



# **Beyond Adrenal Fatigue**

**Using the Functional Medicine Matrix to Crack the  
Energy Code for Fatigued Women Patients**

**Aviva Romm MD**

# Objectives

This class will explore the underlying, or root causes, of the profound “fatigue” epidemic women are currently experiencing. Using the Functional Medicine Matrix as a guide, we’ll look at patient history, conventional and functional testing, and algorithms to apply in identifying and formulating an effective individualized treatment plan for women. We’ll look at the appropriate assessments for hypothyroidism, blood sugar and insulin, adrenal fatigue, intestinal dysbiosis, viral and other infections, and detoxification problems, as well as the role of mind and emotions in fatigue.

By the end of this talk participants will be able to:

- Use the functional medicine matrix as an effective assessment device in clinical practice
- Understand the profound impact of fatigue in women’s lives
- Evaluate the primary causes of fatigue using appropriate conventional and functional medicine testing
- Begin to use the functional medicine matrix to form an individualized treatment plan for women with fatigue.



# The Fatigue Epidemic

- Up to 38% of individuals and 42% of primary care patients experience significant fatigue.
- Rates higher with inflammatory diseases such as rheumatoid arthritis and multiple sclerosis
- Annual cost to employers exceeds \$136 billion in lost productive work time.
- Fatigue results in approximately 7 million office visits per year in the United States.
- Prevalence higher in women; 75% or more of patients with chronic fatigue syndrome [now also called systemic exertion intolerance disease (SEID)] are women.
- EDS is reported by 10-25% of the general population.

Ricci JA et al. . Fatigue in the U.S. workforce: prevalence and implications for lost productive work time *J Occup Environ Med* 2007; 49:1.

R. Fuhrer, S. Wessely. The epidemiology of fatigue and depression: a French primary-care study *Psychol Med*, 25 (5) (1995), pp. 895–905

Pawlikowska, T et al. Population based study of fatigue and psychological distress *BMJ*, 308 (6931) (1994), pp. 763–766

Wolfe, F et al. The prevalence and meaning of fatigue in rheumatic disease. *J Rheumatol.*, 23 (8) (1996), pp. 1407–1417

Heesen C et al. Fatigue in multiple sclerosis: an example of cytokine mediated sickness behaviour? *J. Neurol. Neurosurg. Psy.*, 77 (1) (2006), pp. 34–39

Young TB. Epidemiology of daytime sleepiness: definitions, symptomatology, and prevalence. *J Clin Psychiatry* 2004; 65 Suppl 16:12.

# What is Fatigue?

Defined as subjective or objective:

- Difficulty or inability initiating activity (perception of generalized weakness)
- Reduced capacity maintaining activity (easy fatigability)
- Difficulty with concentration, memory, and emotional stability (mental fatigue)

Note that fatigue chronicity does not mean a patient has chronic fatigue syndrome.

# Diagnostic Criteria for CFS/SEID

2015 IOM diagnostic criteria for CFS/SEID requires that the patient have the following three symptoms:

1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities, that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest, and
2. Post-exertional malaise and
3. Unrefreshing sleep

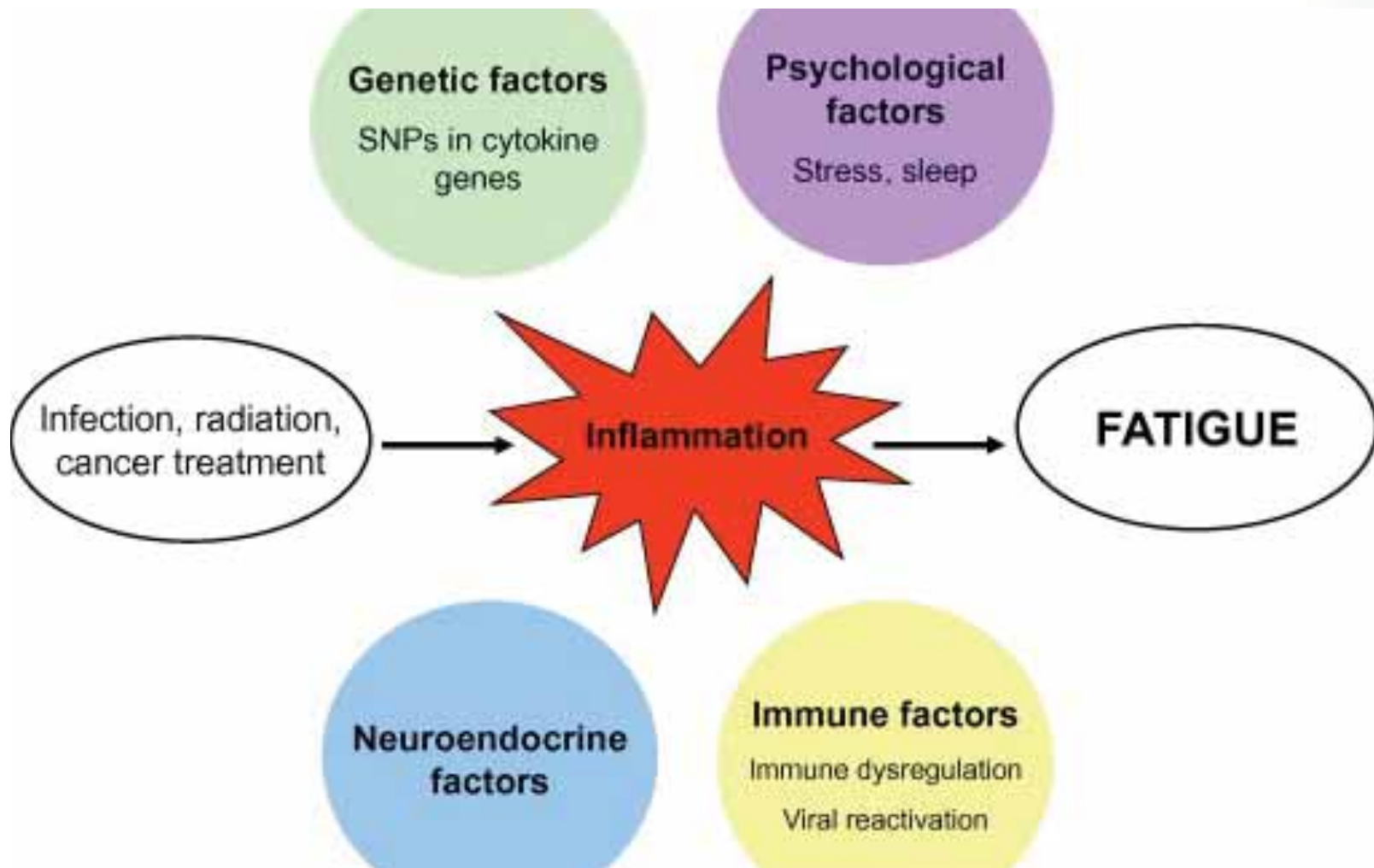
**PLUS** At least one of the two following manifestations is also required:

- Cognitive impairment or
- Orthostatic intolerance

# Common Fatigue-Associated Conditions

- “Adrenal fatigue”
- Anemia
- Autoimmune conditions
- Caffeine use
- Cancer
- Chronic Fatigue Syndrome
- CVD
- Depression
- Diabetes, Dysglycemia
- Fibromyalgia
- Food allergies, intolerances
- Generalized inflammation
- Hypothyroidism
- Hyperthyroidism
- Intimate partner violence
- Lyme disease
- Medications (pains, blood pressure, antidepressants)
- Obesity
- Restless leg syndrome
- Sleep apnea
- Sleep disorders
- Stress, SES factors
- “*UNEXPLAINED*”
- Viral Infections (EBV, HSV, CMV)

# Inflammation: The Root of Fatigue



# Rule Out the Big Bad Things

- CVD, cancer, i.e., new onset/recent fatigue in women >45
- MS, MG, etc., Progressive or recurrent muscle weakness
- HIV, i.e., fatigue frequent infections
- Leukemia, i.e., Bruising



# The Fatigue History

- Understanding the role of fatigue on your patient's QOL
- Describing fatigue
  - Onset (gradual, sudden, related to an illness, exposure)
  - Location (muscle weakness, "in my head," generalized).
  - Type (heaviness in body, brain fog, sleepy, deeply fatigued)
  - Timing (morning, daytime, afternoon, nighttime)
  - Course (stable, improving, worsening)
  - Frequency (daily, constantly, cyclic)
  - Associated symptoms (sinus congestion, bloating, joint pain)
  - Associated behaviors (exercise, postprandial)
  - Alleviating behaviors (sleep, eating protein)
- Primary symptom or secondary symptom (i.e., tired, or tired of being sick)

# The Fatigue Focused Physical Exam

- General appearance: level of alertness, psychomotor agitation or retardation, grooming
- Presence of lymphadenopathy
- Thyroid findings: Goiter, thyroid nodule, ophthalmologic changes
- Cardiopulmonary examination: signs of congestive heart failure and chronic lung disease
- Neurologic examination: muscle bulk, tone, and strength; deep tendon reflexes; sensory and cranial nerve evaluation.

# Initial Conventional Labs for Fatigue

- Complete blood count with differential
- Chemistry screen (including electrolytes, glucose, renal and liver function tests)
- Thyroid stimulating hormone
- Creatine kinase, if pain or muscle weakness present
- Consider ESR
  
- Additional labs *conventionally* recommended only if history or physical exam findings suggest a need.

# Case: A 46 year old woman with chief concern of FATIGUE

- Daytime somnolence
  - Has to nap for hours during the day
  - Even if has a good night's sleep still needs a nap in the afternoon
- “Tired all the time”
- Brain fog – can’t concentrate
- Muscle fatigue
  - With exercise
- Night Eating Syndrome
- Insomnia
  - Has anxiety about getting sleep
  - Wakes up during the night - 3 am -7 am then goes back to sleep

**Let’s go on to rooting out the cause(s) of fatigue...**

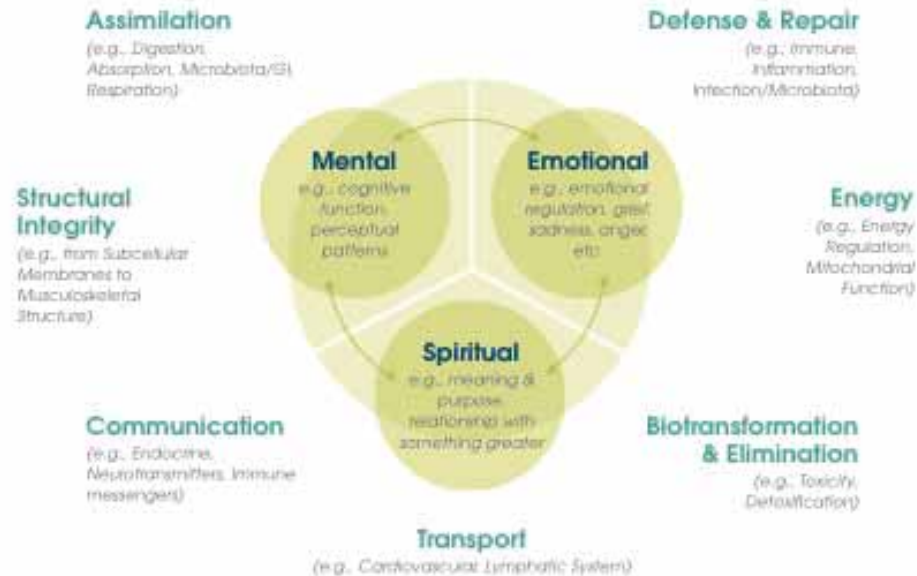
## Retelling the Patient's Story

**Antecedents**  
(Predisposing Factors—  
Genetic/Environmental)

**Triggering Events**  
(Activators)

**Mediators/Perpetuators**  
(Contributors)

## Physiology and Function: Organizing the Patient's Clinical Imbalances



## Modifiable Personal Lifestyle Factors

Sleep & Relaxation

Exercise & Movement

Nutrition

Stress

Relationships

Name: \_\_\_\_\_ Date: \_\_\_\_\_ CC: \_\_\_\_\_ © 2014 Institute for Functional Medicine

# Functional Medicine Approach to Fatigue

# The Matrix & Symptom Organization

The Patient's Story Retold	Physiology and Function: Organizing the Patient's Clinical Imbalances	
<p><b>Antecedents</b></p> <p>FH: Depression DM 2 CVD</p>	<p><b>Assimilation</b></p> <p>GERD (+ PPI) Gas/Bloating Chronic nausea Lactose intolerant, daily dairy intake</p>	<p><b>Defense &amp; Repair</b></p> <p>—</p>
<p><b>Triggering Events</b></p> <p>"Rice diet" Childbirth</p>	<p><b>Structural Integrity</b></p> <p>Osteopenia Dental caries Joint pain</p>	<p><b>Energy</b></p> <p>Daytime somnolence Exercise intolerance</p>
<p><b>Mediators/Perpetuators</b></p>	<p><b>Communication</b></p> <p>35lb weight ↑ NES ↓ Libido</p>	<p><b>Biotransformation &amp; Elimination</b></p> <p>Multiple amalgam fillings</p>

Mental

Anxiety  
BPAD  
Depression  
"Brain fog"  
Hx PPD

Emotional

Spiritual

Transport

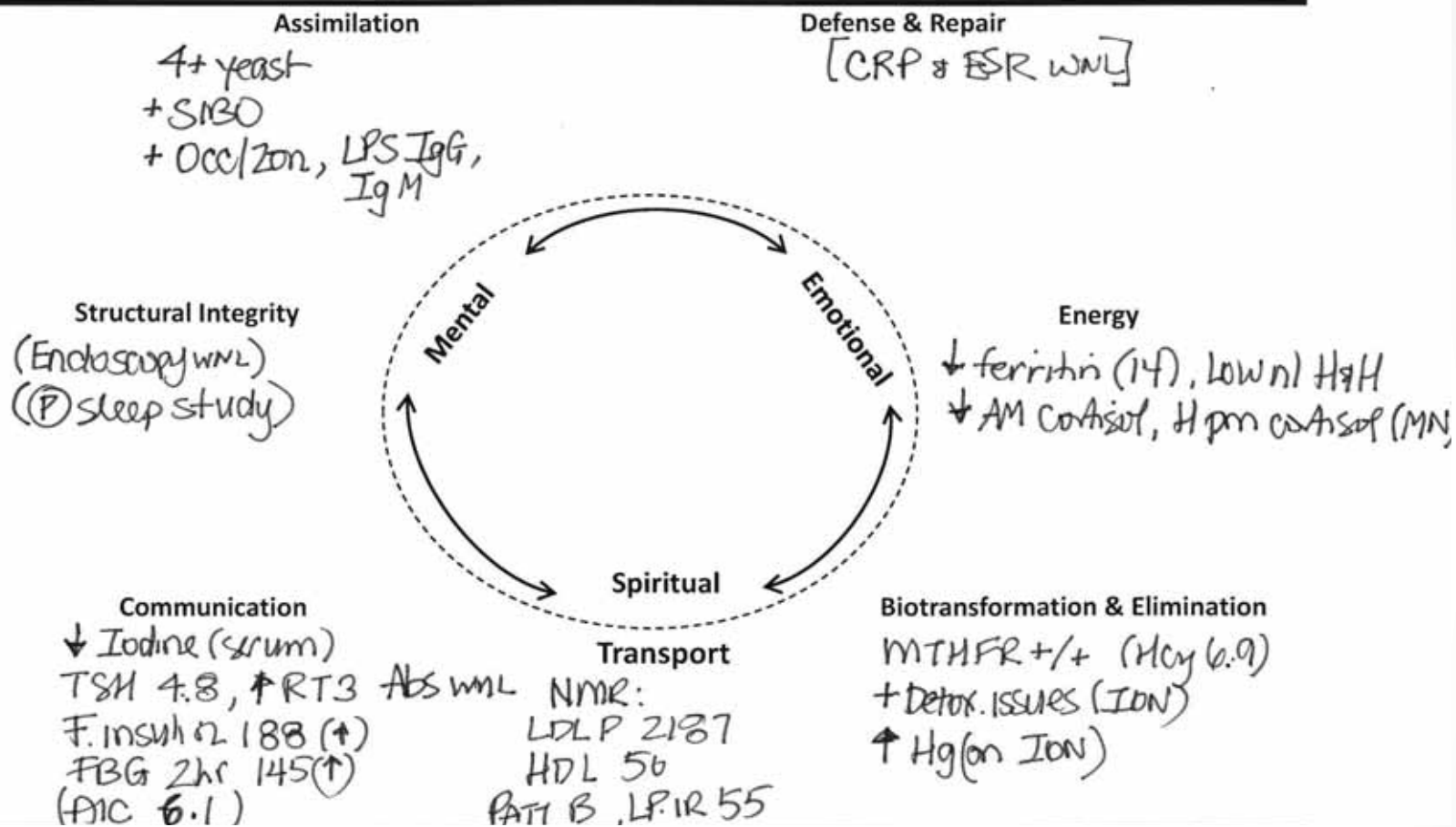
"Cold all the time"

# Food Journal Review

Daily Bowel Movements:

TIME	FOOD/BEVERAGE AMOUNT
AM 7:00	Rice, vegetable, bean soup (500 ml) <del>Mashed</del>
AM 10:00	Half Banana / 1/4 Apple
PM 1:00	<del>Beans</del> 1 cup of soup. (beans)
3:00	Yogurt with rice (100 mg) (cooked) <del>on ground</del>
6:50	Rice with curry (500 mg)

# The Matrix & Labs



Chesson AL Jr, et al. The indications for polysomnography and related procedures. Sleep 1997; 20:423.

Bansal, AS et al Chronic fatigue syndrome, the immune system and viral infection Brain, Behavior, and Immunity, 26 (1) (2012), pp. 24–31

Kumari, M. Cortisol secretion and fatigue: Associations in a community based cohort Psychoneuroendocrinology Volume 34, Issue 10, November 2009, Pages 1476–1485

Fasano, A. Leaky Gut and Autoimmune Diseases. Clinical Reviews in Allergy & Immunology. February 2012, Volume 42, Issue 1, pp 71-78.

Maes, M et al. The gut-brain barrier in major depression: Intestinal mucosal dysfunction with an increased translocation of LPS from gram negative enterobacteria (leaky gut) plays a role in the inflammatory pathophysiology of depression. Neuroendocrinol Lett 2008;29(1): 117–124.

Natividad, J and E Verdu. Modulation of intestinal barrier by intestinal microbiota: Pathological and therapeutic implications. Pharmacological Research Volume 69, Issue 1, March 2013, Pages 42–51



**2100 GI Effects® Function Profile - Stool**

Me

**Pathogenic Bacteria**95% Reference  
Range

Helicobacter pylori	<0.01	<=1.0E+005
E. coli 0157:H7	<0.01	<=1.0E+005
Clostridium difficile	<0.01	<=1.0E+005
Campylobacter sp.	4.2E+006 <b>H</b>	<=1.0E+005

**Yeast/Fungi**Expected  
Value


Yeast/Fungi; taxonomy unavailable. **+4 => 100000 pg DNA/g specimen** Neg

A taxonomy unavailable finding may indicate ingested mold. The higher the number, the greater the indication for treatment, particularly when accompanied by clinical symptoms.

**Parasites**Expected  
Value

No Ova or Parasites

**Adiposity Index**

Firmicutes	55		<= 80
Bacteroidetes	45		>= 20

## 2155 GI Effects® Sensitivity Fungi Profile - Stool

<b>Pharmaceuticals</b>	Sensitive	Resistant
Amphotericin	<b>S</b>	
Fluconazole		<b>R</b>
Itraconazole		<b>R</b>
Ketoconazole		<b>R</b>
Nystatin	<b>S</b>	

<b>Botanicals</b>	Sensitive	Resistant
5-Hydroxy-1,4-naphthoquinone Black Walnut		<b>R</b>
Alliin Garlic		<b>R</b>
Arbutin Uva Ursi		<b>R</b>
Artemisinin Wormwood		<b>R</b>
Berberine Goldenseal	<b>S</b>	
Caprylic acid Octanoic acid	<b>S</b>	
Carvacrol Oregano	<b>S</b>	
Oleuropein Olive Leaf		<b>R</b>
Quinic Acid Cats Claw		<b>R</b>
Thymol Oil of Thyme		<b>R</b>
Undecylenic acid Undecylenic acid	<b>S</b>	

## ARRAY 2

### Intestinal Antigenic Permeability Screen

	Normal	Equivocal*	Out of Range	Nun Va
Actomyosin IgA**			X	25.
Occludin/Zonulin IgG	X			0.
Occludin/Zonulin IgA		X		1.
Occludin/Zonulin IgM	X			1.
Lipopolysaccharides(LPS)IgG			X	3.
Lipopolysaccharides(LPS)IgA	X			1.
Lipopolysaccharides(LPS)IgM			X	2.

Fasano, A. Zonulin and Its Regulation of Intestinal Barrier Function: The Biological Door to Inflammation, Autoimmunity, and Cancer. *Physiological Reviews* Published 1 January 2011 Vol. 91 no. 1, 151-175

Camilleri, M et al. Intestinal barrier function in health and gastrointestinal disease. *Neurogastroenterology & Motility* Volume 24, Issue 6, 503-512, June 2012

## TEST

## RESULTS

## ARRAY 4

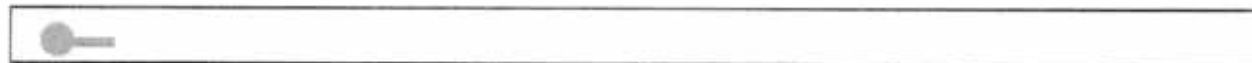
	Normal	Equivocal*	Out of Range	Numeric Value	REFERENCE (ELISA Index)
<b>Gluten-Associated Cross-Reactive Foods &amp; Foods Sensitivity**</b>					
Rye, Barley, Spelt, Polish Wheat	X			<0.4	0.4-1.4
Cow's Milk	X			0.46	0.1-1.3
Casein (Alpha & Beta)	X			0.32	0.1-1.2
Casomorphin	X			0.52	0.2-1.6
Milk Butyrophilin		X	.	0.91	0.1-1.3
Whey Protein		X	.	1.10	0.1-1.3
Chocolate (Milk)	X			0.35	0.1-1.4
Oats			X	1.05	0.2-1.0
Yeast		X	.	1.11	0.2-1.2
Coffee	X			0.59	0.2-1.2
Sesame	X			0.53	0.1-1.3
Buckwheat	X			<0.4	0.4-1.5
Sorghum		X	.	0.98	0.3-1.2
Millet			X	2.10	0.3-1.5
Hemp			X	2.11	0.3-1.5
Amaranth	X			0.34	0.2-1.3
Quinoa	X			0.61	0.5-1.5
Tapioca			X	1.19	0.1-1.1
Teff			X	1.14	0.2-1.1
Soy	X			0.80	0.5-1.5
Egg	X			0.52	0.2-1.7
Corn			X	1.52	0.3-1.4
Rice	X			0.90	0.4-1.6
Potato	X			0.69	0.6-1.4

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 55 Pittfield Road  
 Suite 9  
 Lenox, MA 01240

DoB: 8/27/1966  
 ID: 42127  
 GENDER: F

TEST		RESULTS			
ARRAY 3	Normal	Equivocal*	Out of Range	Numeric Value	Reference (ELISA Index)
<b>Wheat/Gluten Proteome Reactivity &amp; Autoimmunity</b>					
Wheat IgG	X			1.10	0.3-1.5
Wheat IgA	X			0.72	0.1-1.2
Wheat Germ Agglutinin IgG	X			0.87	0.4-1.3
Wheat Germ Agglutinin IgA	X			0.22	0.2-1.1
Native& Deamidated Gliadin 33 IgG	X			0.73	0.2-1.2
Native& Deamidated Gliadin 33 IgA	X			0.59	0.1-1.1
Alpha Gliadin 17-mer IgG		X	.	1.16	0.1-1.5
Alpha Gliadin 17-mer IgA	X			0.61	0.1-1.1
Gamma Gliadin 15-mer IgG		X	.	1.17	0.5-1.5
Gamma Gliadin 15-mer IgA			X	1.22	0.1-1.0
Omega Gliadin 17-mer IgG	X			0.89	0.3-1.2
Omega Gliadin 17-mer IgA		X	.	0.95	0.1-1.2
Glutenin 21-mer IgG	X			0.61	0.1-1.5
Glutenin 21-mer IgA	X			0.94	0.1-1.3
Gluteomorphin + Prodynorphin IgG			X	1.80	0.3-1.2
Gluteomorphin + Prodynorphin IgA	X			0.63	0.1-1.2
Gliadin-Transglutaminase Complex IgG		X	.	1.26	0.3-1.4
Gliadin-Transglutaminase Complex IgA	X			0.95	0.2-1.5
Transglutaminase-2 IgG	X			1.00	0.3-1.6
Transglutaminase-2 IgA	X			1.16	0.1-1.6
Transglutaminase-3 IgG	X			1.05	0.2-1.6
Transglutaminase-3 IgA	X			0.83	0.1-1.5
Transglutaminase-6 IgG		X	.	1.27	0.2-1.5
Transglutaminase-6 IgA		X	.	1.31	0.1-1.5

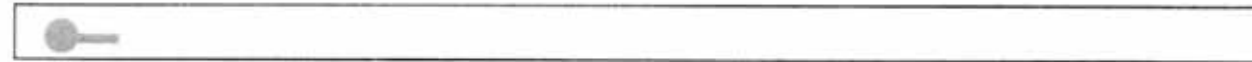
Sulfate



Low significance

High significance

### Essential Fatty Acid Insufficiency



Low significance

High significance

### Disordered Methyl Group (Single carbon) Transfer

Homocysteine		Xanthurenate	X	MeMalonate	H	FIGLU	
Mercury		Citrate		Cis-Aconitate		Isocitrate	
Quinolate	H	2-MeHipp		Orotate	II	Glucarate	II

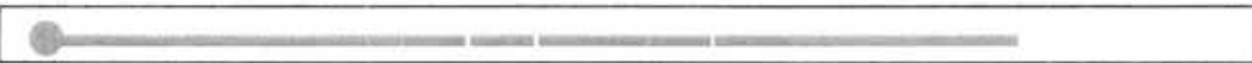


Low significance

High significance

### Detoxification Impairment

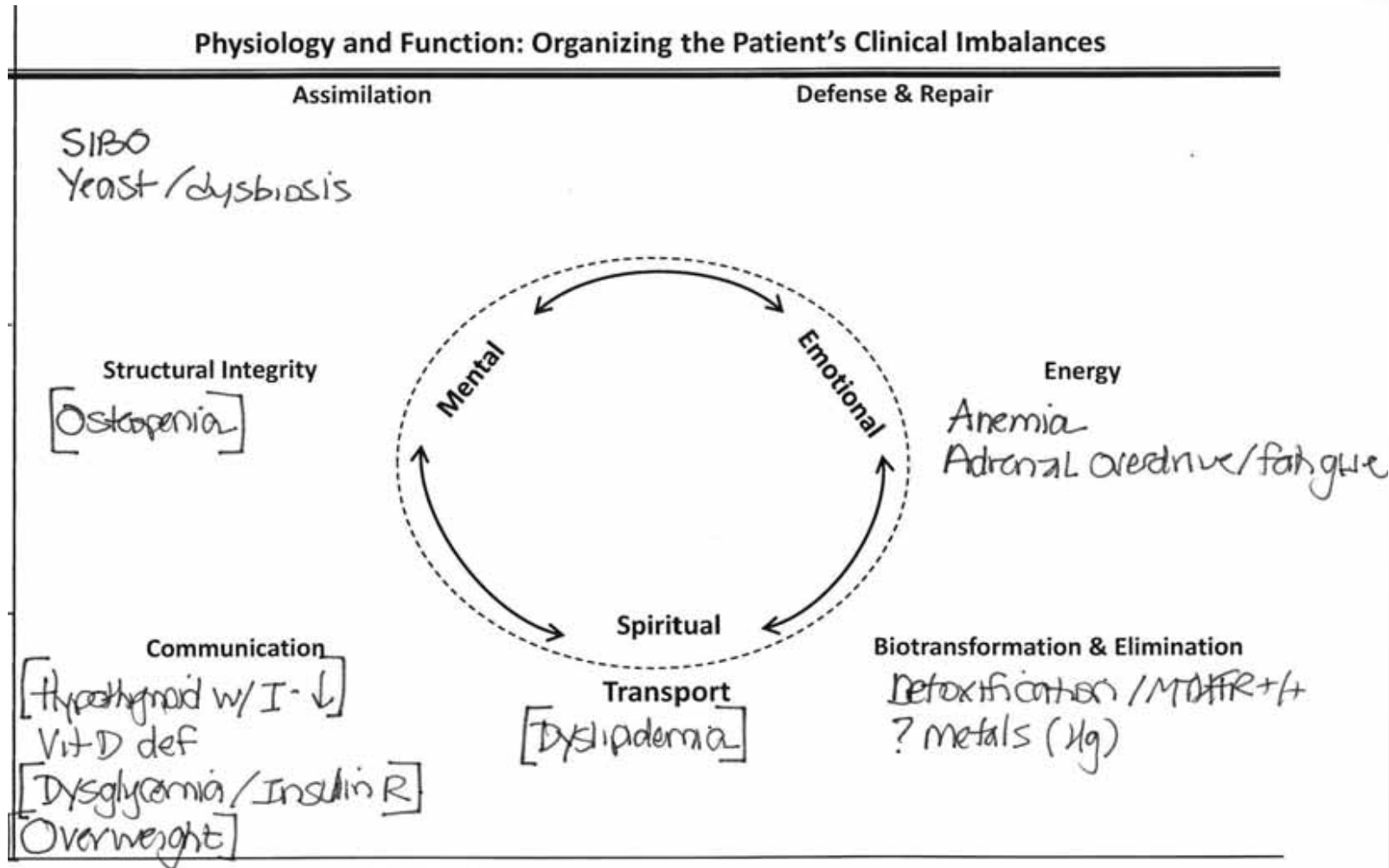
Methionine		Glycine		Serine		Taurine	
Glutamine		Pyroglutamate	II	Sulfate		Benzoate	II



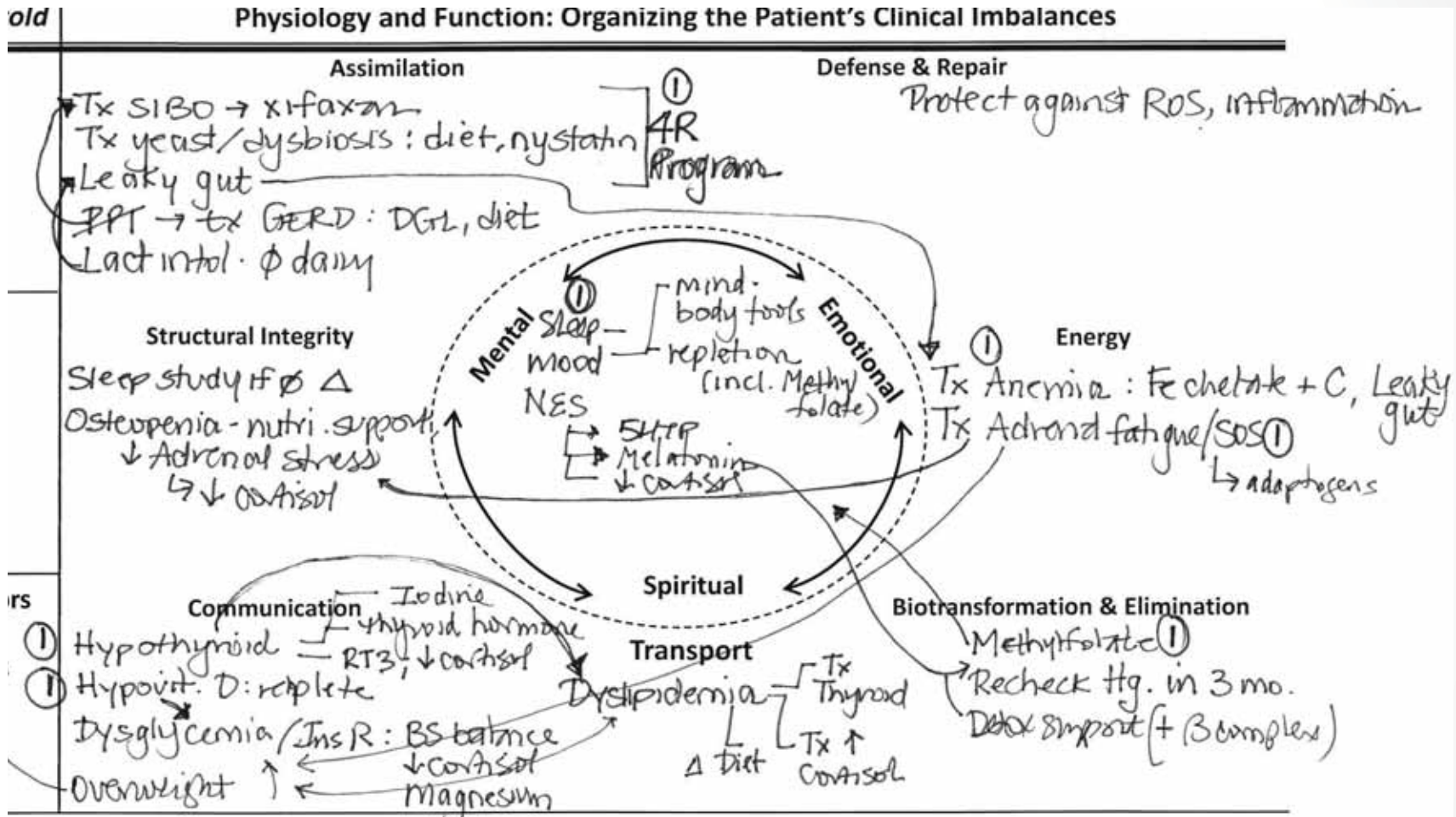
Low significance

High significance

# Matrix: Organize a Root Cause Assessment



# Matrix: Organize Treatment



Lasselin, J et al. Fatigue symptoms relate to systemic inflammation in patients with type 2 diabetes. *Brain, Behavior, and Immunity* Volume 26, Issue 8, November 2012, Pages 1211–1219

Leese G et al. Short-term night-shift working mimics the pituitary-adrenocortical dysfunction of chronic fatigue syndrome. *J Clin Endocrinol Metab* 1996; 81:1867–1870

Lattie, EG, et al Stress management skills, neuroimmune processes and fatigue levels in persons with chronic fatigue syndrome. *Brain Behav. Immun.* (2012)

Clevenger L et al. Sleep disturbance, cytokines, and fatigue in women with ovarian cancer. [Brain Behav Immun.](#) 2012 Oct;26(7):1037-44



# Using the Matrix to Trend Results

- **Mind/Mood**
  - Sleep improved, falling asleep more easily, no night waking
  - No NES on melatonin and 5-HTP
  - Rarely needs more than a brief rest in the early evening
  - Lavender oil and adrenal support with ashwagandha before bed
- **Assimilation**
  - SIBO – resolved after 1 course xifaxan, nausea improved also on HCL now and antimicrobial botanicals for support
  - 4+ yeast – cleared on repeat testing s/p nystatin, no gas, bloating
  - GERD sx resolved, off PPI, taking DGL, dietary changes made
  - Off of dairy
- **Defense/Repair**
  - Taking curcumin 1000 mg BID
- **Energy**
  - Anemia resolved; Hct >30 → 37.4, ferritin from 14 → 23 → 53
- **Biotrans/Detox**
  - Taking 5 mg methylfolate/day
  - To revisit Hg levels and amalgams
- **Transport**
  - LDL-P 1817, LDL-C 103, LDL-p 1084
  - A1C → 5.6
  - Glucose F93, 1hr 166, 2 hr. 116
  - Ins 1 hr 127s
- **Communication**
  - Vitamin D now 61s, reduced to 2000 units/day
  - TSH → started on Armour → TSH 1.0 FT3 2.9
  - Has lost 20 lbs, several pants sizes
- **Structural**
  - Joint pain improved, continuing curcumin

# GIFX Post Treatment

## 2205 Microbial Ecology Profile

Methodology: DNA Analysis, Microscopic, EIA

### Yeast/Fungi

### Expected Value

No clinically significant amounts.

### Yeast/Fungi

Yeast overgrowth has been linked to many chronic conditions, in part because of antigenic responses in some patients to even low rates of yeast growth. Potential symptoms include diarrhea, headache, bloating, atopic dermatitis and fatigue. Positives are reported as +1, +2, +3 or +4 indicating >100, >1000, >10000 or >100000 pg DNA/g.

### Parasitology

#### Microscopic Exam Results:\*

### Parasitology

Parasite Recovery: Literature suggests that >90% of enteric parasitic infections are detected in a sample from a single stool collection. Increased sensitivity results from the collection of additional specimens on separate days. Parasites have been detected in 20-24% of U.S. patients with mild to moderate GI symptoms.

No ova or parasites seen

# SIBO



## Bacterial Overgrowth of the Small Intestine Breath Test

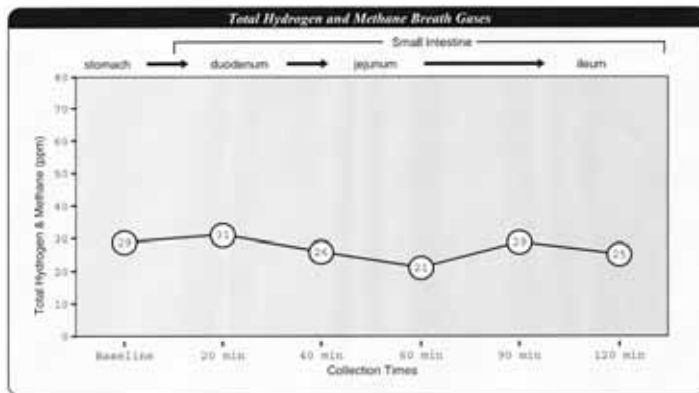


63 Ziliox Street  
Asheville, NC 28801  
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Patient: JAYASREE  
PAREPALLY  
DOB: August 27, 1966  
Sex: F  
MRN: 1232099429

Order Number: G1149219  
Completed: May 16, 2013  
Received: May 14, 2013  
Collected: May 13, 2013

UltraWellness Center  
Aviva Ramon MD  
55 Pittsfield Rd  
Lenox Commons Ste 9  
Lenox, MA 01240-2123



Minutes	Baseline	20	40	60	90	120
Hydrogen (H <sub>2</sub> )	26	29	23	18	26	22
Methane (CH <sub>4</sub> )	3	2	3	3	3	3
Total	29	31	26	21	29	25



This test was developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

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TBO3 RMS 1942 Rev 2



## Bacterial Overgrowth of the Small Intestine Breath Test

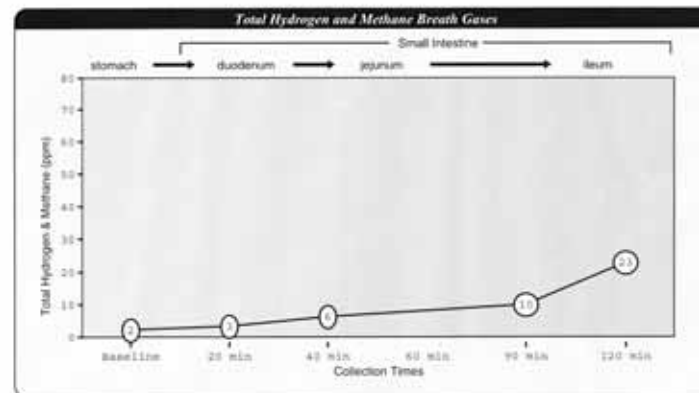


63 Ziliox Street  
Asheville, NC 28801  
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Patient: JAYASREE  
PAREPALLY  
DOB: August 27, 1967  
Sex: F  
MRN: 1232238137

Order Number: G9150149  
Completed: January 17, 2014  
Received: January 15, 2014  
Collected: January 14, 2014

UltraWellness Center  
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Minutes	Baseline	20	40	60	90	120
Hydrogen (H <sub>2</sub> )	2	3	5		9	21
Methane (CH <sub>4</sub> )	0	0	1		1	2
Total	2	3	6		10	23



This test was developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

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TBO3 RMS 1942 Rev 2

# The Long View: Coping with & Supporting the Fatigued Patient

- Can be challenging and frustrating.
  - Fatigued people often more “difficult” and frustrated.
  - High expectations.
  - Compassion fatigue a risk.
  - Have often seen many prior providers who have “failed” them.
- Poorer prognostic factors for complete recovery from fatigue symptoms:
  - More than eight medically unexplained physical symptoms (excluding symptoms in the case criteria for CFS/SEID).
  - A lifetime history of dysthymic disorder or comorbid psychiatric disorder.
  - Multiple chronic illnesses.
  - More than 1.5 years of chronic fatigue.
  - Less than 16 years of formal education.
  - Age exceeding 38 years at presentation.
  - Receipt of sickness or disability benefit.
  - A firm belief that physical causes were responsible for the fatigue.

# What Can Happen...

10 months later...

- Lost 25 + LBS and has kept it off.
- Says "Continue to feel much better because of you"
- "Anxiety has completely disappeared."
- "My stomach doing so well" - able to take her supplements
- "Armour has helped so much" sex drive returning!
- "Sleep is perfect"
- "No joint pain"
- "Mood better than [I] believed possible"
- Still get tired around 5 pm
- Increased self-awareness: Diet - for 3 mo was so religious and lost so much weight. Started eating yogurt and gluten again - after a week started feeling unwell, couldn't walk properly - so went back off completely and within a week the inflammation is gone.