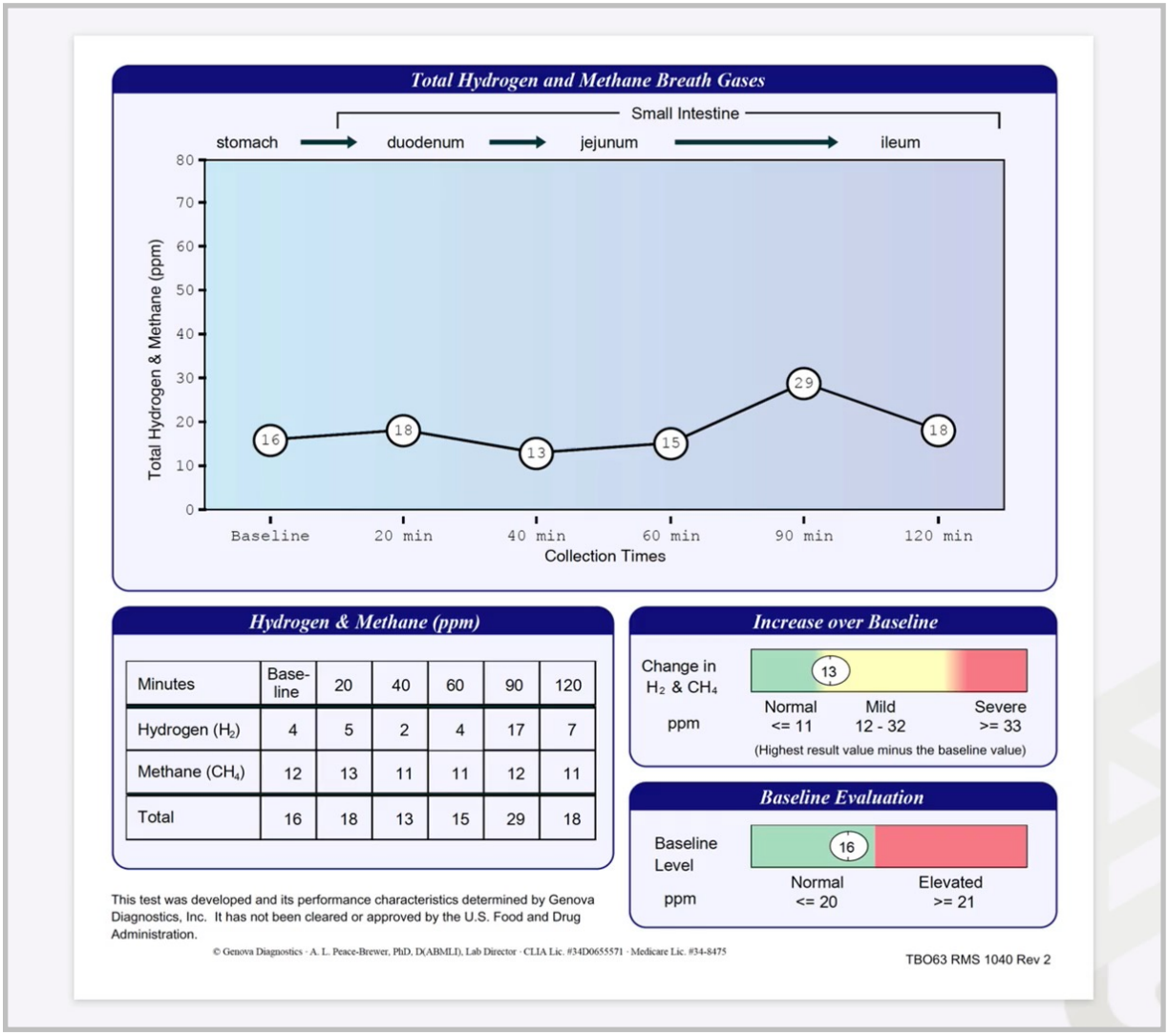
High-powered Executive with Dysbiosis and Gluten Sensitivity

CASE SUMMARY

A high-powered executive wanted to improve his mental and physical performance, lose weight, and lower cholesterol. Laboratory testing showed that he didn't have enough beneficial flora, he had a parasite, and had fungal overgrowth in his gastrointestinal tract. He also was sensitive to gluten, wheat, eggs, dairy, and sesame. After removing the foods and doing a 30-day protocol to remove dysbiotic bacteria, fungi, and parasites, as well as rebuilding beneficial bacteria, this hard-working professional felt a noticeable mental and physical improvement. Lab testing reflected the efficacy of treatments. His cholesterol remained unchanged, however, suggesting familial hypercholesterolemia.

Joe was a 41-year-old, high-powered CEO of a well-known tech corporation. His chief complaint was very high cholesterol. He didn't feel unwell; he just wanted to optimize mental and physical performance and maybe lean out a little bit. Occasionally he experienced post-nasal drip. He also reported infrequent insomnia and fatigue that seemed mostly lifestyle-related. This was no surprise; he was burning the candle at both ends, as is often the case with business CEOs.

FIGURE 1: *Genova Diagnostics Bacterial Overgrowth of the Small Intestine (BOSI/SIBO).*

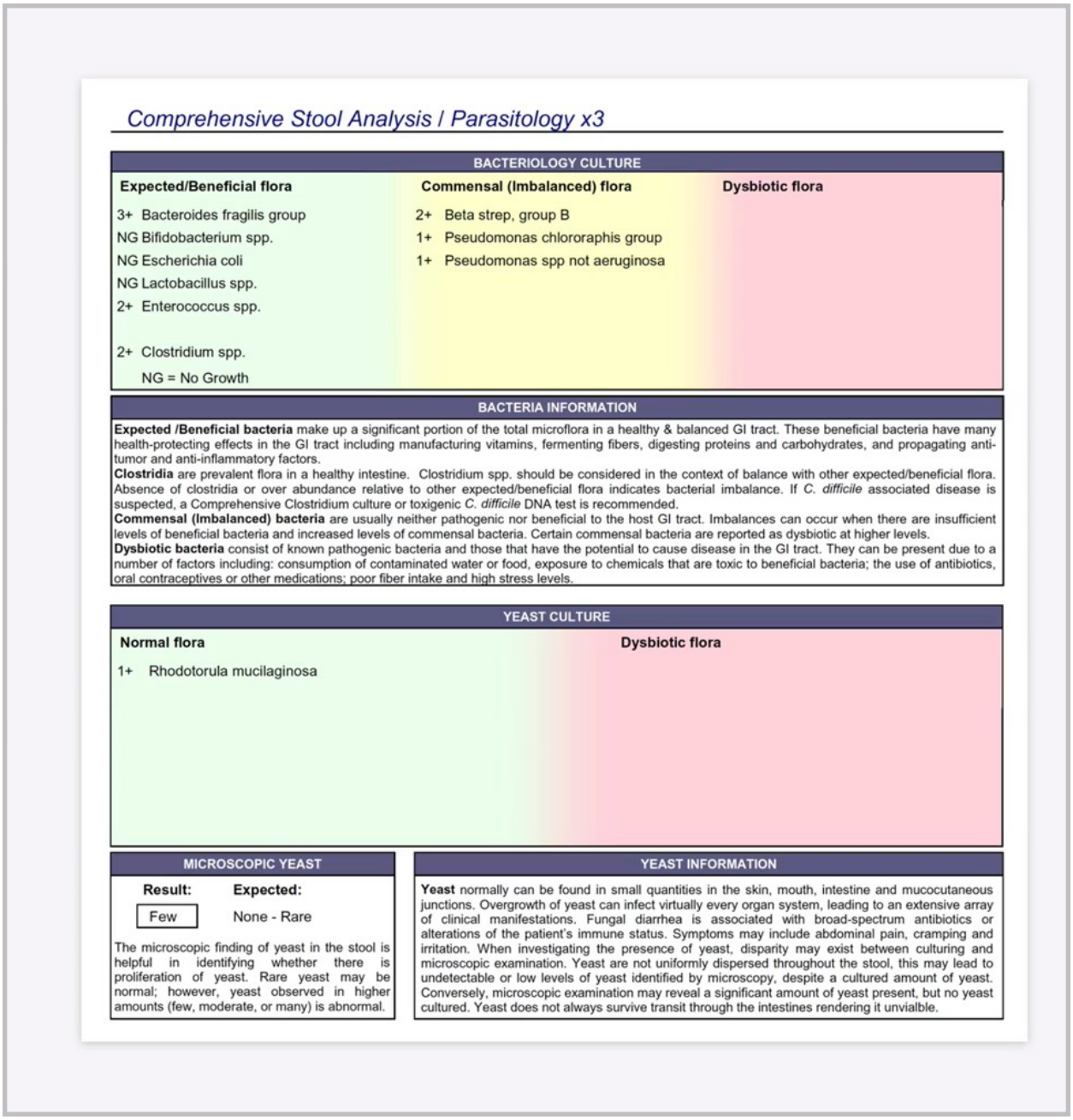


The concept of the small intestinal bacterial overgrowth (SIBO) breath test is that if a patient takes a lactulose challenge drink, excessive levels of bacteria in the small intestine will ferment the lactulose and produce hydrogen and/or methane gas(es). These gases are absorbed into the bloodstream and released into the breath. An early rise in breath gases, within the first hour or so after taking lactulose, typically indicates bacterial overgrowth in the proximal small intestine.

If we use the conventional criteria for interpreting Joe's SIBO breath test results, they would be negative. However, **Dr. Mark Pimentel, a global expert in SIBO diagnosis and treatment**, has suggested that a methane level above three parts per million at any point during the first 120 minutes of the test should be considered a positive result. Using these criteria, Joe's results would be positive, since his methane levels were 12 at baseline and 13 ppm, 20 minutes into

the test. His hydrogen levels were normal. With a borderline result like this, and lack of gut symptoms, other lab findings are necessary to better understand what the breath test means for Joe's gut health.

FIGURE 2: *Doctor's Data Comprehensive Stool Analysis & Parasitology (DD CSAP).*



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
3+ Bacteroides fragilis group	2+ Beta strep, group B	
NG Bifidobacterium spp.	1+ Pseudomonas chlororaphis group	
NG Escherichia coli	1+ Pseudomonas spp not aeruginosa	
NG Lactobacillus spp.		
2+ Enterococcus spp.		
2+ 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+ Rhodotorula mucilaginosa	

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 unvialble.

Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *

Sample 1

None Ova or Parasites
Rare RBC
Rare Yeast

Sample 2

None Ova or Parasites
Rare Yeast

Sample 3

Rare Dientamoeba fragilis trophs
Few Yeast

***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.

Comments:

Date Collected: 09/12/2014
Date Received: 09/12/2014
Date Completed: 09/20/2014

Joe's stool test showed significant dysbiosis. He showed no growth at all of beneficial bacteria such as *Bifidobacterium*, beneficial *E. coli* or *Lactobacillus*. He had mild fungal overgrowth, reported as "few" on the microscopic yeast exam for all three of his stool specimens. Joe was positive for the parasite, *Dientamoeba fragilis*. Its pathogenicity has been somewhat controversial, but many studies suggest that it can cause symptoms in at least some patients.

Joe's results were normal for digestion, inflammation, and immune function in the GI tract. Urinary organic acid results showed that Joe was negative for bacterial or fungal overgrowth in the small intestine.

FIGURE 3: *Gluten, Wheat and Food Sensitivities from Cyrex Laboratories. Array 3 (Wheat/ Gluten Proteome Reactivity & Autoimmunity) measures immune reactions to gluten and other peptides found in wheat, while Array 4 (Gluten-Associated Cross-Reactive Foods and Food Sensitivity) measures immune reactivity to proteins in foods, some of which may be cross-reactive with gluten. For example, in some patients with Celiac disease, antibodies that react with gluten may also react with casein, whey, or other proteins found in dairy products.*

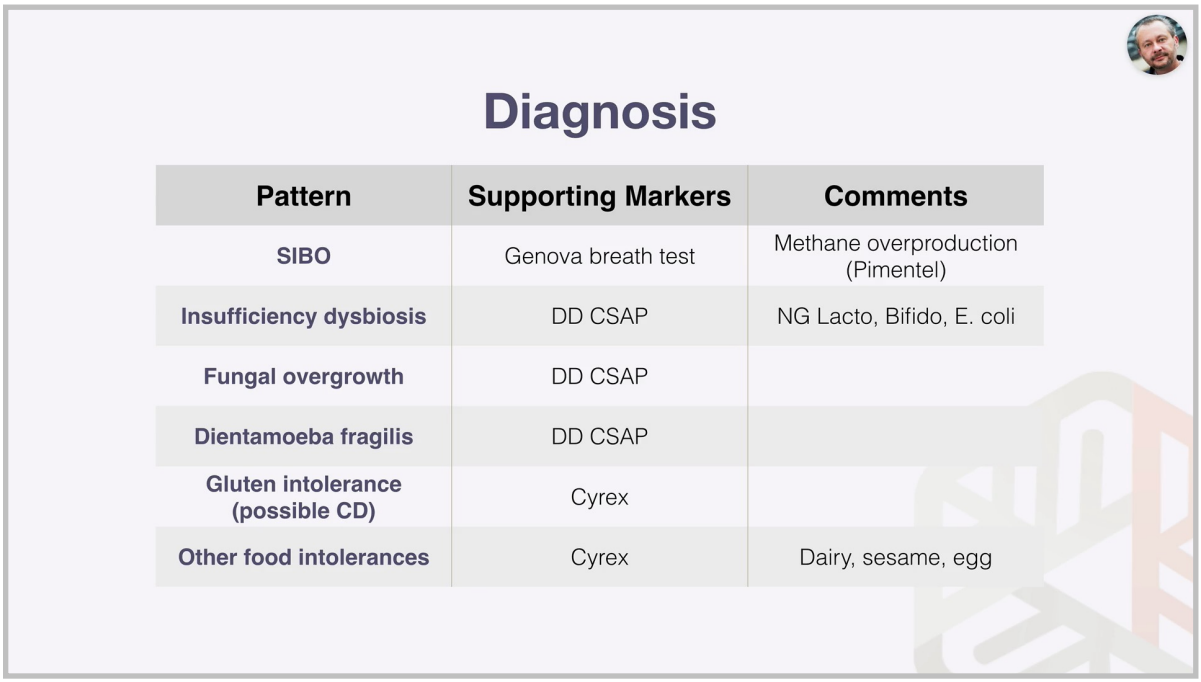
TEST	RESULT			
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	**IN RANGE (Normal)**	**EQUIVOCAL***	**OUT OF RANGE**	**REFERENCE (ELISA Index)**
Wheat IgG	0.47			0.3-1.5
Wheat IgA		1.09		0.1-1.2
Wheat Germ Agglutinin IgG	0.47			0.4-1.3
Wheat Germ Agglutinin IgA	0.65			0.2-1.1
Native & Deamidated Gliadin 33 IgG	0.49			0.2-1.2
Native & Deamidated Gliadin 33 IgA			1.52	0.1-1.1
Alpha Gliadin 17-mer IgG	0.65			0.1-1.5
Alpha Gliadin 17-mer IgA			1.60	0.1-1.1
Gamma Gliadin 15-mer IgG	0.52			0.5-1.5
Gamma Gliadin 15-mer IgA			1.17	0.1-1.0
Omega Gliadin 17-mer IgG	0.51			0.3-1.2
Omega Gliadin 17-mer IgA	0.50			0.1-1.2
Glutenin 21-mer IgG	0.61			0.1-1.5
Glutenin 21-mer IgA	0.62			0.1-1.3
Gluteomorphin + Prodynorphin IgG	0.83			0.3-1.2
Gluteomorphin + Prodynorphin IgA	0.44			0.1-1.2
Gliadin-Transglutaminase Complex IgG	0.59			0.3-1.4
Gliadin-Transglutaminase Complex IgA		1.21		0.2-1.5
Transglutaminase-2 IgG	0.84			0.3-1.6
Transglutaminase-2 IgA	0.72			0.1-1.6
Transglutaminase-3 IgG	1.00			0.2-1.6
Transglutaminase-3 IgA	0.72			0.1-1.5
Transglutaminase-6 IgG	0.45			0.2-1.5
Transglutaminase-6 IgA	1.04			0.1-1.5

TEST	RESULT			
Array 4 – Gluten-Associated Cross-Reactive Foods and Foods Sensitivity **	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Rye, Barley, Spelt, Polish Wheat	0.66			0.4-1.4
Cow's Milk		1.08		0.1-1.3
Casein (Alpha & Beta)		1.46		0.1-1.7
Casomorphin	0.75			0.2-1.6
Milk Butyrophilin	0.94			0.2-1.8
Whey Protein	0.68			0.1-1.3
Chocolate (Milk)		1.39		0.1-1.4
Oats	0.42			0.2-1.0
Yeast	0.52			0.2-1.2
Coffee	1.49			0.3-1.9
Sesame			1.76	0.1-1.3
Buckwheat	0.80			0.4-1.3
Sorghum	0.83			0.3-1.2
Millet	0.92			0.3-1.5
Hemp	0.74			0.3-1.5
Amaranth	0.44			0.2-1.3
Quinoa	0.66			0.5-1.5
Tapioca	0.38			0.1-1.1
Teff	0.79			0.2-1.1
Soy	0.64			0.5-1.5
Egg		1.39		0.2-1.7
Corn	0.87			0.3-1.4
Rice	0.51			0.4-1.6
Potato	<0.60			0.6-1.4

I ran Array 3 and Array 4 from Cyrex Laboratories on Joe to look for immune reactions to wheat and gluten-associated cross-reactive foods. He wasn't eating a lot of gluten, but he was eating it occasionally when he traveled and ate out. Joe wanted to find out whether it was really a problem for him, and sure enough it was. In Array 3, you can see he's got IgA antibodies to native and deamidated gliadin, alpha-gliadin, and gamma-gliadin. Joe is also showing IgA antibodies to gliadin transglutaminase complex and wheat. On Array 4, he tested positive for dairy, cow's milk, casein, and chocolate milk, sesame and egg.

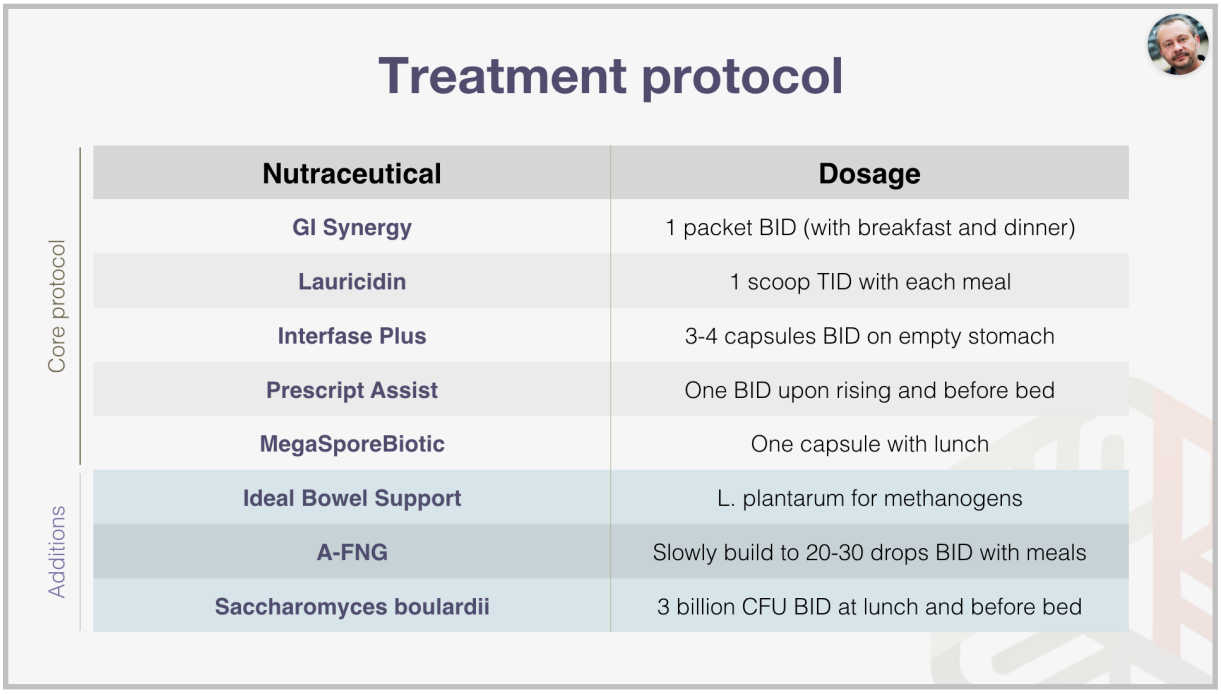
So, interestingly enough, Joe was producing IgA antibodies, rather than IgG antibodies, to wheat and gliadin proteins. Given his immune reactions to native and deamidated gliadin antibodies, alpha-gliadin antibodies and the gliadin transglutaminase complex, I suspected Joe had gluten intolerance, and possibly even celiac disease. Upon my recommendation, Joe agreed to completely cut out gluten and the other foods he tested positive for on Array 4. He didn't really see the need for getting a follow-up test for celiac disease because he was fine with just completely removing wheat and the other proteins he was reacting to.

FIGURE 4: *Assessment and Diagnosis Based on Lab Findings.*



I diagnosed Joe with borderline SIBO, insufficiency dysbiosis (meaning that his good bacteria were too low), fungal overgrowth, and parasitic infection with *Dientamoeba fragilis*. Joe also showed gluten intolerance (possibly celiac disease) and some other food intolerances on the Cyrex panels.

FIGURE 5: *Joe's Treatment Protocol with Dosages.*



Joe's main complaint was high cholesterol; gut issues can be a major contributor to high cholesterol, and I have seen significant changes in cholesterol levels in the past after addressing gut dysfunction, even in patients with no gut symptoms.

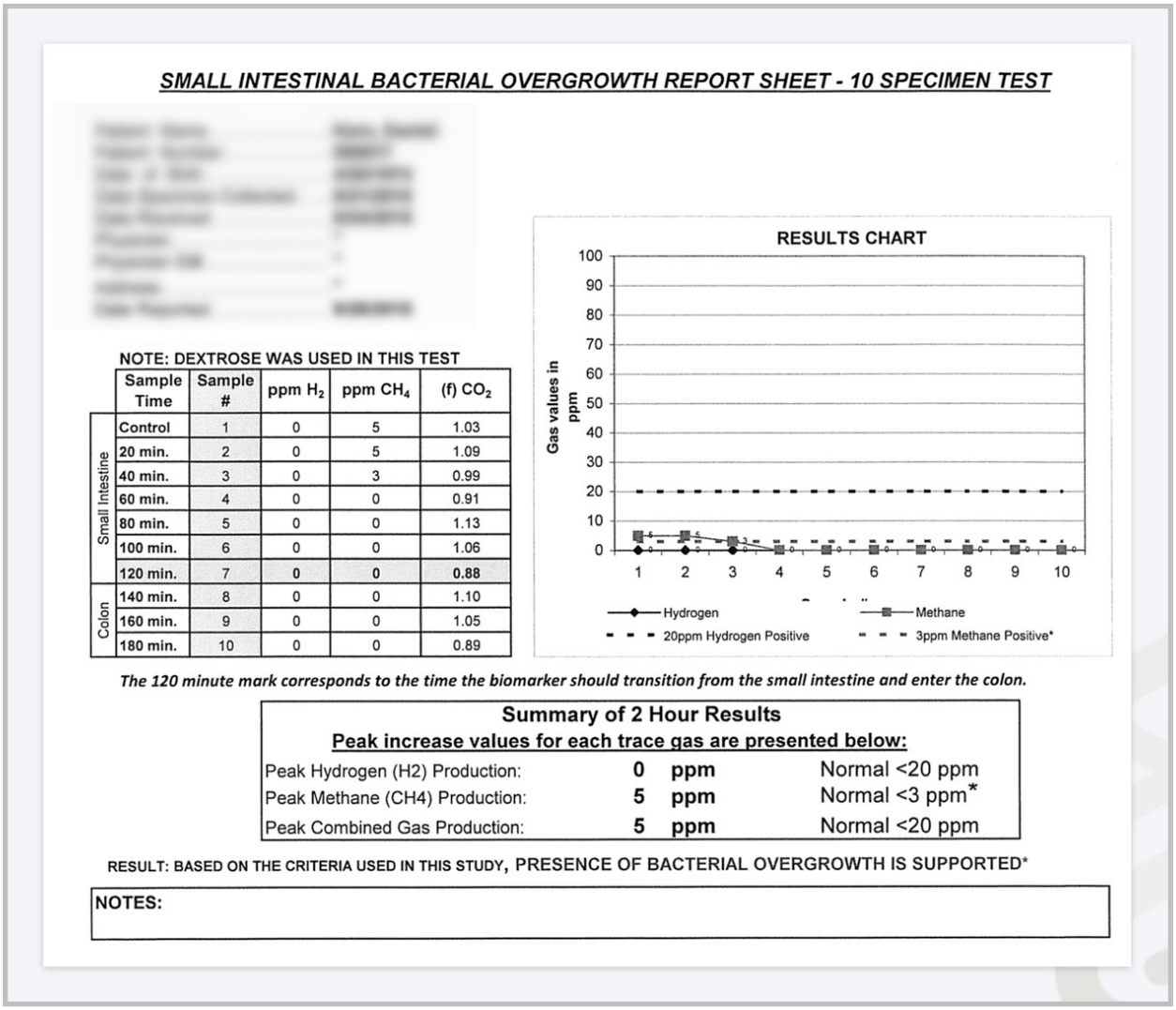
Joe wanted to approach high cholesterol from a functional perspective, instead of just taking statins, so he was motivated to address some of these underlying causes to see if that would bring down his cholesterol levels. Joe didn't want to do pharmaceuticals to begin with so we started with supplements.

I decided to prescribe an antimicrobial botanical protocol for 30 days based on Joe's borderline SIBO, the *D. fragilis*, and the fungal overgrowth. GI Synergy (Apex Energetics), Lauricidin (Med-Chem Labs), and Interfase Plus (Klaire Labs) are designed to remove bacteria, fungi, and parasites in the gastrointestinal tract. MegaSporeBiotic is a probiotic and antioxidant formula that rebuilds beneficial gut bacteria, but also has an antimicrobial effect (it contains *Bacillus* species probiotics, which some pharmaceutical antibiotics have been isolated from).

I added a few things based on his presentation. Because he had elevated methane breath gases, I gave him Ideal Bowel Support (Jarrow Formulas), which is a beneficial bacteria (*Lactobacillus plantarum*) that degrades methane. I gave him A-FNG (Byron White Formulas) and *Saccharomyces boulardii* (Saccharomycin DF from Xymogen) for the fungal overgrowth. *Saccharomyces boulardii* can also help to remove parasites and thereby lower Joe's *D. fragilis*.

If it was just insufficiency dysbiosis, I wouldn't have done antimicrobials. I would have gone right to prebiotics and probiotics to rebuild his beneficial gut flora.

FIGURE 6: *Follow-up Test for Small Intestinal Bacterial Overgrowth (Commonwealth Labs).*



SMALL INTESTINAL BACTERIAL OVERGROWTH REPORT SHEET - 10 SPECIMEN TEST

[redacted]

NOTE: DEXTROSE WAS USED IN THIS TEST

	Sample Time	Sample #	ppm H_2	ppm CH_4	(f) CO_2
Small Intestine	Control	1	0	5	1.03
	20 min.	2	0	5	1.09
	40 min.	3	0	3	0.99
	60 min.	4	0	0	0.91
	80 min.	5	0	0	1.13
	100 min.	6	0	0	1.06
	120 min.	7	0	0	0.88
Colon	140 min.	8	0	0	1.10
	160 min.	9	0	0	1.05
	180 min.	10	0	0	0.89

RESULTS CHART

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

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

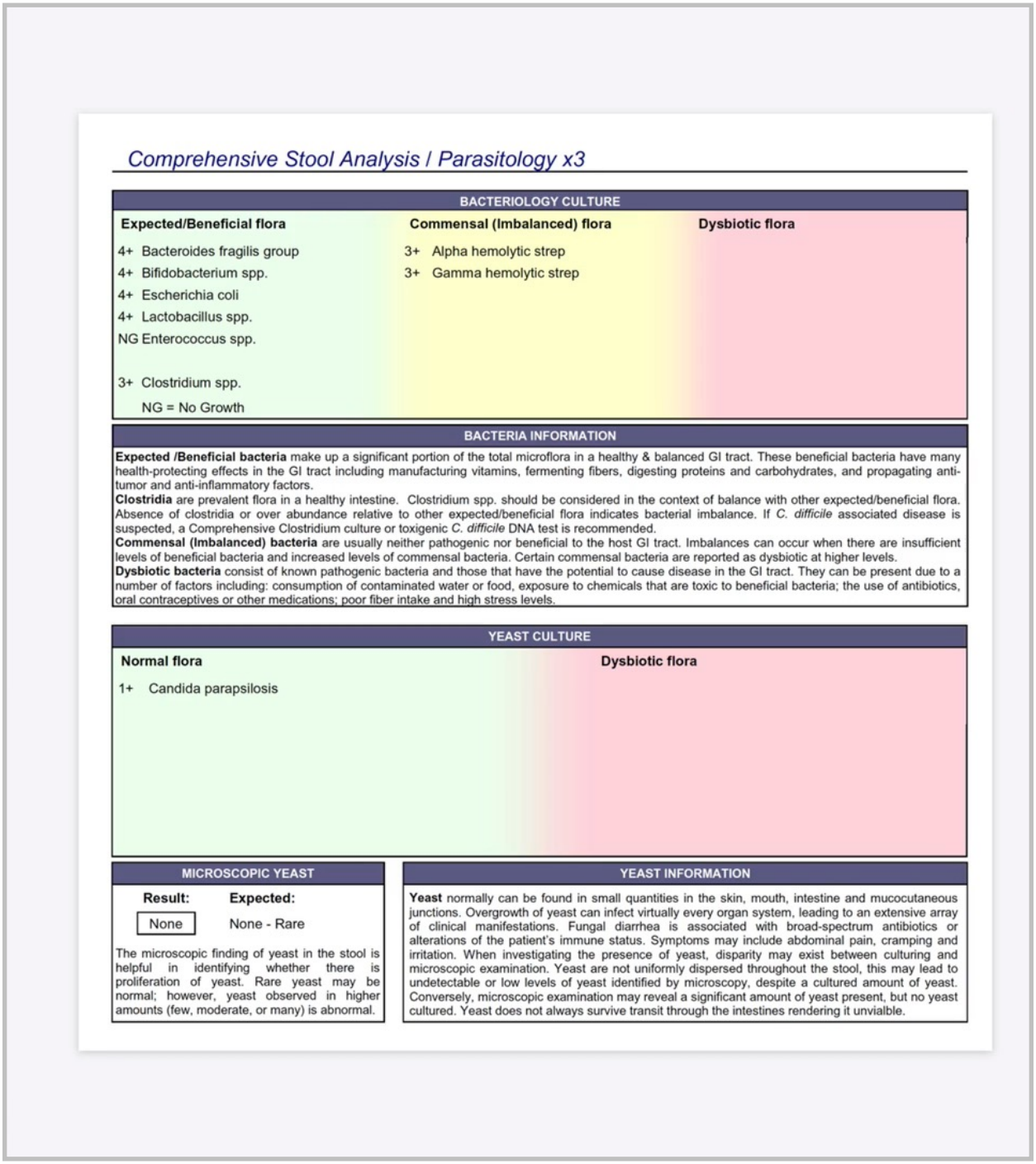
Peak Hydrogen (H2) Production:	**0**	**ppm**	Normal <20 ppm
Peak Methane (CH4) Production:	**5**	**ppm**	Normal <3 ppm*
Peak Combined Gas Production:	**5**	**ppm**	Normal <20 ppm

RESULT: BASED ON THE CRITERIA USED IN THIS STUDY, PRESENCE OF BACTERIAL OVERGROWTH IS SUPPORTED*

NOTES:

A follow-up SIBO breath test with Commonwealth Labs showed all zeroes for hydrogen (negative). Joe's methane was lower than it was on the initial test, but still *slightly* elevated at baseline. Although these results would still be considered positive according to Dr. Pimentel's criteria, given that he had no gut symptoms, and his highest methane value was only three parts per million, I did not feel that further treatment was necessary.

FIGURE 7: *Follow-up Comprehensive Stool Analysis & Parasitology (DD CSAP) Test*



Comprehensive Stool Analysis / Parasitology x3

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	3+ Alpha hemolytic strep	
4+ Bifidobacterium spp.	3+ Gamma hemolytic strep	
4+ Escherichia coli		
4+ Lactobacillus spp.		
NG 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
1+ Candida parapsilosis	

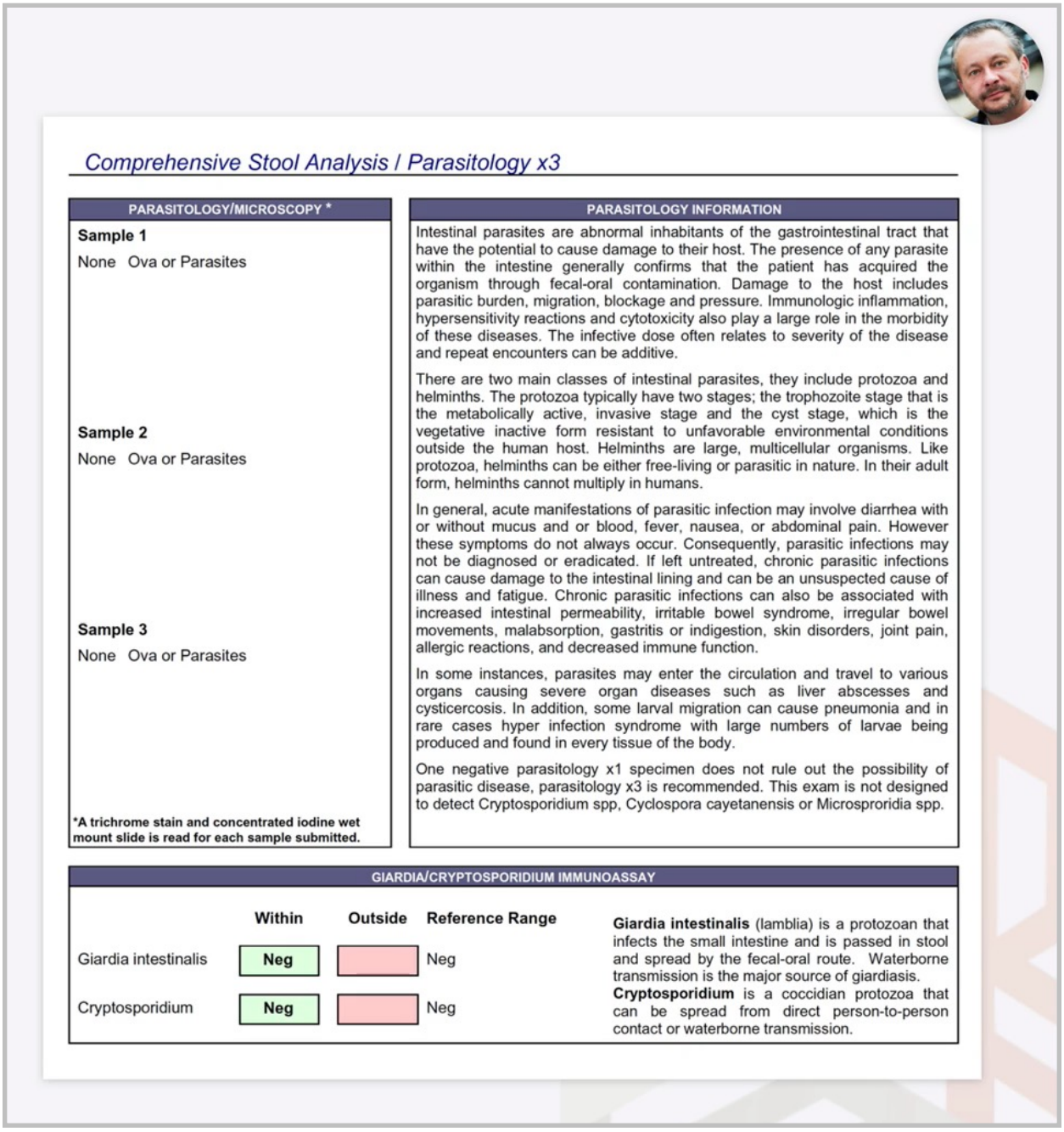
MICROSCOPIC YEAST

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 unvialble.



Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *	PARASITOLOGY INFORMATION
Sample 1 None Ova or Parasites **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.**	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.

Joe's follow-up stool test showed significant improvement in beneficial bacteria: *Bifidobacterium*, *E. coli,* and *Lactobacillus*. Fungi were no longer detected on the microscopic exam, suggesting that we got his fungal overgrowth under control. There was 1+ for *Candida* still showing, but that can be just normal flora, so it didn't require treatment. Joe's follow-up test was negative for the parasite, *D. fragilis.*

Unfortunately, in this case, Joe's cholesterol didn't come down after addressing his gut issues. His cholesterol was very high, over 300. If cholesterol levels are that high, and they don't respond to addressing these underlying problems, it's most likely genetic in origin. This patient probably has familial hypercholesterolemia. On the other hand, his mental and physical performance did improve, and he lost weight and felt better overall, so the treatment was successful from
that perspective.

The next step with Joe would be to make specific dietary, lifestyle, and supplement recommendations to manage his high cholesterol levels, and to do further testing to determine his overall level of risk (e.g. inflammatory markers like Lp-PLA2, L(p)a, ox-LDL and CT scans to determine his calcium score and carotid intima media thickness).

Clinician's Guide to Hypothalamic–Pituitary–Adrenal Axis Dysregulation: Case Study

Dietary and Lifestyle Treatments Alone Improve Energy and Normalize Sleep Patterns in a High-Performance Mother and Business Owner

CASE SUMMARY

A 42-year-old mother of four and business owner complained of fatigue and exhaustion, sleep disturbance, anxiety, and weight gain. Analysis of her lifestyle and diet revealed that she was suffering from hypothalamic–pituitary–adrenal axis dysregulation (HPA-D) due to overtraining; she was eating a low-carb Paleo diet that was ill suited to her activity level; she had poor sleep hygiene; and she wasn't managing her stress appropriately. Ninety days of a customized diet that was higher in calories and carbohydrates, a temporary break from high-intensity exercise, better sleep habits, meditation, and changes to her business structure led to marked improvements in anxiety, sleep patterns, energy, stress tolerance, and weight loss. This case shows that it is possible to achieve significant improvements in a patient's symptoms simply by focusing on the basics: a thorough patient intake and history, coupled with targeted diet and lifestyle recommendations.

A 42-year-old mother of four and business owner complained of fatigue and exhaustion, sleep disturbance, anxiety, and weight gain. Analysis of her lifestyle and diet revealed that she was suffering from hypothalamic–pituitary–adrenal axis dysregulation (HPA-D) due to overtraining; she was eating a low-carb Paleo diet that was ill suited to her activity level; she had poor sleep hygiene; and she wasn't managing her stress appropriately. Ninety days of a customized diet that was higher in calories and carbohydrates, a temporary break from high-intensity exercise, better sleep habits, meditation, and changes to her business structure led to marked improvements in anxiety, sleep patterns, energy, stress tolerance, and weight loss. This case shows that it is possible to achieve significant improvements in a patient's symptoms simply by focusing on the basics: a thorough patient intake and history, coupled with targeted diet and lifestyle recommendations.

INITIAL PRESENTATION

Macy was a 42-year-old female that presented with fatigue, especially in the afternoons, as her primary complaint. She was a business owner and mother of four children, one of whom was on the autism spectrum, and she never felt like she had enough energy to make it

through the day. She woke up in the morning feeling unrefreshed, and her sense of exhaustion worsened as the day progressed.
She also had difficulty sleeping without medication or supplements, anxiety, and high levels of perceived stress. She worked out at a CrossFit gym a few times a week and reported that her performance and exercise tolerance had declined steadily over the past eighteen months. She had also recently started to notice fat gain around her waistline and underneath her chin.

During our appointment, I noticed that several aspects of her current diet and lifestyle could be either entirely responsible for, or contributing significantly to, her primary complaints. For example:

- Due to the increasing demands of her business and her ongoing familial obligations, she was averaging just under six hours of sleep per night.
- She did high-intensity CrossFit workouts a few times a week, despite increasing feelings of fatigue.
- She started a strict Paleo diet 18 months ago. This entirely resolved her acne, digestive issues, and premenstrual dysphoric disorder (PMDD), but it also corresponded with the decline in her energy and exercise tolerance.

In short, Macy was burning the candle at both ends—a perfect recipe for HPA axis dysregulation. What's more, I suspected that her intake of both calories and carbohydrates was insufficient for her activity level and energy needs. This is unfortunately common in lean, active women and men that adopt a strict Paleo diet.

When Macy switched to Paleo, she eliminated all starchy vegetables, fruits, grains, and sugars, and consumed high levels of protein at each meal. She reported that at first, this regimen worked well for her; she lost excess weight, was more fit, and felt good about how she looked. As mentioned above, her longstanding acne, digestive issues, and PMDD also disappeared. But as time progressed, her energy started to flag, she developed difficulties falling and staying asleep, and her levels of anxiety and stress increased.

After analyzing Macy's three-day food diary, I determined that she was significantly undereating both calories and carbohydrates. Her average calorie intake was about 1,400 to 1,600 per day, with less than 50 grams of carbohydrate on most days. These were far from optimal for a woman of her height, weight, and activity level.

There are standardized formulas for calculating calorie needs based on activity level, such as the Harris-Benedict and Mifflin-St. Jeor formulas. However, a quick and dirty approximation of these can be obtained by simply multiplying the patient's weight in pounds by 12 to 14 to establish their baseline calorie needs, and then adding 100 calories for every 10 minutes of moderate- to high-intensity activity that they perform per day.

Using this calculation, on her CrossFit training days, Macy should have been eating 2,200 calories—a full 600 to 800 more than she was typically consuming (1,400 to 1,600 per day). On her resting days, she should have been eating 1,900 calories, which was still 300 to 500 more calories than she regularly ate.

Next, we examined her carbohydrate intake. Carbohydrate is the most variable macronutrient for each patient, depending their condition. The chart below illustrates suggested starting places for experimentation, given specific populations and goals:

TABLE 1: *Dietary Carbohydrate Recommendations for Different Populations.*

	% Carbs	Carbs (Grams) for Men (2600 kcal diet)	Carbs (Grams) for Women (2000 kcal diet)	Goal/Population
Very Low Carb	<10%	<65g	<50g	• Neurological issues (Epilepsy, Alzheimer's, etc.) • Severe blood sugar problems
Low Carb	10-15%	65-100g	50-75g	• Weight loss • Blood sugar regulation • Mood disturbances • Digestive problems
Moderate Carb	15-30%	100-200g	75-150g	• Generally healthy • Maintain weight • Adrenal fatigue • Hypothyroidism • Familial Hypercholesterolemia
High Carb	>30%	>200g	>150g	• Athletes and highly active people • Trying to gain weight/ muscle • Fast metabolism • Pregnant/breastfeeding

As you can see, for athletes I suggest a carbohydrate intake of at least 30 percent of total calories, with a range of 30 to 40 percent being a good starting place for most recreational athletes doing CrossFit-style training. I also suggest a moderate carbohydrate intake for patients who are suffering from HPA-D.

At 50 grams of carbohydrate per day, and an average of 1,500 calories total per day, Macy's carbohydrate intake was 13 percent—far below the recommended threshold of 30 percent.

In Macy's case, her low carbohydrate intake was in part due to a fear that eating too many carbohydrates (even Paleo-friendly ones) would make her gain weight. After all, she had lost weight when she switched to the Paleo diet and cut out refined carbs.

Macy was shocked when I told her she was eating only 13 percent of calories as carbohydrate, as it was not her intention to drop this low. Unfortunately, I've found that this is all too common, particularly among women. It's so common, in fact, that I came up with a name for it (the "accidental low-carb Paleo diet") and I **wrote an article about it**.

TREATMENT PLAN

Here are the targets for total calorie, carbohydrate, fat, and protein intake that I suggested for Macy:

Crossfit training days	Non-training days
2200 calories	**1900 calories**
160-220 g carbs	100-150 g carbs
120-140 g protein	120-140 g protein
75-110 g fat	75-110 g fat
(30-40% carbohydrates, 20-25% protein, and 30-45% fat.)	(She was instructed to add 1 cup of non-starchy vegetables to each meal.)

Note that on her training days, I was asking her to eat anywhere from three- to four-fold the amount of carbohydrate she was eating previously! This is impossible to do on a Paleo-style diet without including significant amounts of starchy plants like plantain, yuca, taro, and sweet potatoes, as well as fruit. For this reason, I recommended that Macy add some non-Paleo carbohydrate sources such as white rice and white potatoes (see Discussion).

In addition to the dietary changes I recommended, I also suggested she get at least eight hours of sleep. This meant giving up her use of Facebook and other social media at night, which she typically did after she put her kids to bed, and hiring two employees to help her with her business. These changes were not easy, but Macy was willing to make them because she was alarmed by the recent changes in her health—and because I explained to her that healing from HPA-D is not possible without adequate sleep.

I also suggested that she dial back her exercise routine significantly. This can be difficult for CrossFitters to do for two reasons. First, the CrossFit gym is more than a place to exercise for many people; it's also a source of community and social support. Second, many CrossFit gyms emphasize competition and personal achievement and unfortunately do not recognize the potential for serious harm that can come from overtraining. I asked her to avoid CrossFit entirely until she was able to start sleeping better and her energy levels recovered. Fortunately, Macy was again willing to make this change.

Finally, I suggested that Macy begin a meditation practice in order to help her to manage her stress and anxiety. Given her technology orientation (her company was a tech start-up), busy

lifestyle, and several unsuccessful attempts to start meditating in the past, I suggested Macy try using the **Headspace app**. This worked very well for her.

NINETY-DAY FOLLOW-UP:

After three months of treatment, Macy experienced some remarkable changes:

- She began falling asleep without medication or supplements and sleeping through the night on most nights (with the exception of occasionally waking to attend to her special-needs child).
- She woke up feeling refreshed and no longer felt tired during the day or had energy crashes in the afternoon.
- Much to her surprise, adding carbohydrates to her diet not only didn't lead to weight gain, but it had the opposite effect: the extra fat she had gained around her midsection and under her chin began to decrease.
- She reported feeling less background anxiety and greater stress tolerance, despite the fact that the circumstances of her busy life hadn't changed much.
- Her exercise tolerance gradually improved and she was again able to start increasing her performance at the gym.

Once Macy's energy levels and sleep were better, I then suggested she work with the trainers at her gym to create a routine that was more appropriate for her particular circumstances and needs. She was eventually able to return to training three days a week, but at a much lower intensity than she was before.

DISCUSSION

So far we've focused on relatively complex cases where extensive laboratory testing was needed to determine the underlying cause(s) of the patient's symptoms and comprehensive treatment protocols involving several supplements and botanicals were needed to resolve the pathologies that were identified. This case study, on the other hand, illustrates the importance of "the basics"—taking a thorough new patient history and addressing diet and lifestyle before anything else. Occasionally this is all that's needed to resolve the patient's concerns.

Macy's case is also a good reminder that HPA-D is ultimately a clinical diagnosis. We did run a panel of tests (including a Dried Urine Test Comprehensive Hormones, or DUTCH, HPA axis assessment), but the results in most cases were normal or equivocal. Nevertheless, Macy presented with classic symptoms of HPA-D, and I was confident that approaching her from that perspective would yield positive results. After treatment, her considerable clinical improvement in the areas of stress tolerance, sleep, anxiety, and weight loss confirmed that HPA-D was the

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correct diagnosis.

Paleo Diet, Calories, and Carbohydrates
Strict Paleo is a fantastic starting place for many people, since it removes many of the antigenic foods that can provoke digestive distress, immune dysregulation, and inflammation. This is why Macy saw a nearly complete resolution of her acne, digestive issues, and PMDD when she adopted a Paleo diet.

However, there is no one-size-fits-all approach to diet. Instead, diet must be customized to meet each individual's particular genetic predisposition, goals, health status, activity levels, and goals. For an athlete or active person, calorie and carbohydrate intake are particularly important factors to address. This is even more true when significant stress is present, since ongoing stress (including excessive exercise) can have a catabolic effect on the body. Without sufficient calories and carbohydrates to support activity and stress levels, the body will progressively break down. This is what was happening with Macy.

Reaching an appropriate carbohydrate level (>30 percent) for athletes, active people, those trying to gain weight and muscle mass, and pregnant women can be difficult without adding some non-Paleo carb sources such as white rice and white potatoes. For example, imagine Macy consumed the following Paleo-style meal plan in one day:

- Breakfast: two scrambled eggs, two pieces of bacon, and a cup of fresh blueberries
- Lunch: half of an acorn squash stuffed with ground beef, kale, red peppers, and other non-starchy veggies
- Snack: an apple with almond butter
- Dinner: an 8-ounce New York strip, a medium sweet potato with butter, and steamed broccoli

What would her total carbohydrate intake be? Non-starchy vegetables are excellent sources of micronutrients and fiber, but overall they are quite low in carbohydrates. Most have fewer than 80 calories of carbohydrates per pound, and those are typically in the form of glucose and fructose. What's more, some evidence indicates that the human body expends up to 40 calories for every pound of non-starchy vegetables consumed. This suggests a net gain of a mere 40 calories per pound of vegetables eaten.

For this reason, I recommend not counting non-starchy vegetables toward the total carbohydrate intake. That means that we only count carbohydrates from starchy plants and fruit. If we do that from the example above, we get the following amounts:

- 1 cup of fresh blueberries: 21 grams
- 1 cup of acorn squash: 30 grams

- 1 apple: 25 grams
- 1 medium sweet potato: 37 grams

This plan—even with starchy plants and fruit—provides a total of only 113 grams of carbohydrate. Remember that Macy needed approximately 160 to 220 grams of carbohydrate on her training days and somewhere between 100 and 150 grams on her resting days. So, although the meal plan above might be sufficient on resting days (albeit in the low end of the recommended range), it would be well below the recommended target for her training days.

You can see that customizing the diet, especially for a patient who needs a higher carbohydrate intake, is important and requires attention to detail. Knowledge of foods that are high in carbohydrates can help tailor the diet for a particular patient. I've listed the carbohydrate content of starchy plants and fruits (Tables 2 & 3) below to illustrate the most carbohydrate-dense foods on a Paleo-style diet. I've also included white rice and white potatoes in the starch section to give you an idea of why these may be helpful carb sources, if tolerated, for athletes and active people.

TABLE 2: *Carbohydrate Content of Starchy Plants.*

CARBOHYDRATE CONTENT OF SELECTED STARCHY PLANTS		
STARCHY PLANT	**MEASURE**	**CARBOHYDRATE, G**
Potato, russet	1 large	64
Tapioca	1/2 cup	63
Plantain	1 cup, slices	48
Taro	1 cup, sliced	46
Yuca* (aka manioc, cassava)	1/2 cup	39
Sweet potato	1 large	37
Yam	1 cup, cubes	37
Breadfruit	1/2 cup	30
Acorn squash	1 cup, cubes	30
Butternut squash	1 cup, cubes	22
Lotus root	10 slices	14

As you can see, the most carbohydrate-dense starches on a strict Paleo diet are tapioca, plantain, taro, and yuca (also called manioc or cassava)—foods that are not typically consumed by most Americans, even those on a Paleo diet.

Notice, as well, that white potatoes are higher in carbohydrates than any Paleo source, and white rice is higher than any Paleo source with the exception of tapioca. If your active patients tolerate white potatoes and rice, I don't think there's any reason to avoid these foods, and in fact, they may be highly beneficial.

TABLE 3: *List of the Carbohydrate Content of Fruits.*

CARBOHYDRATE CONTENT OF SELECTED FRUITS		
FRUIT	**MEASURE**	**CARBOHYDRATE, G**
Banana	1 medium	27
Pear	1 fruit, medium	27
Pomegranate	1/2 fruit (4-inch piece)	27
Mango	1 cup, pieces	25
Apple	1 fruit (3-inch piece)	25
Pineapple	1 cup, chunks	22
Orange	1 fruit (3-inch piece)	18
Grapes	1 cup	16
Papaya	1 cup, 1-inch pieces	16
Peach	1 medium (2 2/3 inch)	14
Cantaloupe	1 cup, cubes	13
Strawberries	1 cup, halves	12
Watermelon	1 cup, diced	12
Blueberries	1/2 cup	11
Raspberries	1/2 cup	8
Plum	1 fruit (2 1/8 inch)	8
Tomato	1 cup, chopped	7

As you can see, even the most carbohydrate-dense fruits like bananas and pears contain less than half of the carbohydrate than a serving of potatoes. So, while fruit can certainly contribute to overall carbohydrate intake, it should not be the sole source for athletes and active people.

Why do so many people who adopt a Paleo diet follow a low-carb version of it? In many cases, it is simply an unintentional result of removing highly refined carbohydrate sources like bread, flour, and sugar, and not replacing them with Paleo-friendly starches and fruit.

In other cases, people have been led to believe that carbohydrates—even Paleo-friendly starches and fruit—are potentially harmful even for healthy people and should be limited as a result. Macy was afraid that eating too many carbohydrates (even Paleo-friendly ones) would make her gain weight. There is, however, no research that I am aware of that supports this

viewpoint. On the contrary, the majority of the peer-reviewed studies that have shown the Paleo diet to reduce weight, blood sugar, total and LDL cholesterol, inflammatory markers, and blood pressure employed moderate carbohydrate versions of Paleo. For example, in a study of patients with type 2 diabetes, participants experienced significant improvements in metabolic and lipid parameters following a Paleo diet that averaged 32 percent of calories from carbohydrate.[1]

In addition, traditional hunter-gatherer societies typically consume between 30 and 40 percent of their total calories from carbohydrate, though the range can vary between 3 and 50 percent, depending on the population studied and the latitude at which they live.[2,3] The only hunter-gatherer societies observed to eat fewer than 20 percent of calories as carbohydrate were those living at latitudes quite distant from the equator, often in marginalized environments where fruits, vegetables, starches, and honey were not readily available.

Both clinicians and patients need to understand that Paleo-friendly carbs do not affect the body in the same way that highly refined carbohydrates do. Refined carbohydrates have been shown to alter our gut microbiota in ways that may predispose us to weight gain.[4] They are also much higher in total calories and lower in nutrients than whole-food sources of carbohydrates, which means we're more likely to gain weight when we eat them.

CONCLUSIONS

Macy presented with fatigue, anxiety, sleep disturbance, and weight gain. After a careful intake, it was clear that she was eating a diet poorly suited to her personal circumstances. She was undereating calories and carbohydrates because she had inadvertently adopted a low-carb Paleo diet. Macy was overtraining, had poor sleep hygiene, and needed to make changes at work to decrease her stress level. Her symptoms suggested HPA axis dysregulation. A straightforward protocol of dietary and lifestyle changes over three months led to increased energy, restorative sleep, weight loss, less anxiety, and better stress tolerance. She was eventually able to resume her active lifestyle (though not high intensity) without diminishing her newfound energy levels.

As clinicians, we have an increasingly sophisticated array of laboratory tests and other diagnostic methods available to us. In some cases, we'll need to make full use of these in order to successfully treat our patients. Yet in a surprising number of cases, such as this one, we can accomplish our goals simply by focusing on the basics: a thorough patient intake and history, coupled with targeted diet and lifestyle recommendations. Unfortunately, these are all too often overlooked—not only in conventional primary care, but also in functional medicine.

As a final note, I encourage clinicians to consider either hiring or developing a referral relationship with a registered dietitian or nutritionist who is familiar with Paleo-style, nutrient-dense diets. Calculating the necessary calorie and macronutrient intakes for each patient based on their individual needs can be time-consuming and beyond what most full-time clinicians will be able to do in their practice. This is where a well-trained RD or nutritionist can be a fantastic resource for you, as a clinician, and your patients.

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