Specialty Diagnostics for Nutritional Assessment:

Organix Comprehensive®

Overview of Topics

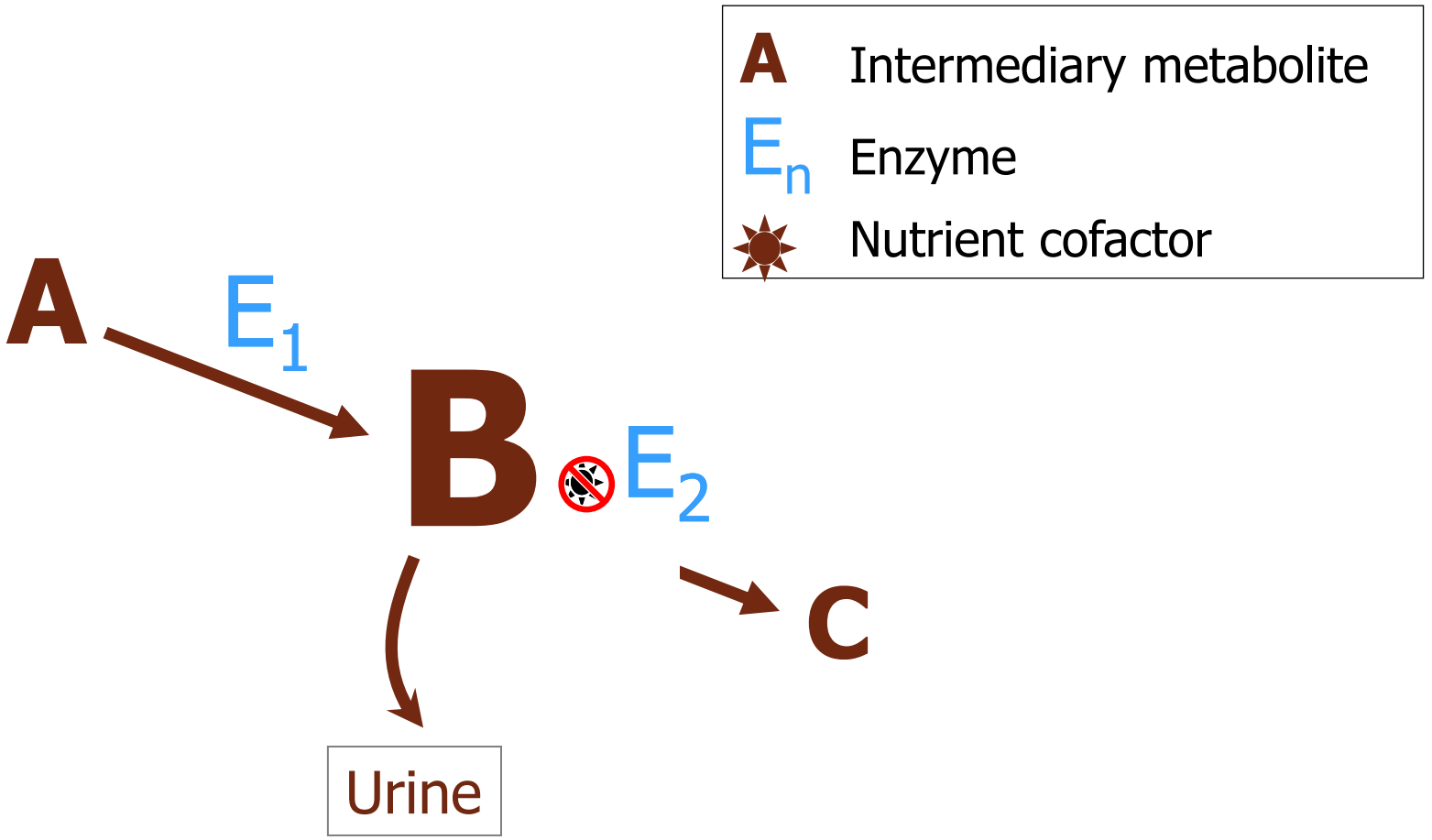
- Brief review of related biochemistry
- Learn when to consider an **Organix** profile
- Review some of the most important markers in the **Organix**
- **Organix** case study
- Discuss treatment considerations
- Incorporating the **Organix** into clinical practice

What are Organic Acids?

- Organic (carbon containing) compounds that possess acidic properties
- Metabolic intermediates in many different biochemical pathways in the body
  - Energy production
  - Detoxification
  - Metabolites of neurotransmitters and intestinal bacteria
  - Biotransformation
- Accumulation of specific organic acids can signify metabolic inhibition or blockage
  - Possibly due to nutrient deficiency, toxic interference, enzyme defect, and/or drug effect

Conceptual Framework:

Functional Indicators of Nutrient Deficiency



Organic Acids in Medical Literature

Published in final edited form as:
Diabetes Res Clin Pract. 2014 June ; 104(3): 393–400. doi:10.1016/j.diabres.2014.03.001.

Early pregnancy urinary biomarkers of fatty acid and carbohydrate metabolism in pregnancies complicated by gestational diabetes

Chunfang Qiu[a,*], Daniel A. Enquobahrie[a,b], Ihunnaya O. Frederick[a], Tanya K. Sorensen[a], Miguel Angel Luque Fernandez[c], Robert M. David[d], J. Alexander Bralley[d], and Michelle A. Williams[a,c]

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[c]Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA

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Abstract

Aims—Alterations in organic acid biomarkers from fatty acid and carbohydrate metabolism have been documented in type 2 diabetes patients. However, their association with gestational diabetes mellitus (GDM) is largely unknown.

Methods—Participants were 25 GDM cases and 25 non-GDM controls. Biomarkers of fatty acid (adipate, suberate and ethylmalonate) and carbohydrate (pyruvate, ι-lactate and β-hydroxybutyrate) metabolism were measured in maternal urine samples collected in early pregnancy (17 weeks) using liquid chromatography–mass spectrometry methods. Logistic regression were used to calculate odds ratios (OR) and 95% confidence intervals (CI).

Results—GDM cases and controls differed in median urinary concentrations of ethylmalonate (3.0 vs. 2.3 μg/mg creatinine), pyruvate (7.4 vs. 2.1 μg/mg creatinine), and adipate (4.6 vs. 7.3 μg/mg creatinine) (all *p*-values <0.05). Women in the highest tertile for ethylmalonate or pyruvate concentrations had 11.4-fold (95%CI 1.10–117.48) and 3.27-fold (95%CI 0.72–14.79) increased risk of GDM compared with women in the lowest tertile for ethylmalonate and pyruvate concentrations, respectively. Women in the highest tertile for adipate concentrations, compared with women in the lowest tertile, had an 86% reduction in GDM risk (95%CI 0.02–0.97).

Conclusions—These preliminary findings underscore the importance of altered fatty acid and carbohydrate metabolism in the pathogenesis of GDM.

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Conflict of interest statement
There is no conflict of interest to declare.

Appendix A. Supplementary data
Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.diabres.2014.03.001.

Organic acid … human blood and
urine, are deg … intestinal bacterial
action on foo … tion, neurotransmitter
metabolism, … metabolism [13].
Measuremen … lipate reflect metabolic
processes inv … ine-dependent
pathways) an … ed concentrations of
organic acids … ological markers of
disturbed car …

Qiu C, et al. *Diabetes Res Clin Pract*. 2014; 104(3): 393–400.

Xanthurenate

- Produced in tryptophan catabolism
- Functional marker of Vitamin B6 insufficiency

J Nutr. 2013 Sep;143(9):1509-19. doi: 10.3945/jn.113.174599. Epub 2013 Jul 31.

A mathematical model of tryptophan metabolism via the kynurenine pathway provides insights into the effects of vitamin B-6 deficiency, tryptophan loading, and induction of tryptophan 2,3-dioxygenase on tryptophan metabolites.

Rios-Avila L[1], Nijhout HF, Reed MC, Sitren HS, Gregory JF 3rd.

Author information

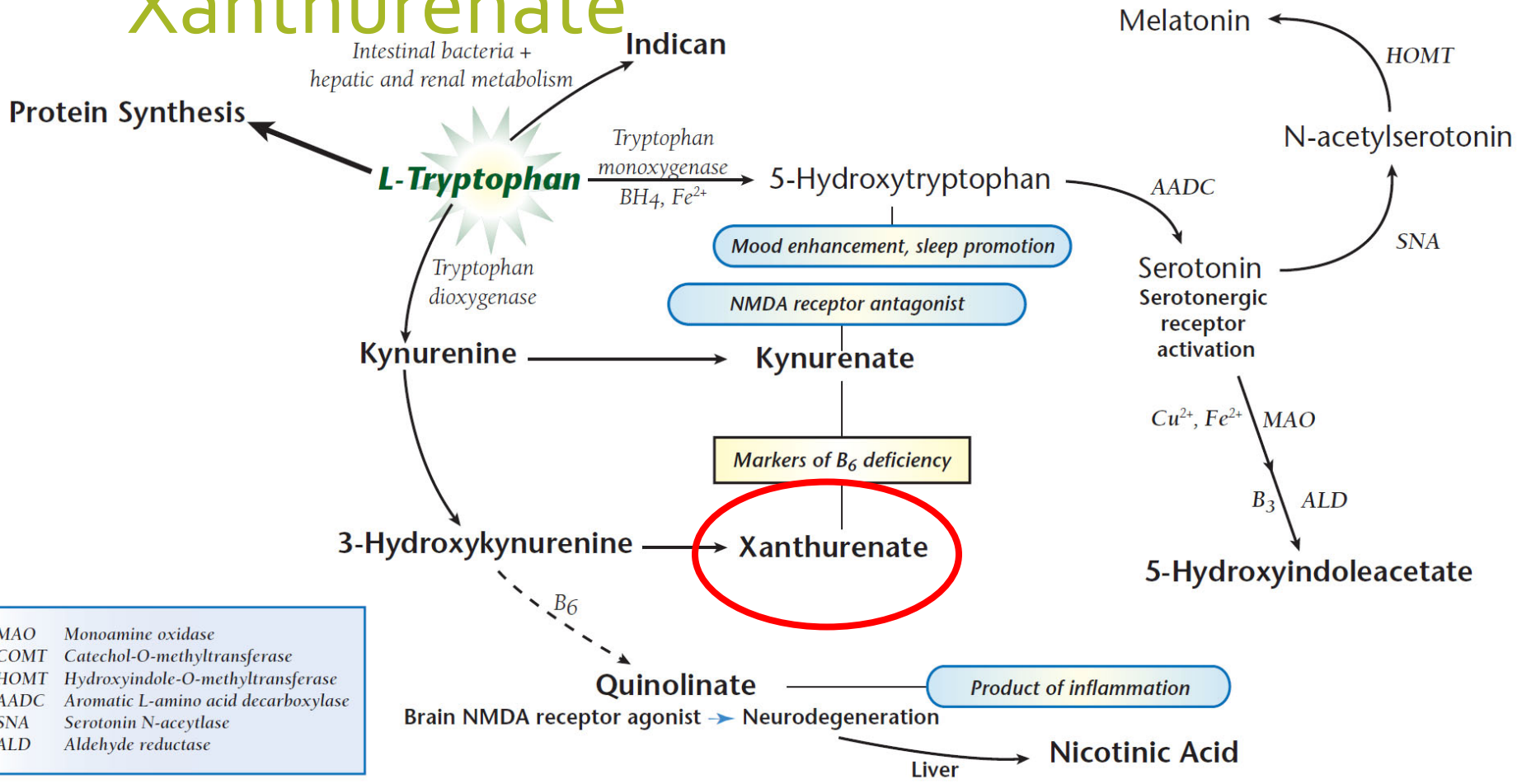
Abstract

Vitamin B-6 deficiency is associated with impaired tryptophan metabolism because of the coenzyme role of pyridoxal 5'-phosphate (PLP) for kynureninase and kynurenine aminotransferase. To investigate the underlying mechanism, we developed a mathematical model of tryptophan metabolism via the kynurenine pathway. The model includes mammalian data on enzyme kinetics and tryptophan transport from the intestinal lumen to liver, muscle, and brain. Regulatory mechanisms and inhibition of relevant enzymes were included. We simulated the effects of graded reduction in cellular PLP concentration, tryptophan loads and induction of tryptophan 2,3-dioxygenase (TDO) on metabolite profiles and urinary excretion. The model predictions matched experimental data and provided clarification of the response of metabolites in various extents of vitamin B-6 deficiency. We found that moderate deficiency yielded increased 3-hydroxykynurenine and a decrease in kynurenic acid and anthranilic acid. More severe deficiency also yielded an increase in kynurenine and xanthurenic acid and more pronounced effects on the other metabolites. Tryptophan load simulations with and without vitamin B-6 deficiency showed altered metabolite concentrations consistent with published data. Induction of TDO caused an increase in all metabolites, and TDO induction together with a simulated vitamin B-6 deficiency, as has been reported in oral contraceptive users, yielded increases in kynurenine, 3-hydroxykynurenine, and xanthurenic acid and decreases in kynurenic acid and anthranilic acid. These results show that the model successfully simulated tryptophan metabolism via the kynurenine pathway and can be used to complement experimental investigations.

PMID: 23902960 PMCID: PMC3743279 DOI: 10.3945/jn.113.174599

Rios-Avila L, et al. *J Nutr.* 2013;143(9):1509-19.

Xanthurenate



Methylmalonate (MMA)

- Functional marker of Vitamin B12 insufficiency
- Intermediate in the catabolism of valine
- MMA is converted into succinyl-CoA by methylmalonyl-CoA mutase, a B12-dependent enzyme

J Diabetes Res. 2014;2014:921616. doi: 10.1155/2014/921616. Epub 2014 Feb 26.

Urinary methylmalonic acid as an indicator of early vitamin B12 deficiency and its role in polyneuropathy in type 2 diabetes.

Sun AL[1], Ni YH[1], Li XB[1], Zhuang XH[1], Liu YT[1], Liu XH[2], Chen SH[3].

Author information

Abstract

The rising incidence of diabetes and its negative impact on quality of life highlights the urgent need to develop biomarkers of early nerve damage. Measurement of total vitamin B12 has some limitations. We want to determine the levels of urinary methylmalonic acid and its relationships with serum vitamin B12 and polyneuropathy. The 176 Chinese patients with Type 2 diabetes mellitus were divided into 3 groups according to the levels of vitamin B12. A gas chromatography mass spectrometric technique was used to determine blood methylmalonic acid and urinary methylmalonic acid. The diagnosis of distal diabetic polyneuropathy was based on the determination of bilateral limb sensory and motor nerve conduction velocity and amplitude with electromyogram. Multiple regression analysis revealed that urinary methylmalonic acid/creatinine, blood methylmalonic acid, and so forth were variables that influenced diabetic polyneuropathy significantly. Nerve sensory conduction velocity and nerve amplitude in the group of urinary methylmalonic acid/creatinine >3.5 mmol/mol decreased significantly. Superficial peroneal nerve sensory and motor conduction velocity and ulnar nerve compound motor active potential amplitude were inversely correlated with urinary methylmalonic acid/creatinine. Urinary methylmalonic acid correlates with serum vitamin B12 levels in person with diabetes and is a sensitive marker of early polyneuropathy.

PMID: 24719898 PMCID: PMC3955587 DOI: 10.1155/2014/921616

Sun AL, et al. *J Diabetes Res*. 2014;2014:921616.

Organix Rationale

Why not just measure vitamin B12 in serum?

"Several studies have suggested that the determination of serum or urinary methylmalonic acid could be a more reliable marker of cobalamin deficiency than direct cobalamin determination."

Mayo Clinic Laboratories Interpretive Handbook, 2020

Organix Comprehensive®

- Energy production markers
- B-Complex vitamin markers
- Methylation cofactor markers
- Neurotransmitters metabolism markers
- Oxidative damage and antioxidant markers
- Detoxification indicators
- Intestinal dysbiosis markers

When to Consider

- Mood imbalances
- Sleep disturbance
- Myalgia
- Fatigue
- Immune dysfunction

When to Consider

- Nutrient-depleted diets
- Sports fitness
- Nutrient depletions 2° or 3° to other interventions:
  - Medications
  - Special diets (vegan, etc.)
  - GI surgeries (gastric bypass, gall bladder removal, etc.)

Case History

Case: 32 y/o Female

- **Chief complaint**: fatigue x 2 years
  - Normal CBC, CMP, thyroid, and Fe
- ROS: constipation and occasional loose stools; diagnosed with IBS by her primary doctor
- Abundance of processed foods in the diet
- No medications or dietary supplements
- Drinks a few glasses of wine per night; stays up very late and eats biggest meal at night; skips breakfast

3301 Organix ® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectrometry, Colorimetric

Summary of Abnormal Findings		
Biomarkers	**Findings**	**Metabolic Pathway**
Fatty Acid Metabolism		
Suberate	**Borderline High**	Fatty acid oxidation
Carbohydrate Metabolism		
L-Lactate	**Borderline High**	Glycolysis
b-Hydroxybutyrate	**Borderline High**	Ketone production
Energy Production Markers		
Citrate	**Borderline High**	Citric acid cycle
Cis-Aconitate	**Borderline High**	Citric acid cycle
Isocitrate	**Borderline High**	Citric acid cycle
Fumarate	**Borderline High**	Citric acid cycle
B-Complex Vitamin Markers		
a-Keto-b-Methylvalerate	**Borderline High**	Amino acid metabolism
Xanthurenate	H	Amino acid metabolism
b-Hydroxyisovalerate	H	Amino acid metabolism
Methylation Cofactor Markers	No Abnormality Found	
Neurotransmitter Metabolism Markers		
5-Hydroxyindoleacetate	**Borderline High**	Serotonin metabolism
Kynurenate	H	Tryptophan pathway
Oxidative Damage and Antioxidant Markers		
p-Hydroxyphenyllactate	H	Gut bacterial metabolism
Detoxification Indicators		

Summary of Abnormal Findings (Continued)

Summary of Abnormal Findings		
Biomarkers	**Findings**	**Metabolic Pathway**
Pyroglutamate	**Borderline High**	Glutathione pathway
Sulfate	**Borderline High**	Transsulfuration pathway
Bacterial - General		
Phenylacetate	H	Gut bacterial metabolism
p-Hydroxybenzoate	H	Gut bacterial metabolism
p-Hydroxyphenylacetate	**Borderline High**	Gut bacterial metabolism
L. acidophilus/General Bacteria		
D-Lactate	**Borderline High**	Bacterial or human metabolism byproduct
Clostridial Species	No Abnormality Found	
Yeast/Fungal	No Abnormality Found	

3301 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectrometry, Colorimetric

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

Ranges: Ages 13 and over

	Results mcg/mg creatinine	QUINTILE DISTRIBUTION (1st | 2nd | 3rd | 4th | 5th)	95% Reference Range
Nutrient Markers			
Fatty Acid Metabolism *(Carnitine & B2)*			
1. Adipate	3.5	6.2	<= 11.1
2. Suberate	2.2	2.1	<= 4.6
3. Ethylmalonate	2.9	3.6	<= 6.3
Carbohydrate Metabolism *(B1, B3, Cr, Lipoic Acid, CoQ10)*			
4. Pyruvate	<DL	3.9	<= 6.4
5. L-Lactate	9.7	8.5	0.6 - 16.4
6. β-Hydroxybutyrate	3.4	2.1	<= 9.9
Energy Production (Citric Acid Cycle) *(B Comp., CoQ10, Amino Acids, Mg)*			
7. Citrate	726	601	56 - 987
8. Cis-Aconitate	66	51	18 - 78
9. Isocitrate	113	98	39 - 143
10. α-Ketoglutarate	1.0	19.0	<= 35.0
11. Succinate	2.5	11.6	<= 20.9
12. Fumarate	0.95	0.59	<= 1.35
13. Malate	1.3	1.4	<= 3.1
14. Hydroxymethylglutarate	2.8	3.6	<= 5.1

Organix: Clinical Application of Findings

Fatty Acid Metabolism
(Carnitine & B2)

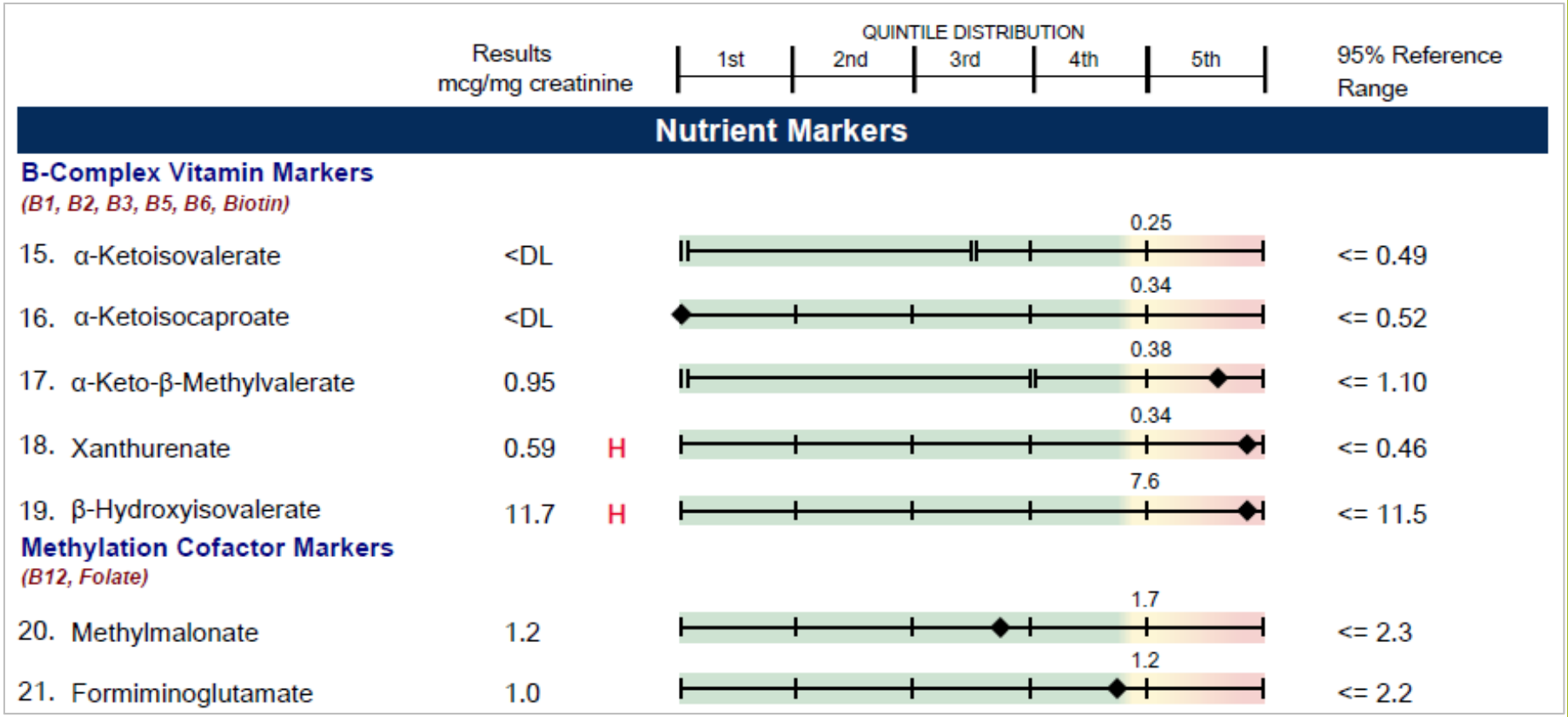
1. Adipate
2. Suberate
3. Ethylmalonate

Carbohydrate Metabolism
(B1, B3, Cr, Lipoic Acid, CoQ10)

4. Pyruvate
5. L-Lactate
6. β-Hydroxybutyrate

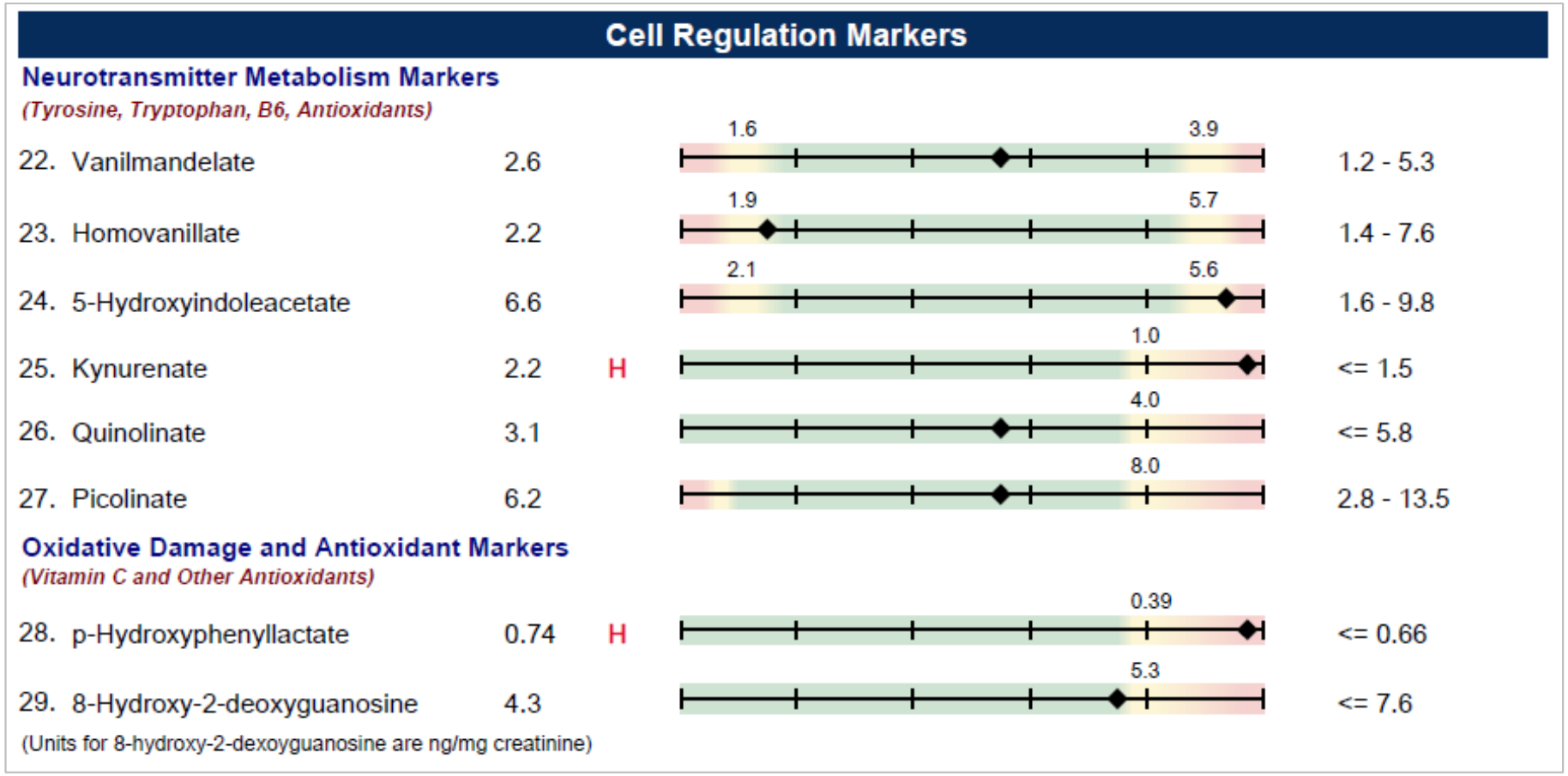
Energy Production (Citric Acid Cycle)
(B Comp., CoQ10, Amino Acids, Mg)

7. Citrate
8. Cis-Aconitate
9. Isocitrate
10. α-Ketoglutarate
11. Succinate
12. Fumarate
13. Malate
14. Hydroxymethylglutarate



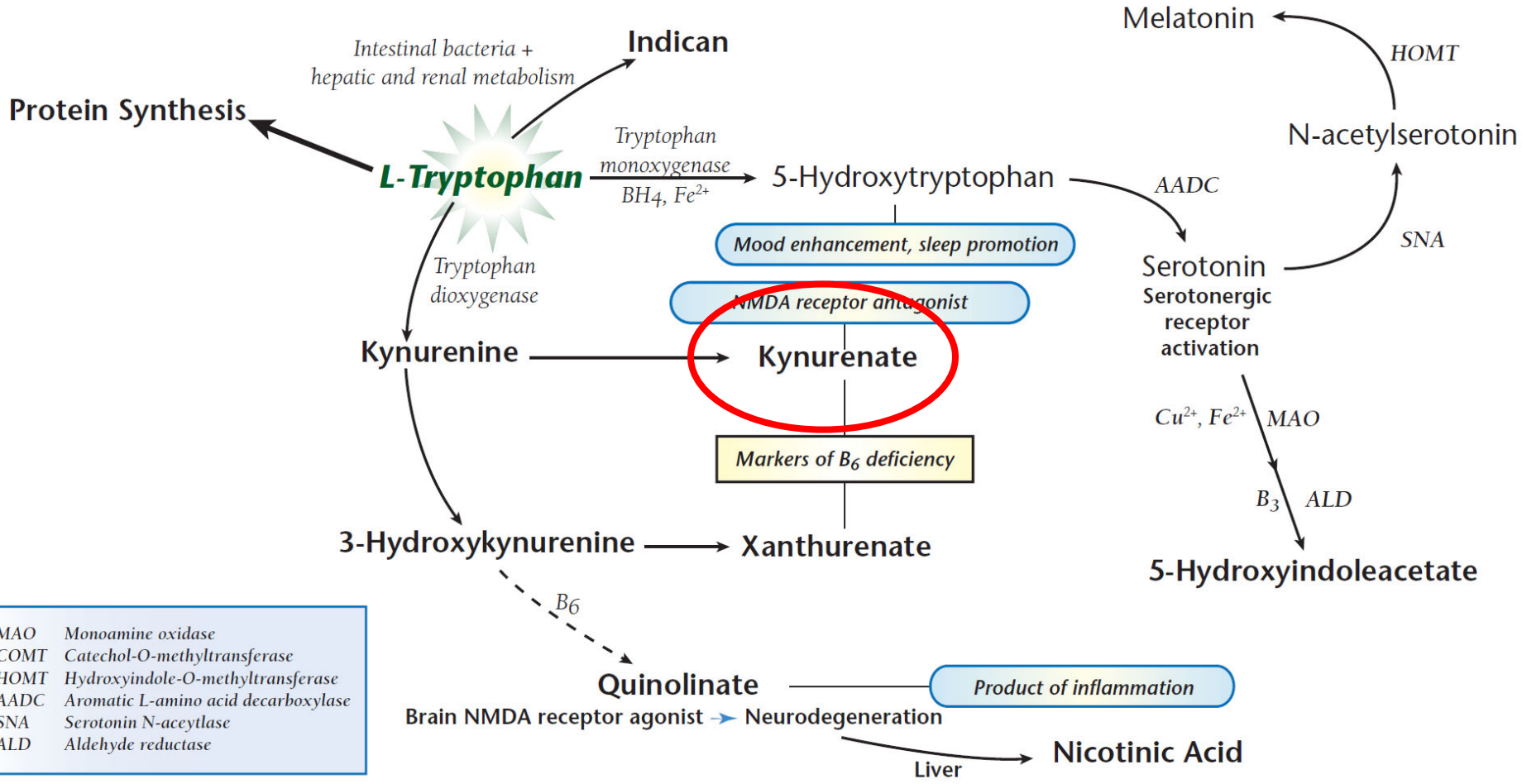
- Elevated Xanthurenate suggests a need for vitamin B6
- Elevated β-Hydroxyisovalerate suggests a need for biotin

Rios-Avila L, et al. *J Nutr*. 2013;143(9):1509-19.
Wolf, B. *Genetics in Medicine.* 2012;14:565–575.



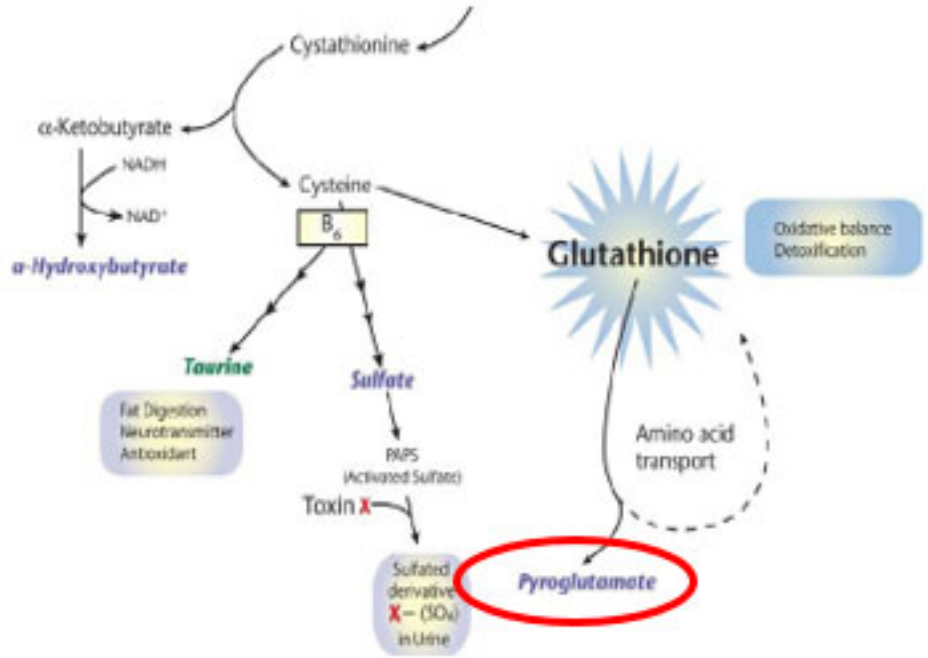
- Elevated Kynurenate suggests a need for vitamin B6
- Elevated p-hydroxyphenyllactate suggests a need for antioxidant support

Ueland, PM. et al. *Mol Aspects Med*. 2016;53:10-27.
Beloborodova, N. et al. *J Biomed Sci*. 2012; 19(1): 89.



Ueland, PM. et al. *Mol Aspects Med*. 2016;53:10-27.

	Results mcg/mg creatinine	QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	95% Reference Range
Toxicants and Detoxification			
Detoxification Indicators *(Arg, NAC, Met, Mg, Antioxidants)*			
30. 2-Methylhippurate	0.056	0.084	<= 0.192
31. Orotate	0.17	0.69	<= 1.01
32. Glucarate	<DL	6.3	<= 10.7
33. α-Hydroxybutyrate	<DL	0.3	<= 0.9
34. Pyroglutamate	60	59	28 - 88
35. Sulfate	2,663	958 2,347	690 - 2,988



Compounds of Bacterial or Yeast/Fungal Origin

Bacterial - General				
36. Benzoate	<DL		0.6	<= 9.3
37. Hippurate	283		548	<= 1,070
38. Phenylacetate	0.55	H	0.11	<= 0.18
39. Phenylpropionate	<DL			<= 0.06
40. p-Hydroxybenzoate	2.1	H	1.1	<= 1.8
41. p-Hydroxyphenylacetate	28		19	<= 34
42. Indican	36		64	<= 90
43. Tricarballylate	<DL		0.73	<= 1.41
L. acidophilus / General Bacterial				
44. D-Lactate	3.5		2.0	<= 4.1
Clostridial Species				
45. 3,4-Dihydroxyphenylpropionate	<DL			<= 0.05
Yeast / Fungal				
46. D-Arabinitol	17		36	<= 73

Creatinine = 126 mg/dL

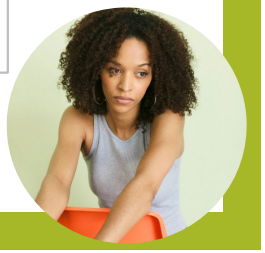
- Compounds of Bacterial or Yeast/Fungal Origin are created by organisms in the bowel, absorbed by the body, and excreted in the urine
- These organic acids can suggest dysbiosis, but can also be influenced by diet
  - Dietary sources include: preserved foods, diet sodas, strawberries, high intake of polyphenols or phenylalanine

3301 Organix® Comprehensive Profile - Urine

Additional Considerations

Nutrient supplementation is at the ***discretion of the treating clinician.*** The supplement dose ranges provided below are meant for educational purposes only. These dosage ranges relate to findings commonly found on Genova's nutritional panels and do not apply to specific disease conditions where different dosages may be warranted. Final recommendations should be based on consideration of the patient's medical history and current clinical condition.

Nutrient	Nutrient Need	Clinician Recommendations
Vitamin C	High: 1000-2000 mg	
Vitamin E (mixed tocopherols)	Moderate: 100-200 IU	
Vitamin B-1 (Thiamin)	Optional: 0-10 mg	
Vitamin B-2 (Riboflavin)	Optional: 0-10 mg	
Vitamin B-3 (Niacin)	Optional: 0-50 mg	
Vitamin B-5 (Pantothenic Acid)	Optional: 0-10 mg	
Vitamin B-6 (Pyridoxine)	High: 50-100 mg	
Biotin	High: 400-800 mcg	
Magnesium	Optional: 0-100 mg	
Carnitine	Optional: 0-250 mg	
Coenzyme Q10	Optional: 0-20 mg	
Lipoic Acid	Optional: 0-100 mg	
N-Acetylcysteine	Optional: 0-100 mg	
L-Arginine	Optional: 0-250 mg	
Glycine	Optional: 0-1000 mg	
Need for other antioxidants	Moderate	



Additional testing Considerations

- Adrenal stress profile
- GI health testing
- Neurotransmitter testing
- Amino acids
- Fatty acids
- Toxic mold testing
- Lyme testing
- Toxic element testing
- Nutrient testing

Clinical Connections:

NutrEval® Interpretation for Patients with Chronic Fatigue

Pamela W. Smith, M.D., MPH, MS

Lahnor Powell, ND, MPH

NutrEval: Comprehensive Nutritional Analysis

- The NutrEval provides a framework for assessing functional nutrient needs in 5 key areas:
  - Antioxidants
  - B Vitamins
  - Digestive Support
  - Essential Fatty Acids
  - Minerals

Physician Copy

SUGGESTED

Patient: FEMALE TEST

Supplements	Recor Intal
Antioxidants	
Vitamin A / Carotenoids	2,3
Vitamin C	75
Vitamin E / Tocopherols	2
α-Lipoic Acid	
CoQ10	
B-Vitamins	
Thiamin - B1	1.
Riboflavin - B2	1.
Niacin - B3	14
Pyridoxine - B6	1.
Biotin - B7	30
Folic Acid - B9	40
Cobalamin - B12	2.4
Minerals	
Magnesium	32
Manganese	1.
Molybdenum	45
Zinc	8
Essential Fatty Acids	
Omega-3 Oils	50
Digestive Support	
Probiotics	
Pancreatic Enzymes	
Other Vitamins	
Vitamin D	80

Amino Acid	mg/day
Arginine	473
Asparagine	0
Cysteine	165
Glutamine	64
Glycine	0
Histidine	0
Isoleucine	200
Leucine	415
Lysine	0
Taurine	40
Threonine	0
Tryptophan	0
Tyrosine	196
Valine	291

NutrEval Results Overview

APNTI.2

Clinical Considerations in Chronic Fatigue

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Bedside-to-Bench Conference: Research Agenda for Idiopathic Fatigue and Aging

Neil B. Alexander, MD[*], **George E. Taffet, MD**[†], **Frances McFarland Horne, PhD**[‡], **Basil A. Eldadah, MD, PhD**[§], **Luigi Ferrucci, MD**[||], **Susan Nayfield, MD, MSc**[§], and **Stephanie Studenski, MD, MPH**[#,**]

[*] Mobility Research Center, Geriatrics Center and Division of Geriatric Medicine, University of Michigan Hospitals and Veterans Affairs Ann Arbor Health Care System Geriatric Research Education and Clinical Center, Ann Arbor, Michigan [†] Baylor College of Medicine, Methodist Hospital, Houston, Texas [‡] American Geriatrics Society, New York, New York [§] Division of Geriatrics and Clinical Gerontology, National Institute on Aging, Bethesda, Maryland [||] Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, Baltimore, Maryland [#] Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania [**] Geriatric Research, Education and Clinical Center, Department of Veterans Affairs Pittsburgh Healthcare Center, Pittsburgh, Pennsylvania

Abstract

The American Geriatrics Society, with support from the National Institute on Aging and the John A. Hartford Foundation, held its fifth Bedside-to-Bench research conference, "Idiopathic Fatigue and Aging," to provide participants with opportunities to learn about cutting-edge research developments, draft recommendations for future research, and network with colleagues and leaders in the field.

Fatigue is a symptom that older persons, especially by those with chronic diseases, frequently experience. Definitions and prevalence of fatigue may vary across studies, across diseases, and even between investigators and patients. The focus of this review is on physical fatigue, recognizing that there are other related domains of fatigue (such as cognitive fatigue).

Many definitions of fatigue involve a sensation of "low" energy, suggesting that fatigue could be a disorder of energy balance. Poor energy utilization efficiency has not been considered in previous studies but is likely to be one of the most important determinants of fatigue in older individuals. Relationships between activity level, capacity for activity, a tolerable rate of activity, and a tolerable fatigue threshold or ceiling underlie a notion of fatiguability. Mechanisms probably contributing to fatigue in older adults include decline in mitochondrial function, alterations in brain neurotransmitters, oxidative stress, and inflammation. The relationships between muscle function and fatigue are complex. A number of diseases (such as cancer) are known to cause

Address correspondence to Neil B. Alexander, VA Ann Arbor Health Care System GRECC, 2215 Fuller Road, Ann Arbor, MI 48105. nalexand@med.umich.edu.

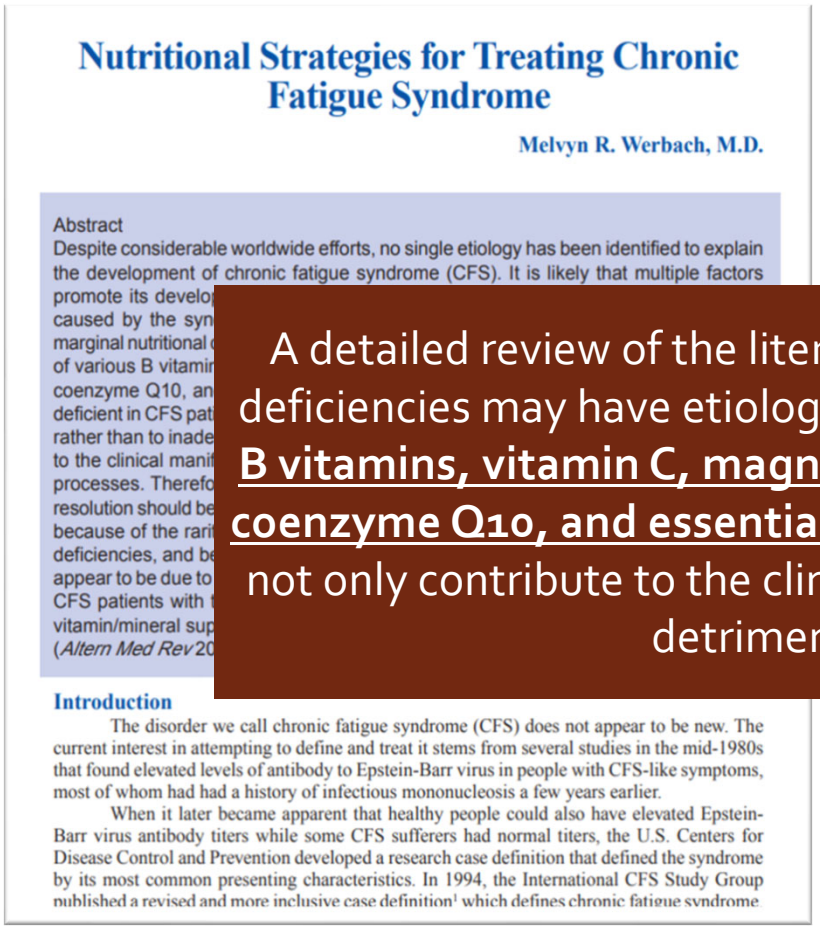
Conflict of Interest: The authors declare no conflict of interest.

Author Contributions: All of the authors contributed to the review, concept, design, and preparation of this manuscript.

Probable contributing mechanisms to fatigue:

- Decline in mitochondrial function
- Alterations in brain neurotransmitters
- Oxidative Stress
- Inflammation

Alexanfer NB, et al. *J Am Geriatr So*. 2010;58(5):967-975



Nutritional Strategies for Treating Chronic Fatigue Syndrome

Melvyn R. Werbach, M.D.

Abstract
Despite considerable worldwide efforts, no single etiology has been identified to explain the development of chronic fatigue syndrome (CFS). It is likely that multiple factors promote its develo
caused by the syn
marginal nutritional
of various B vitamin
coenzyme Q10, an
deficient in CFS pat
rather than to inade
to the clinical mani
processes. Therefo
resolution should be
because of the rari
deficiencies, and be
appear to be due to
CFS patients with
vitamin/mineral sup
(*Altern Med Rev* 20

Introduction

The disorder we call chronic fatigue syndrome (CFS) does not appear to be new. The current interest in attempting to define and treat it stems from several studies in the mid-1980s that found elevated levels of antibody to Epstein-Barr virus in people with CFS-like symptoms, most of whom had had a history of infectious mononucleosis a few years earlier.

When it later became apparent that healthy people could also have elevated Epstein-Barr virus antibody titers while some CFS sufferers had normal titers, the U.S. Centers for Disease Control and Prevention developed a research case definition that defined the syndrome by its most common presenting characteristics. In 1994, the International CFS Study Group published a revised and more inclusive case definition[1] which defines chronic fatigue syndrome

A detailed review of the literature suggests a number of marginal nutritional deficiencies may have etiologic relevance. These include deficiencies of **various B vitamins, vitamin C, magnesium, sodium, zinc, L-tryptophan, L-carnitine, coenzyme Q10, and essential fatty acids**... It is likely that marginal deficiencies not only contribute to the clinical manifestations of the syndrome, but also are detrimental to the healing processes.

Werbach MR, et al. *Altern Med Rev*. 2000;5(2):93-108

NutrEval Case History

40-year-old male with the chief complaint of fatigue for the last 4 years. He went to see a personalized medicine physician and had his hormones tested which were all optimal including his cortisol.

PH: + appendectomy at the age or 24

SH: works as an autoworker in a plant

Meds: none. He is also not taking any nutrients.

Diet: eats a healthy diet that is somewhat ketogenic. He drinks 6 ounces of coffee a day and dose not eat a lot of sugar.

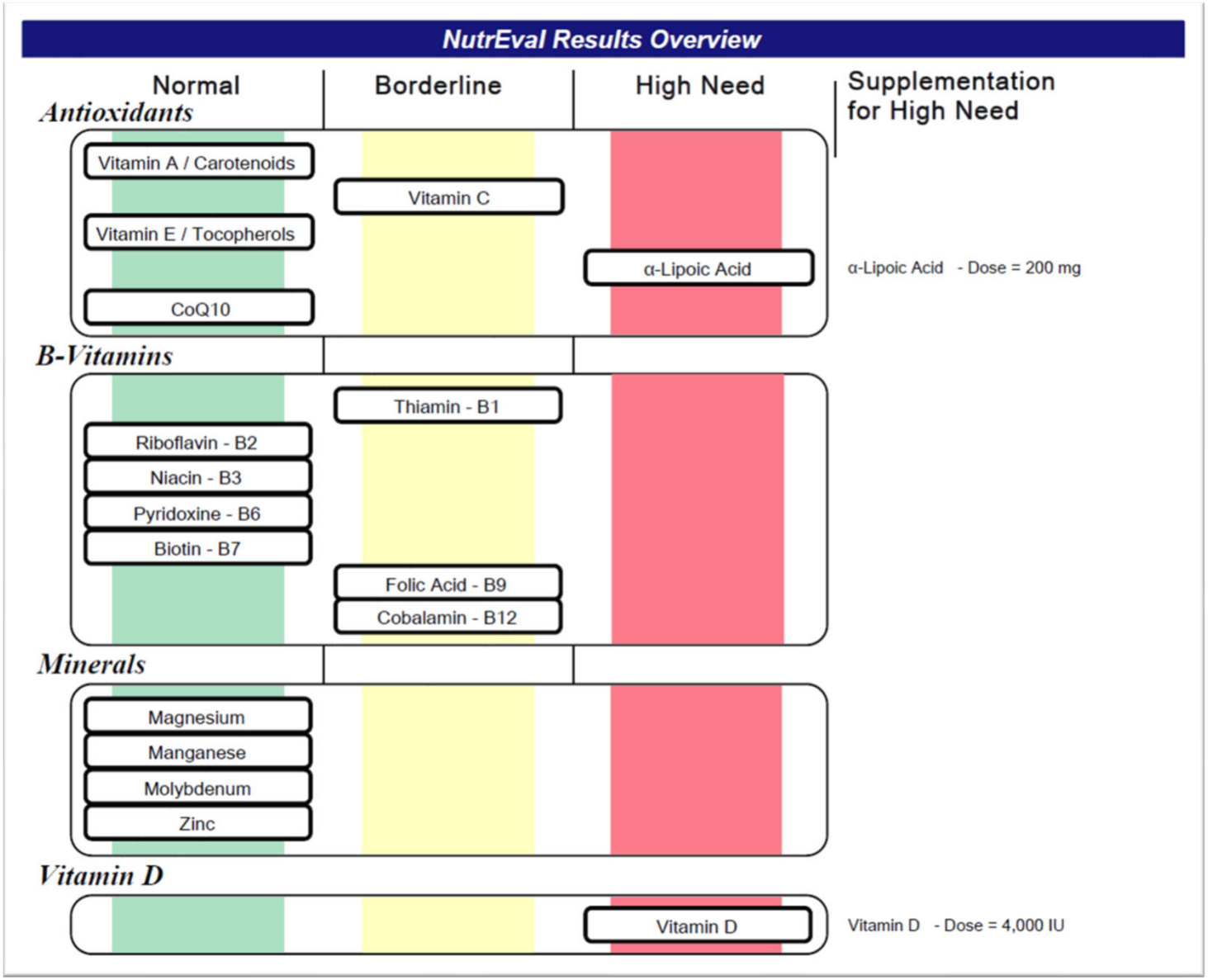
Exercise: cross fit 3 x a week for 45 minutes. Feels more tired after working out.

ROS: Patient sleeps 6 hours a night but it is un-refreshed sleep. He has one bowel movement a day. He complains of indigestion. He also has headaches and difficulty concentrating.

P/E: is unremarkable except for patient appears older than stated age and looks tired.

What Do You Want to Look at Next?

- A NutrEval test is a great test as a next step to evaluate his fatigue to try and find the etiology of his symptom.


NutrEval Results Overview
Normal
Borderline
High Need
Supplementation for High Need
Antioxidants
Vitamin A / Carotenoids
Vitamin C
Vitamin E / Tocopherols
α-Lipoic Acid
α-Lipoic Acid - Dose = 200 mg
CoQ10
B-Vitamins
Thiamin - B1
Riboflavin - B2
Niacin - B3
Pyridoxine - B6
Biotin - B7
Folic Acid - B9
Cobalamin - B12
Minerals
Magnesium
Manganese
Molybdenum
Zinc
Vitamin D
Vitamin D
Vitamin D - Dose = 4,000 IU

SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	3,000 IU	3,000 IU	
Vitamin C	90 mg	500 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		200 mg	
CoQ10		30 mg	

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	384
Asparagine	206	Phenylalanine	317
Cysteine	0	Serine	0
Glutamine	1,505	Taurine	7
Glycine	3,858	Threonine	0
Histidine	1,188	Tryptophan	0
Isoleucine	272	Tyrosine	799
Leucine	0	Valine	0
Lysine	1,480		

NutrEval FMV — *Interpretation At-A-Glance*

Nutritional Needs

Antioxidants

Vitamin A / Carotenoids

3,000 IU | 5,000 IU | 10,000 IU

- Beta-carotene & other carotenoids are converted to vitamin A (retinol), involved in vision, antioxidant & immune function, gene expression & cell growth.
- Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, or oral contraceptives containing estrogen & progestin.
- Deficiency may result in night blindness, impaired immunity, healing & tissue regeneration, increased risk of infection, leukoplakia or keratosis.
- Food sources include cod liver oil, fortified cereals & milk, eggs, sweet potato, pumpkin, carrot, cantaloupe, mango, spinach, broccoli, kale & butternut squash.

Vitamin C

- Vitamin C is an a
- It is involved in c
- antibodies, and t
- Deficiency may c
- Deficiency can re
- teeth, sore mout
- Food sources inc
- pepper, broccoli

Vitamin E / Tocopherols

100 IU | 200 IU | 400 IU

- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital, phenytoin).
- Deficiency may result in peripheral neuropathy, ataxia, muscle weakness, retinopathy, and increased risk of CVD, prostate cancer and cataracts.
- Food sources include oils (olive, soy, corn, canola, safflower, sunflower), eggs, nuts, seeds, spinach, carrots, avocado, dark leafy greens and wheat germ.

α-Lipoic Acid

- α-Lipoic acid pla
- (including the re
- signaling and the
- High biotin intake
- Optimal levels of
- against diabetic
- Main food source
- include tomato,

CoQ10

30 mg | 60 mg | 90 mg

- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) or beta-blockers.
- Low levels may aggravate oxidative stress, diabetes, cancer, congestive heart failure, cardiac arrhythmias, gingivitis and neurologic diseases.
- Main food sources include meat, poultry, fish, soybean, canola oil, nuts and whole grains. Moderate sources include fruits, vegetables, eggs and dairy.

Glutathione

- Glutathione (GSH
- source of sulfate
- of toxins.
- GSH requiremen
- chronic alcoholis
- toxic exposure.
- Deficiency may r
- altered immunity
- Food sources of
- nuts, seeds, whe

Plant-based Antioxidants

- Oxidative stress is the imbalance between the production of free radicals and the body's ability to readily detoxify these reactive species and/or repair the resulting damage with anti-oxidants.
- Oxidative stress can be endogenous (energy production and inflammation) or exogenous (exercise, exposure to environmental toxins).
- Oxidative stress has been implicated clinically in the development of neurodegenerative diseases, cardiovascular diseases and chronic fatigue syndrome.
- Antioxidants may be found in whole food sources (e.g., brightly colored fruits & vegetables, green tea, turmeric) as well as nutraceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).

NutrEval FMV — *Interpretation At-A-Glance*

Nutritional Needs

B-Vitamins

Thiamin - B1

10 mg | 25 mg | 50 mg

- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency may lead to dry beriberi (e.g., neuropathy, muscle weakness), wet beriberi (e.g., cardiac problems, edema), encephalopathy or dementia.
- Food sources include lentils, whole grains, wheat germ, Brazil nuts, peas, organ meats, brewer's yeast, blackstrap molasses, spinach, milk & eggs.

Pyridoxine - B6

- B6 (as P5P) is a cofa
- genesis, and synthe
- Low B6 may result fr
- contraceptives and H
- B6 deficiency may re
- seizures), oral inflam
- Food sources includ
- soybean, lentils, nut

Riboflavin - B2

10 mg | 25 mg | 50 mg

- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.
- B2 deficiency may result in oxidative stress, mitochondrial dysfunction, low uric acid, low B3 or B6, high homocysteine, anemia or oral & throat inflammation.
- Food sources include milk, cheese, eggs, whole grains, beef, chicken, wheat germ, fish, broccoli, asparagus, spinach, mushrooms and almonds.

Biotin - B7

- Biotin is a cofactor fo
- synthesis, mitochon
- transcription.
- Deficiency may resu
- whites, long-term TP
- antibiotics.
- Low levels may resu
- hair loss, scaly rash
- Food sources includ
- meats, fish, wheat, n
- cauliflower.

Niacin - B3

20 mg | 30 mg | 50 mg

- B3 is used to form NAD and NADP, involved in energy production from food, fatty acid & cholesterol synthesis, cell signaling, DNA repair & cell differentiation.
- Low B3 may result from deficiencies of tryptophan (B3 precursor), B6, B2 or Fe (cofactors in B3 production), or from long-term isoniazid or oral contraceptive use.
- B3 deficiency may result in pellagra (dermatitis, diarrhea, dementia), neurologic symptoms (e.g., depression, memory loss), bright red tongue or fatigue.
- Food sources include poultry, beef, organ meats, fish, whole grains, peanuts, seeds, lentils, brewer's yeast and lima beans.

Folic Acid - B9

- Folic acid plays a ke
- methylation, nucleic
- Low folate may resu
- blockers, some diure
- trimethoprim, pyrime
- Folate deficiency ca
- homocysteine, impai
- Food sources includ

Cobalamin - B12

- B12 plays important
- methylation, synthes
- cells, DNA & RNA.
- Low B12 may result
- atrophic gastritis, H.
- diets, diabetic meds,
- B12 deficiency can k
- paresthesias, memo
- chromosome breaks
- Food sources includ

NutrEval FMV — *Interpretation At-A-Glance*

Nutritional Needs

Minerals

Manganese

3.0 mg | 5.0 mg | 7.0 mg

- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing antacids or laxatives.
- Deficiency may result in impaired bone/connective tissue growth, glucose & lipid dysregulation, infertility, oxidative stress, inflammation or hyperammonemia.
- Food sources include whole grains, legumes, dried fruits, nuts, dark green leafy vegetables, liver, kidney and tea.

Magnesium

400 mg | 600 mg | 800 mg

- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses of zinc.
- Low Mg may result in muscle weakness/spasm, constipation, depression, hypertension, arrhythmias, hypocalcemia, hypokalemia or personality changes.
- Food sources include dark leafy greens, oatmeal, buckwheat, unpolished grains, chocolate, milk, nuts & seeds, lima beans and molasses.

Molybdenum

75 mcg | 150 mcg | 300 mcg

- Molybdenum is a cofactor for enzymes that convert sulfites to sulfate, and nucleotides to uric acid, and that help metabolize aldehydes & other toxins.
- Low Mo levels may result from long-term TPN that does not include Mo.
- Mo deficiency may result in increased sulfite, decreased plasma uric acid (and antioxidant function), deficient sulfate, impaired sulfation (detoxification), neurologic disorders or brain damage (if severe deficiency).
- Food sources include buckwheat, beans, grains, nuts, beans, lentils, meats and vegetables (although Mo content of plants depends on soil content).

Zinc

10 mg | 20 mg | 30 mg

- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency can result in hair loss and skin rashes, also impairments in growth & healing, immunity, sexual function, taste & smell and digestion.
- Food sources include oysters, organ meats, soybean, wheat germ, seeds, nuts, red meat, chicken, herring, milk, yeast, leafy and root vegetables.

Essential Fatty Acids

Need for Essential Fatty Acids

500 mg | 1,000 mg | 2,000 mg

- Omega-3 (O3) and Omega-6 (O6) fatty acids are polyunsaturated fatty acids that cannot be synthesized by the human body. They are classified as essential nutrients and must be obtained from dietary sources.
- The standard American diet is much higher in O6 than O3 fatty acids. Deficiency of EFAs may result from poor dietary intake and/or poor conversion from food sources.
- EFA deficiency is associated with decreased growth & development of infants and children, dry skin/rash, poor wound healing, and increased risk of infection, cardiovascular and inflammatory diseases.
- Dietary sources of the O6 Linoleic Acid (LA) include vegetable oils, nuts, seeds and some vegetables. Dietary sources of the O3 a-Linolenic Acid (ALA) include flaxseeds, walnuts, and their oils. Fish (mackerel, salmon, sardines) are the major dietary sources of the O3 fatty acids EPA and DHA.

Digestive Support

Need for Probiotics

10 B CFU | 25 B CFU | 50 B CFU

- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhance digestion & absorption; decrease severity of diarrheal illness; modulate of immune function & intestinal permeability.
- Alterations of gastrointestinal microflora may result from C-section delivery, antibiotic use, improved sanitation, decreased consumption of fermented foods and use of certain drugs.
- Some of the diseases associated with microflora imbalances include: IBS, IBD, fibromyalgia, chronic fatigue syndrome, obesity, atopic illness, colic and cancer.
- Food sources rich in probiotics are yogurt, kefir and fermented foods.

Need for Pancreatic Enzymes

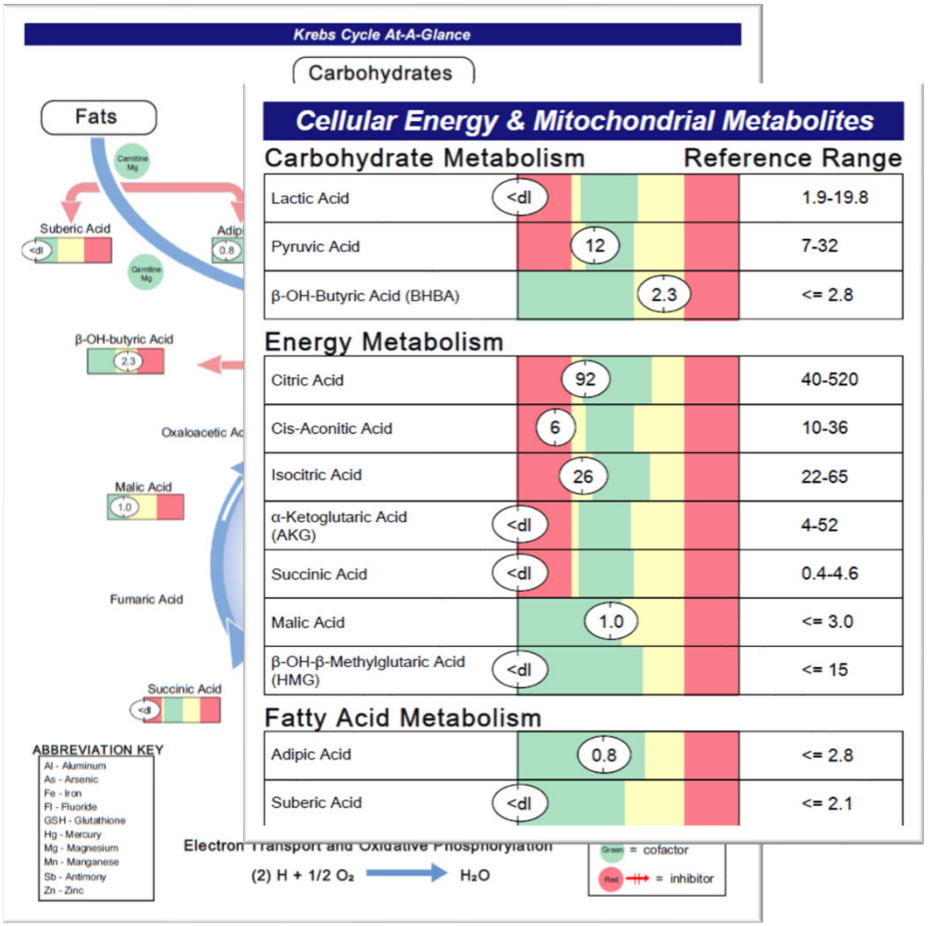
0 IU | 5,000 IU | 10,000 IU

- Pancreatic enzymes are secreted by the exocrine glands of the pancreas and include protease/peptidase, lipase and amylase.
- Pancreatic exocrine insufficiency may be primary or secondary in nature. Any indication of insufficiency warrants further evaluation for underlying cause (i.e., celiac disease, small intestine villous atrophy, small bowel bacterial overgrowth).
- A high functional need for digestive enzymes suggests that there is an impairment related to digestive capacity.
- Determining the strength of the pancreatic enzyme support depends on the degree of functional impairment. Supplement potency is based on the lipase units present in both prescriptive and non-prescriptive agents.

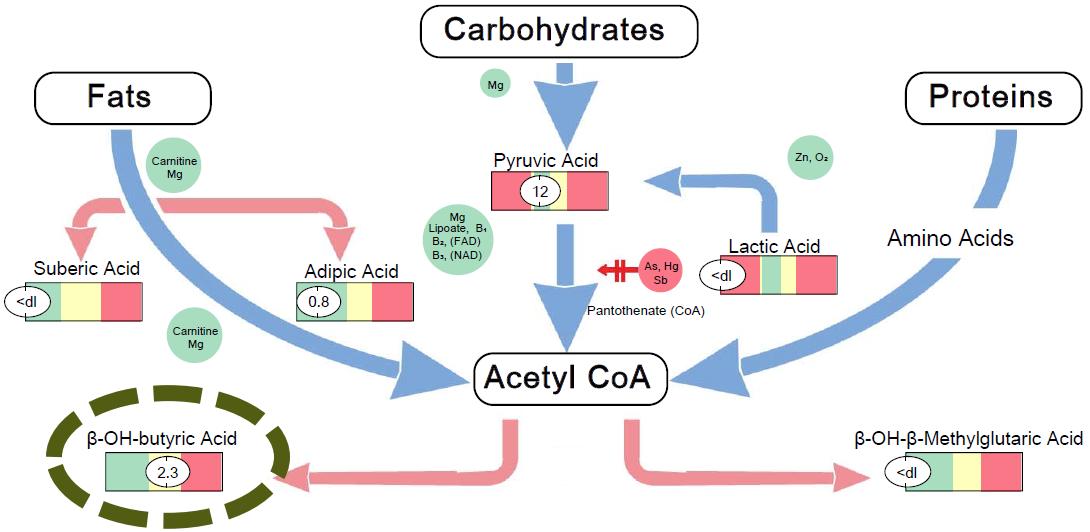
Fatigue Pattern: CAC/TCA

Kreb cycle dysfunction can be supported with specific nutrient co-factors:

- CoQ10
- Carnitine
- B-vitamins
- Magnesium
- Manganese
- Iron
- Glutathione
- Zinc
- Alpha lipoic acid

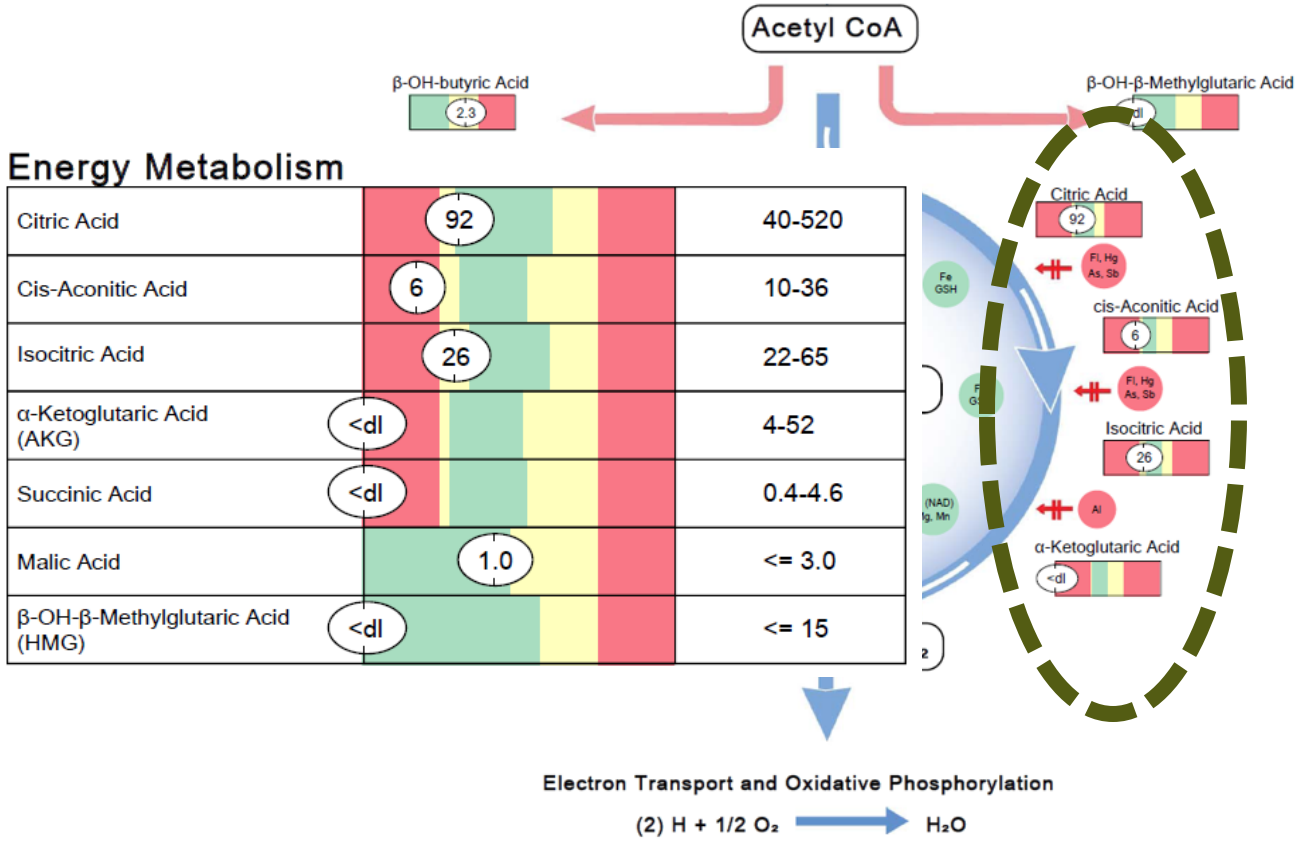


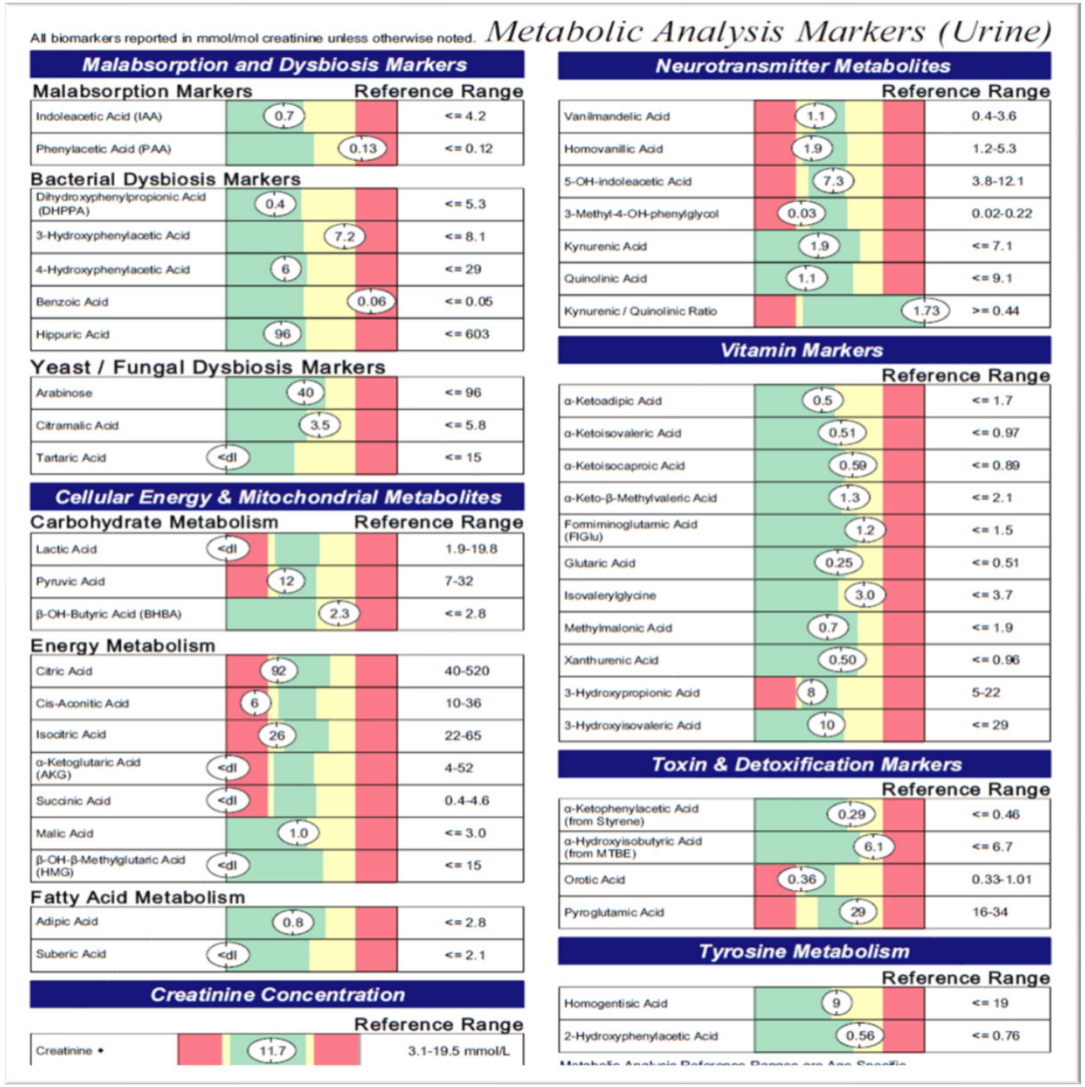
Fatigue Pattern: CAC/TCA



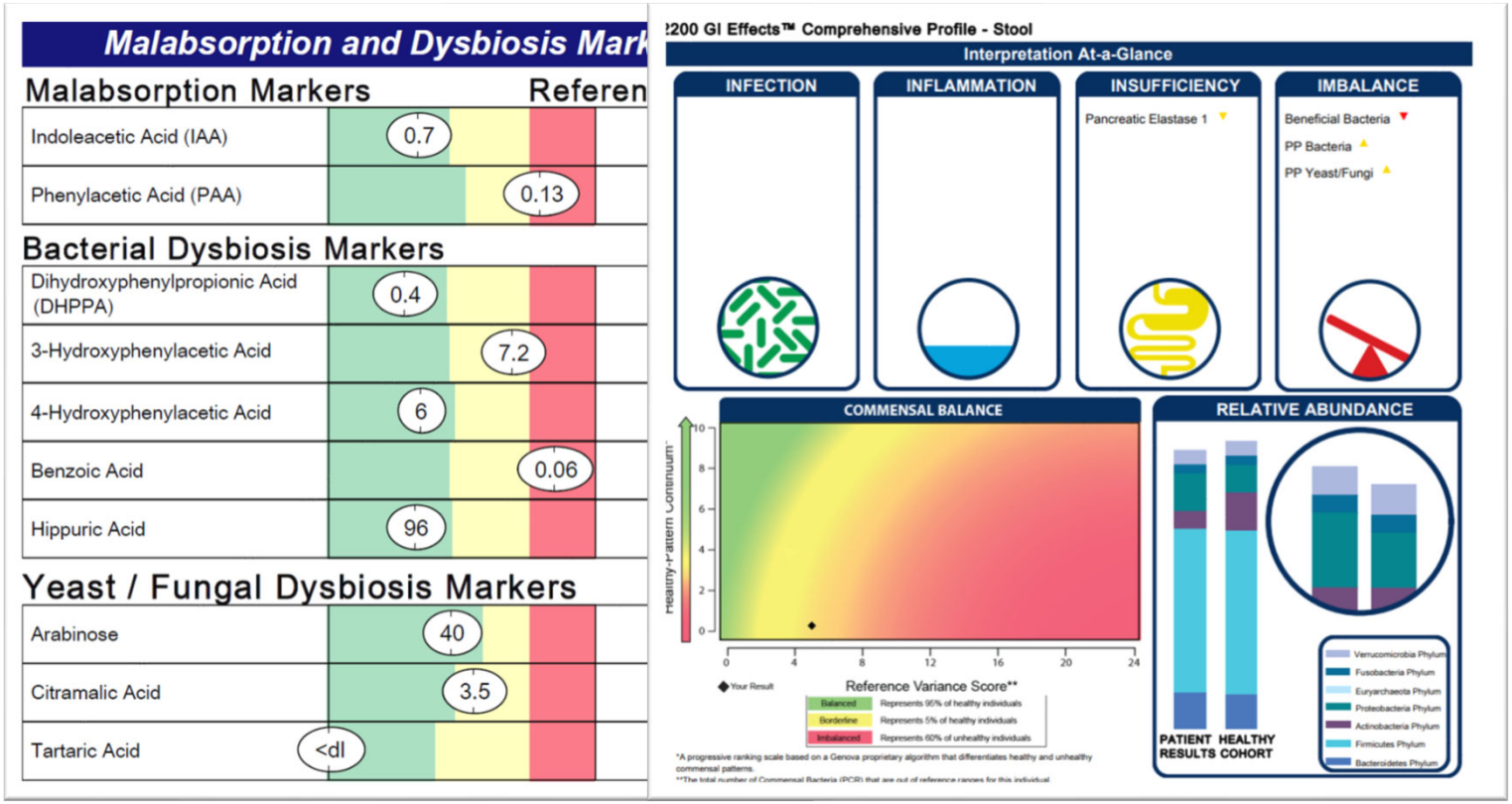
- Beta (β) – OH – butyric acid or BHBA (ketone body)
  - Ketones are formed by the liver from fatty acids during periods of low food intake or starvation (i.e. fasting or anorexia), **carbohydrate restrictive diets**, prolonged intense exercise, alcoholism, and diabetes.

Fatigue Pattern: CAC/TCA




All biomarkers reported in mmol/mol creatinine unless otherwise noted.
Metabolic Analysis Markers (Urine)
Malabsorption and Dysbiosis Markers
Malabsorption Markers
Reference Range
Indoleacetic Acid (IAA) 0.7 <= 4.2
Phenylacetic Acid (PAA) 0.13 <= 0.12
Bacterial Dysbiosis Markers
Dihydroxyphenylpropionic Acid (DHPPA) 0.4 <= 5.3
3-Hydroxyphenylacetic Acid 7.2 <= 8.1
4-Hydroxyphenylacetic Acid 6 <= 29
Benzoic Acid 0.06 <= 0.05
Hippuric Acid 96 <= 603
Yeast / Fungal Dysbiosis Markers
Arabinose 40 <= 96
Citramalic Acid 3.5 <= 5.8
Tartaric Acid <dl <= 15
Cellular Energy & Mitochondrial Metabolites
Carbohydrate Metabolism
Reference Range
Lactic Acid <dl 1.9-19.8
Pyruvic Acid 12 7-32
β-OH-Butyric Acid (BHBA) 2.3 <= 2.8
Energy Metabolism
Citric Acid 92 40-520
Cis-Aconitic Acid 6 10-36
Isocitric Acid 26 22-65
α-Ketoglutaric Acid (AKG) <dl 4-52
Succinic Acid <dl 0.4-4.6
Malic Acid 1.0 <= 3.0
β-OH-β-Methylglutaric Acid (HMG) <dl <= 15
Fatty Acid Metabolism
Adipic Acid 0.8 <= 2.8
Suberic Acid <dl <= 2.1
Creatinine Concentration
Reference Range
Creatinine • 11.7 3.1-19.5 mmol/L
Neurotransmitter Metabolites
Reference Range
Vanilmandelic Acid 1.1 0.4-3.6
Homovanillic Acid 1.9 1.2-5.3
5-OH-indoleacetic Acid 7.3 3.8-12.1
3-Methyl-4-OH-phenylglycol 0.03 0.02-0.22
Kynurenic Acid 1.9 <= 7.1
Quinolinic Acid 1.1 <= 9.1
Kynurenic / Quinolinic Ratio 1.73 >= 0.44
Vitamin Markers
Reference Range
α-Ketoadipic Acid 0.5 <= 1.7
α-Ketoisovaleric Acid 0.51 <= 0.97
α-Ketoisocaproic Acid 0.59 <= 0.89
α-Keto-β-Methylvaleric Acid 1.3 <= 2.1
Formiminoglutamic Acid (FIGlu) 1.2 <= 1.5
Glutaric Acid 0.25 <= 0.51
Isovalerylglycine 3.0 <= 3.7
Methylmalonic Acid 0.7 <= 1.9
Xanthurenic Acid 0.50 <= 0.96
3-Hydroxypropionic Acid 8 5-22
3-Hydroxyisovaleric Acid 10 <= 29
Toxin & Detoxification Markers
Reference Range
α-Ketophenylacetic Acid (from Styrene) 0.29 <= 0.46
α-Hydroxyisobutyric Acid (from MTBE) 6.1 <= 6.7
Orotic Acid 0.36 0.33-1.01
Pyroglutamic Acid 29 16-34
Tyrosine Metabolism
Reference Range
Homogentisic Acid 9 <= 19
2-Hydroxyphenylacetic Acid 0.56 <= 0.76

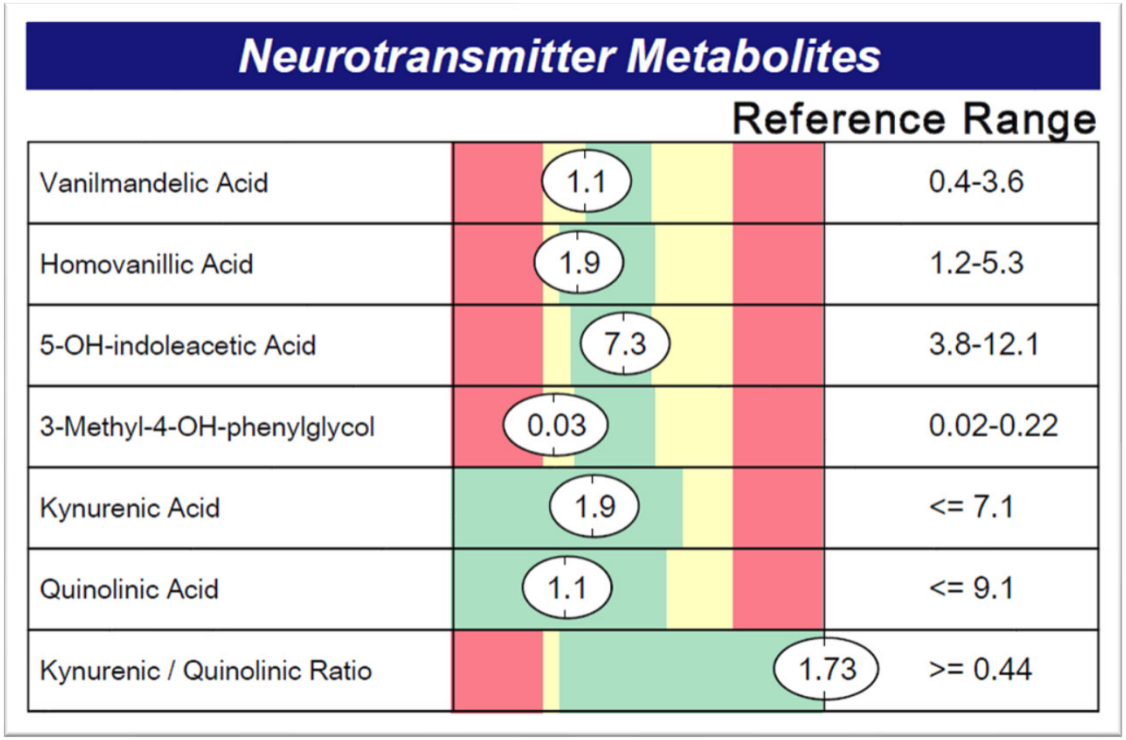
Fatigue Pattern: Organic Acids



Malabsorption and Dysbiosis Mark

Malabsorption Markers	Referen
Indoleacetic Acid (IAA)	0.7
Phenylacetic Acid (PAA)	0.13
Bacterial Dysbiosis Markers	
Dihydroxyphenylpropionic Acid (DHPPA)	0.4
3-Hydroxyphenylacetic Acid	7.2
4-Hydroxyphenylacetic Acid	6
Benzoic Acid	0.06
Hippuric Acid	96
Yeast / Fungal Dysbiosis Markers	
Arabinose	40
Citramalic Acid	3.5
Tartaric Acid	<dl

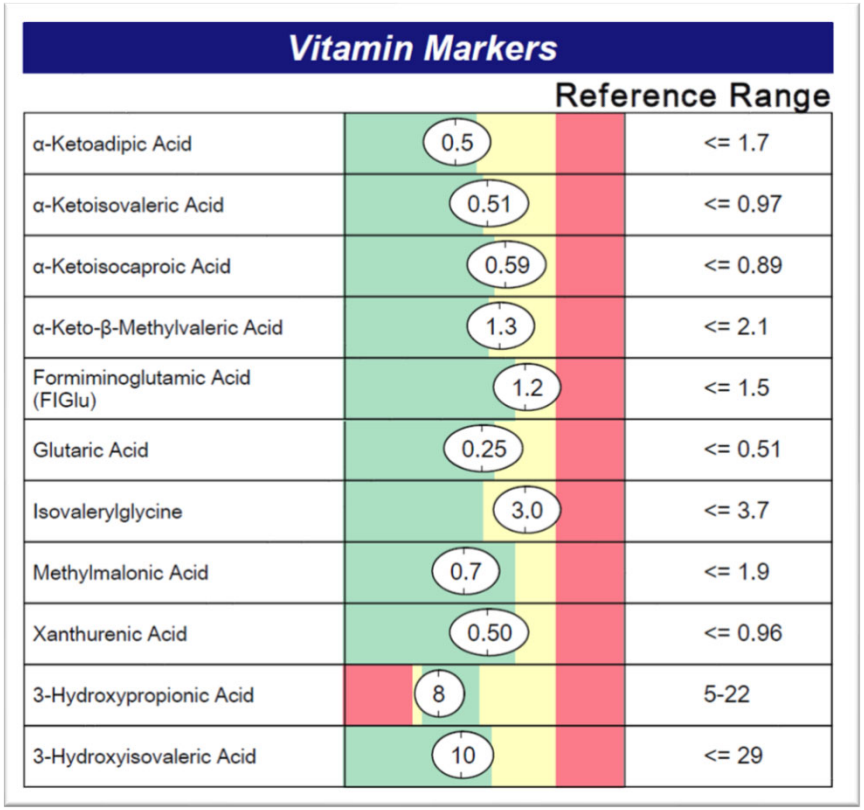
Fatigue Pattern: Organic Acids



Neurotransmitter Metabolites

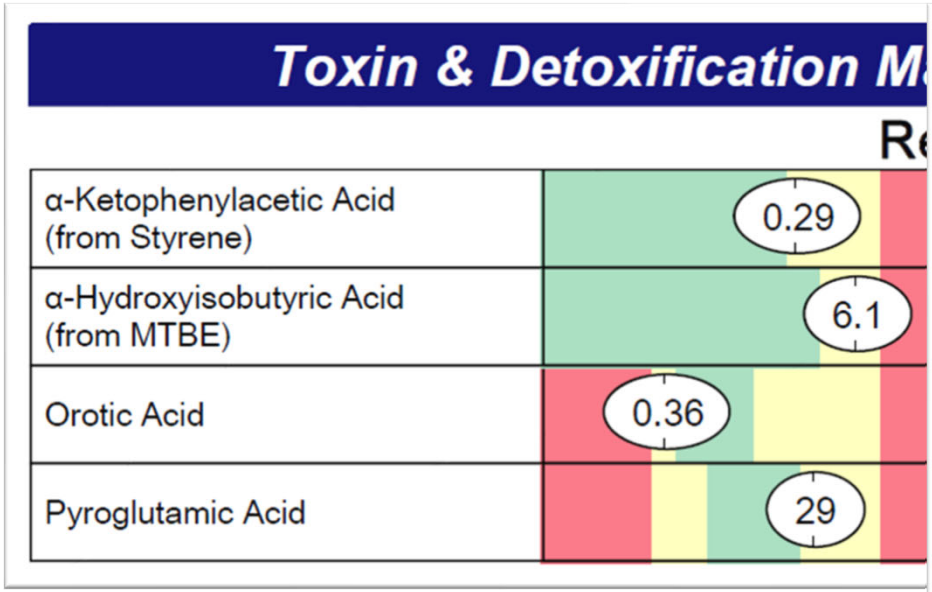
		Reference Range
Vanilmandelic Acid	1.1	0.4-3.6
Homovanillic Acid	1.9	1.2-5.3
5-OH-indoleacetic Acid	7.3	3.8-12.1
3-Methyl-4-OH-phenylglycol	0.03	0.02-0.22
Kynurenic Acid	1.9	<= 7.1
Quinolinic Acid	1.1	<= 9.1
Kynurenic / Quinolinic Ratio	1.73	>= 0.44

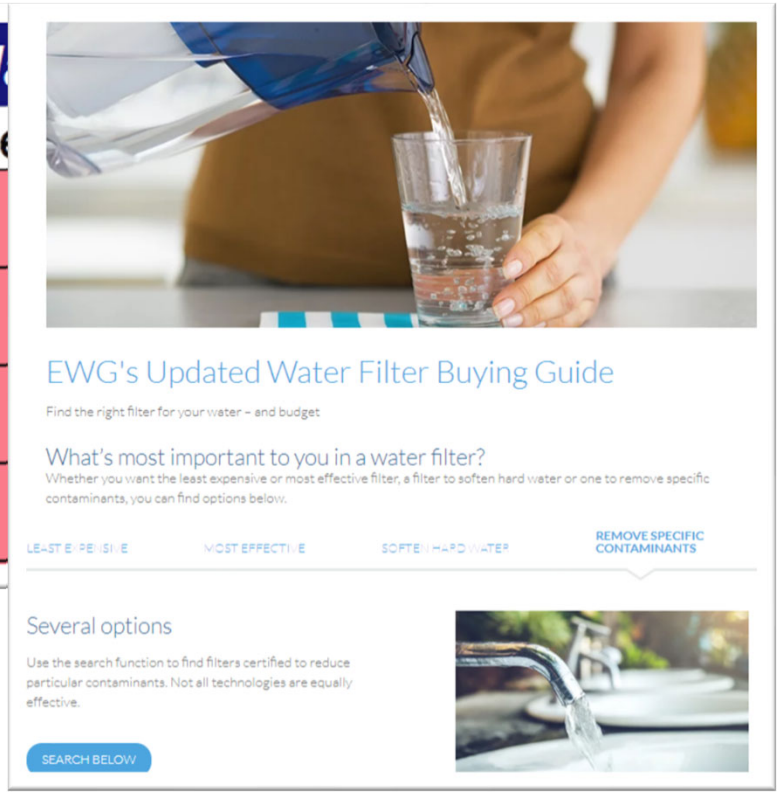
Fatigue Pattern: Organic Acids



Vitamin Markers		Reference Range
α-Ketoadipic Acid	0.5	<= 1.7
α-Ketoisovaleric Acid	0.51	<= 0.97
α-Ketoisocaproic Acid	0.59	<= 0.89
α-Keto-β-Methylvaleric Acid	1.3	<= 2.1
Formiminoglutamic Acid (FIGlu)	1.2	<= 1.5
Glutaric Acid	0.25	<= 0.51
Isovalerylglycine	3.0	<= 3.7
Methylmalonic Acid	0.7	<= 1.9
Xanthurenic Acid	0.50	<= 0.96
3-Hydroxypropionic Acid	8	5-22
3-Hydroxyisovaleric Acid	10	<= 29

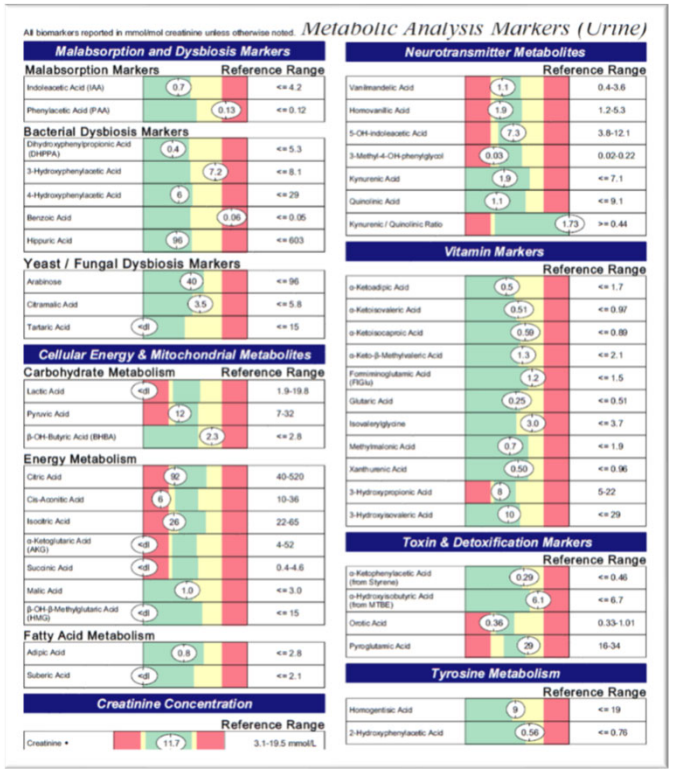
Fatigue Pattern: Organic Acids





Fatigue Pattern: Organic Acids Review

- Maldigestion and Dysbiosis Markers
  - Pancreatic enzymes and/or probiotics
- Cellular Energy
  - Low energy metabolism: Amino acids
  - High energy metabolism markers: B-vitamins and/or CoQ10
- Neurotransmitter Metabolites
  - High neurotransmitter metabolites: B-vitamins and/or methylation
  - Low neurotransmitter metabolites: Amino acid sufficiency
- Vitamin Markers
  - B-vitamins
- Toxin & Detoxification Markers
  - Antioxidants



Fatigue Pattern: Amino Acids

Amino Acids (Urine FMV)

All biomarkers reported in micromol/g creatinine unless otherwise noted.

Nutritionally Essential Amino Acids

Amino Acid	Reference Range
Arginine	3-43
Histidine	102-763
Isoleucine	3-25
Leucine	6-61
Lysine	15-231
Methionine	2-16
Phenylalanine	7-92
Taurine	39-568
Threonine	9-97
Tryptophan	8-58
Valine	5-43

Nonessential Protein Amino Acids

Amino Acid	Reference Range
Alanine	26-275
Asparagine	12-115
Aspartic Acid	<= 9
Cysteine (FMV urine)	9-60
Cystine (FMV Urine)	10-116
γ-Aminobutyric Acid	<= 3
Glutamic Acid	2-16
Glutamine	85-518
Proline	1-9
Tyrosine	19-135

Intermediary Metabolites

B Vitamin Markers	Reference Range
α-Aminoadipic	6-56
α-Amino-N-butyric Acid	2-21
β-Aminoisobutyric Acid	4-194
Cystathionine	4-48
3-Methylhistidine	47-232

Urea Cycle Markers	
Citrulline	0.7-3.4
Ornithine	3-17
Urea ♦	150-380 mmol/g creatinine

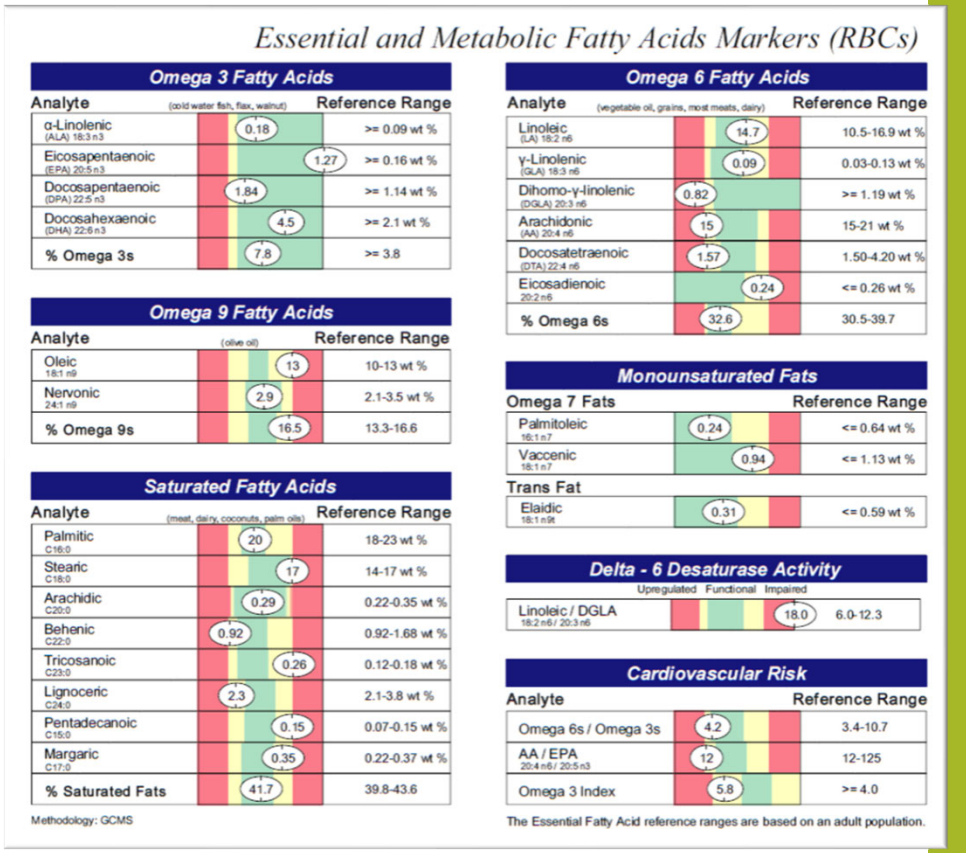
Glycine/Serine Metabolites	
Glycine	47-435
Serine	24-140
Ethanolamine	40-226
Phosphoethanolamine	1-9
Phosphoserine	2-13
Sarcosine	<= 1.0

Dietary Peptide Related Markers

	Reference Range
Anserine (dipeptide)	0.7-76.1
Carnosine (dipeptide)	1-32
1-Methylhistidine	18-887
β-Alanine	<= 18

Fatigue Pattern: Fatty Acids

- Can provide an overall assessment of the proportions of the classes of fatty acids and their relationship to each other
- Specific information about Omega-3 fatty acids: ALA, EPA and DHA



Essential and Metabolic Fatty Acids Markers (RBCs)

Omega 3 Fatty Acids

Analyte (cold water fish, flax, walnut)		Reference Range
α-Linolenic (ALA) 18:3 n3	0.18	>= 0.09 wt %
Eicosapentaenoic (EPA) 20:5 n3	1.27	>= 0.16 wt %
Docosapentaenoic (DPA) 22:5 n3	1.84	>= 1.14 wt %
Docosahexaenoic (DHA) 22:6 n3	4.5	>= 2.1 wt %
% Omega 3s	7.8	>= 3.8

Omega 9 Fatty Acids

Analyte (olive oil)		Reference Range
Oleic 18:1 n9	13	10-13 wt %
Nervonic 24:1 n9	2.9	2.1-3.5 wt %
% Omega 9s	16.5	13.3-16.6

Saturated Fatty Acids

Analyte (meat, dairy, coconuts, palm oils)		Reference Range
Palmitic C16:0	20	18-23 wt %
Stearic C18:0	17	14-17 wt %
Arachidic C20:0	0.29	0.22-0.35 wt %
Behenic C22:0	0.92	0.92-1.68 wt %
Tricosanoic C23:0	0.26	0.12-0.18 wt %
Lignoceric C24:0	2.3	2.1-3.8 wt %
Pentadecanoic C15:0	0.15	0.07-0.15 wt %
Margaric C17:0	0.35	0.22-0.37 wt %
% Saturated Fats	41.7	39.8-43.6

Methodology: GCMS

Omega 6 Fatty Acids

Analyte (vegetable oil, grains, most meats, dairy)		Reference Range
Linoleic (LA) 18:2 n6	14.7	10.5-16.9 wt %
γ-Linolenic (GLA) 18:3 n6	0.09	0.03-0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3 n6	0.82	>= 1.19 wt %
Arachidonic (AA) 20:4 n6	15	15-21 wt %
Docosatetraenoic (DTA) 22:4 n6	1.57	1.50-4.20 wt %
Eicosadienoic 20:2 n6	0.24	<= 0.26 wt %
% Omega 6s	32.6	30.5-39.7

Monounsaturated Fats

Omega 7 Fats		Reference Range
Palmitoleic 16:1 n7	0.24	<= 0.64 wt %
Vaccenic 18:1 n7	0.94	<= 1.13 wt %
Trans Fat		
Elaidic 18:1 n9t	0.31	<= 0.59 wt %

Delta - 6 Desaturase Activity

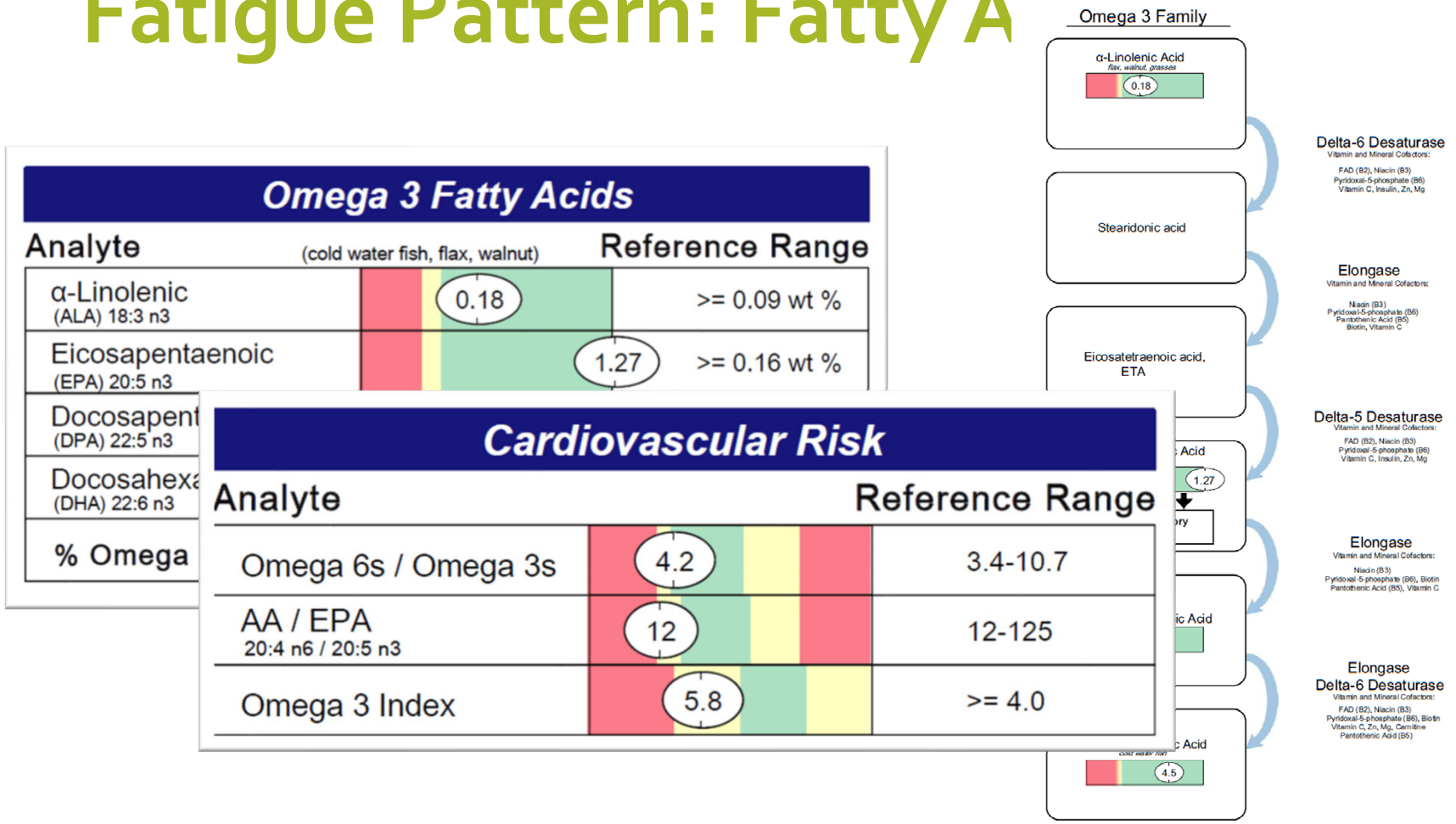
	Upregulated Functional Impaired	
Linoleic / DGLA 18:2 n6 / 20:3 n6	18.0	6.0-12.3

Cardiovascular Risk

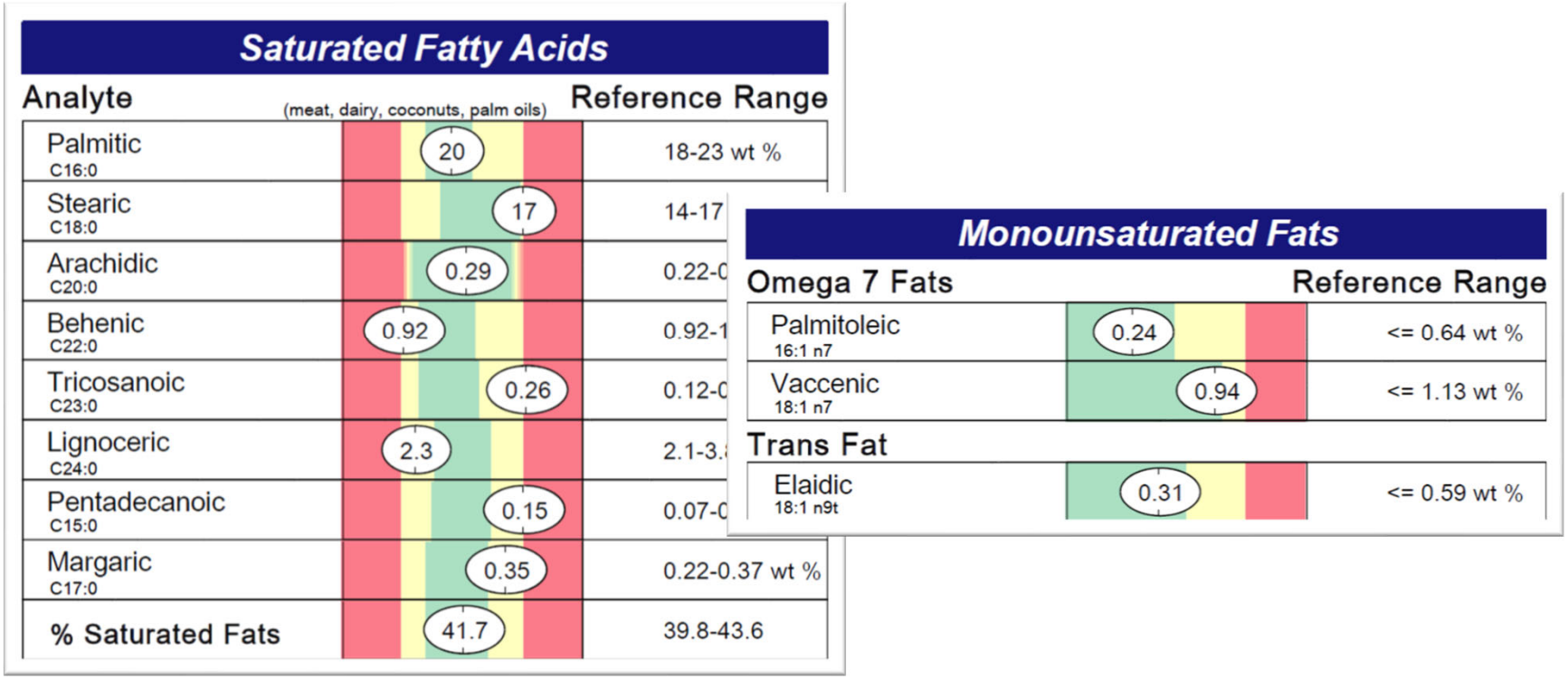
Analyte		Reference Range
Omega 6s / Omega 3s	4.2	3.4-10.7
AA / EPA 20:4 n6 / 20:5 n3	12	12-125
Omega 3 Index	5.8	>= 4.0

The Essential Fatty Acid reference ranges are based on an adult population.

Fatigue Pattern: Fatty A



Fatigue Pattern: Fatty Acids



Fatigue Pattern: Amino Acids & Fatty Acids

Amino Acids (Urine FMV)

All biomarkers reported in micromol/g creatinine unless otherwise noted.

Nutritionally Essential Amino Acids

Amino Acid	Reference Range
Arginine	3-43
Histidine	102-763
Isoleucine	3-25
Leucine	6-61
Lysine	15-231
Methionine	2-16
Phenylalanine	7-92
Taurine	39-568
Threonine	9-97
Tryptophan	8-58
Valine	5-43

Nonessential Protein Amino Acids

Amino Acid	Reference Range
Alanine	26-275
Asparagine	12-115
Aspartic Acid	<= 9
Cysteine (FMV urine)	9-60
Cystine (FMV Urine)	10-116
γ-Aminobutyric Acid	<= 3
Glutamic Acid	2-16
Glutamine	85-518
Proline	1-9
Tyrosine	19-135

Intermediary Metabolites

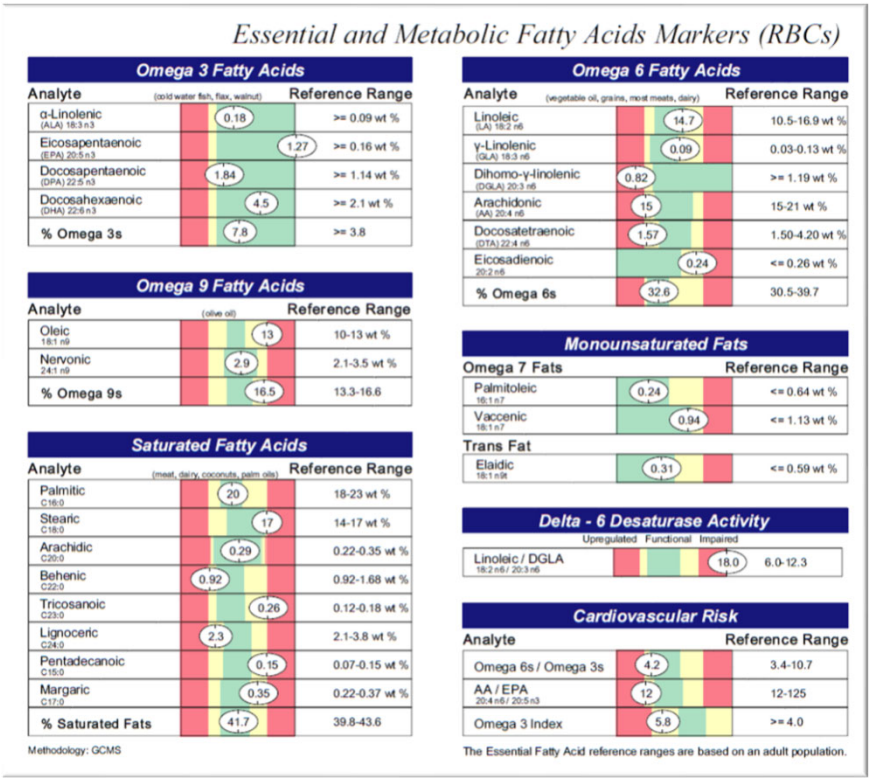
B Vitamin Markers	Reference Range
α-Aminoadipic	6-56
α-Amino-N-butyric Acid	2-21
β-Aminoisobutyric Acid	4-194
Cystathionine	4-48
3-Methylhistidine	47-232

Urea Cycle Markers	
Citrulline	0.7-3.4
Ornithine	3-17
Urea *	150-380 mmol/g creatinine

Glycine/Serine Metabolites	
Glycine	47-435
Serine	24-140
Ethanolamine	40-226
Phosphoethanolamine	1-9
Phosphoserine	2-13
Sarcosine	<= 1.0

Dietary Peptide Related Markers

	Reference Range
Anserine (dipeptide)	0.7-76.1
Carnosine (dipeptide)	1-32
1-Methylhistidine	18-887
β-Alanine	<= 18



Essential and Metabolic Fatty Acids Markers (RBCs)

Omega 3 Fatty Acids

Analyte (cold water fish, flax, walnut)	Reference Range
α-Linolenic (ALA) 18:3 n3	>= 0.09 wt %
Eicosapentaenoic (EPA) 20:5 n3	>= 0.16 wt %
Docosapentaenoic (DPA) 22:5 n3	>= 1.14 wt %
Docosahexaenoic (DHA) 22:6 n3	>= 2.1 wt %
% Omega 3s	>= 3.8

Omega 9 Fatty Acids

Analyte (olive oil)	Reference Range
Oleic 18:1 n9	10-13 wt %
Nervonic 24:1 n9	2.1-3.5 wt %
% Omega 9s	13.3-16.6

Saturated Fatty Acids

Analyte (meat, dairy, coconuts, palm oils)	Reference Range
Palmitic C16:0	18-23 wt %
Stearic C18:0	14-17 wt %
Arachidic C20:0	0.22-0.35 wt %
Behenic C22:0	0.92-1.68 wt %
Tricosanoic C23:0	0.12-0.18 wt %
Lignoceric C24:0	2.1-3.8 wt %
Pentadecanoic C15:0	0.07-0.15 wt %
Margaric C17:0	0.22-0.37 wt %
% Saturated Fats	39.8-43.6

Methodology: GCMS

Omega 6 Fatty Acids

Analyte (vegetable oil, grains, most meats, dairy)	Reference Range
Linoleic (LA) 18:2 n6	10.5-16.9 wt %
γ-Linolenic (GLA) 18:3 n6	0.03-0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3 n6	>= 1.19 wt %
Arachidonic (AA) 20:4 n6	15-21 wt %
Docosatetraenoic (DTA) 22:4 n6	1.50-4.20 wt %
Eicosadienoic 20:2 n6	<= 0.26 wt %
% Omega 6s	30.5-39.7

Monounsaturated Fats

Omega 7 Fats	Reference Range
Palmitoleic 16:1 n7	<= 0.64 wt %
Vaccenic 18:1 n7	<= 1.13 wt %
Trans Fat	
Elaidic 18:1 n9t	<= 0.59 wt %

Delta - 6 Desaturase Activity

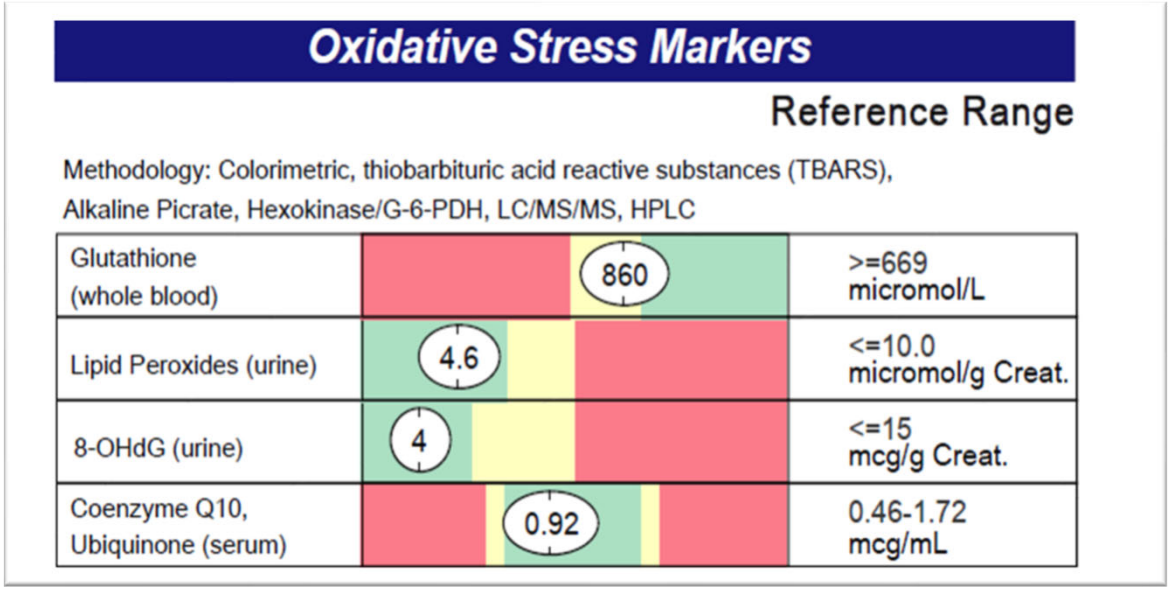
	Upregulated	Functional	Impaired	
Linoleic / DGLA 18:2 n6 / 20:3 n6			18.0	6.0-12.3

Cardiovascular Risk

Analyte	Reference Range
Omega 6s / Omega 3s	3.4-10.7
AA / EPA 20:4 n6 / 20:5 n3	12-125
Omega 3 Index	>= 4.0

The Essential Fatty Acid reference ranges are based on an adult population.

Fatigue Pattern: Oxidative Stress

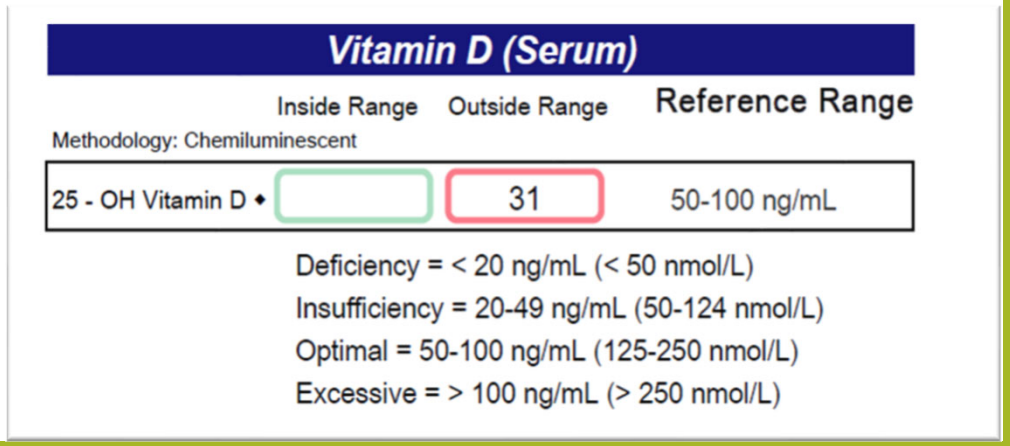


Oxidative Stress Markers

Reference Range

Methodology: Colorimetric, thiobarbituric acid reactive substances (TBARS), Alkaline Picrate, Hexokinase/G-6-PDH, LC/MS/MS, HPLC

Glutathione (whole blood)	860	>=669 micromol/L
Lipid Peroxides (urine)	4.6	<=10.0 micromol/g Creat.
8-OHdG (urine)	4	<=15 mcg/g Creat.
Coenzyme Q10, Ubiquinone (serum)	0.92	0.46-1.72 mcg/mL

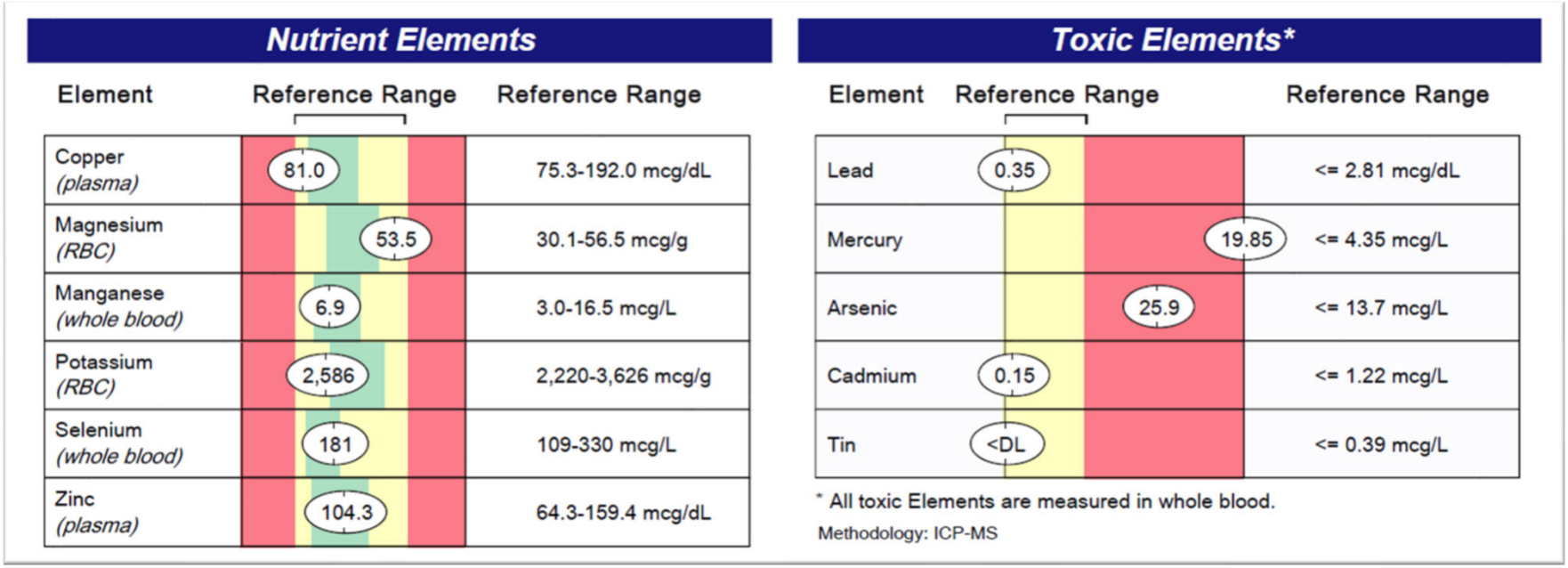


Vitamin D (Serum)

	Inside Range	Outside Range	Reference Range
Methodology: Chemiluminescent			
25 - OH Vitamin D ◆		31	50-100 ng/mL

Deficiency = < 20 ng/mL (< 50 nmol/L)
Insufficiency = 20-49 ng/mL (50-124 nmol/L)
Optimal = 50-100 ng/mL (125-250 nmol/L)
Excessive = > 100 ng/mL (> 250 nmol/L)

Fatigue Pattern: Elemental Markers



Nutrient Elements

Element	Reference Range	Reference Range
Copper *(plasma)*	81.0	75.3-192.0 mcg/dL
Magnesium *(RBC)*	53.5	30.1-56.5 mcg/g
Manganese *(whole blood)*	6.9	3.0-16.5 mcg/L
Potassium *(RBC)*	2,586	2,220-3,626 mcg/g
Selenium *(whole blood)*	181	109-330 mcg/L
Zinc *(plasma)*	104.3	64.3-159.4 mcg/dL

Toxic Elements*

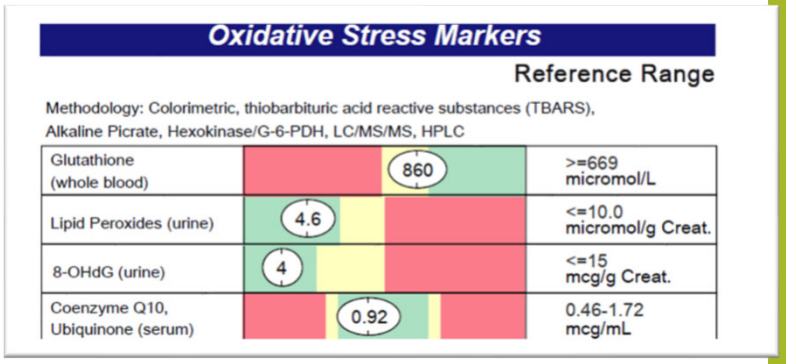
Element	Reference Range	Reference Range
Lead	0.35	<= 2.81 mcg/dL
Mercury	19.85	<= 4.35 mcg/L
Arsenic	25.9	<= 13.7 mcg/L
Cadmium	0.15	<= 1.22 mcg/L
Tin	<DL	<= 0.39 mcg/L

* All toxic Elements are measured in whole blood.

Methodology: ICP-MS

Fatigue Pattern: Oxidative Stress and Elemental Markers

- Oxidative Stress Pattern
  - Low glutathione, elevated lipid peroxides and/or 8-OHdG, and low CoQ10
    - Support when needed
- Nutrient Elements
  - Support with diet or supplementation with low elements
  - Toxic Elements
    - Identify the source
    - Eliminate or reduce the source
    - Antioxidants
    - Clearance (bowels and hydration)



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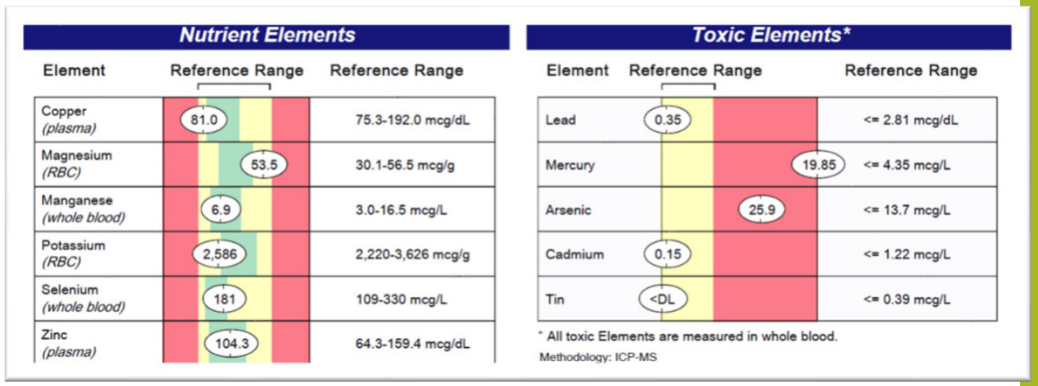

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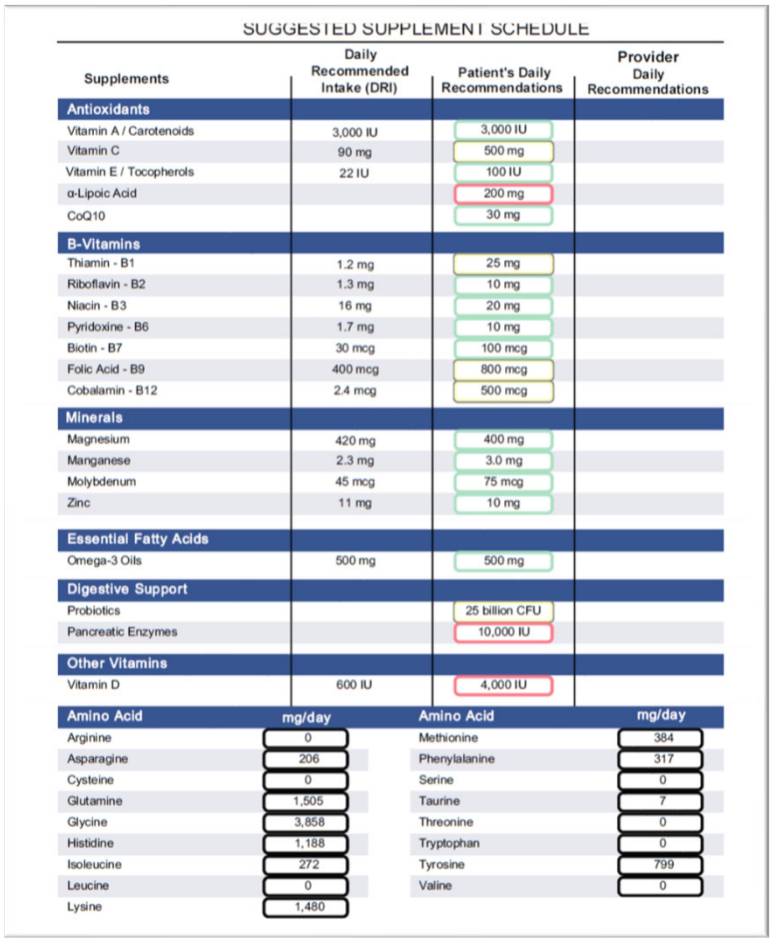
* All toxic Elements are measured in whole blood.

Methodology: ICP-MS

Fatigue Pattern: Summary

- Decline in mitochondria function & alteration in brain neurotransmitters
  - B-vitamins, CoQ10, amino acids, and minerals
- Oxidative stress
  - ID source, avoid/minimize, and support detoxification (hydration, antioxidants, elimination)
- Inflammation
  - Essential fatty acids
- Genomic SNPs
  - B-vitamins, minerals, anti-oxidants, and anti-inflammatory



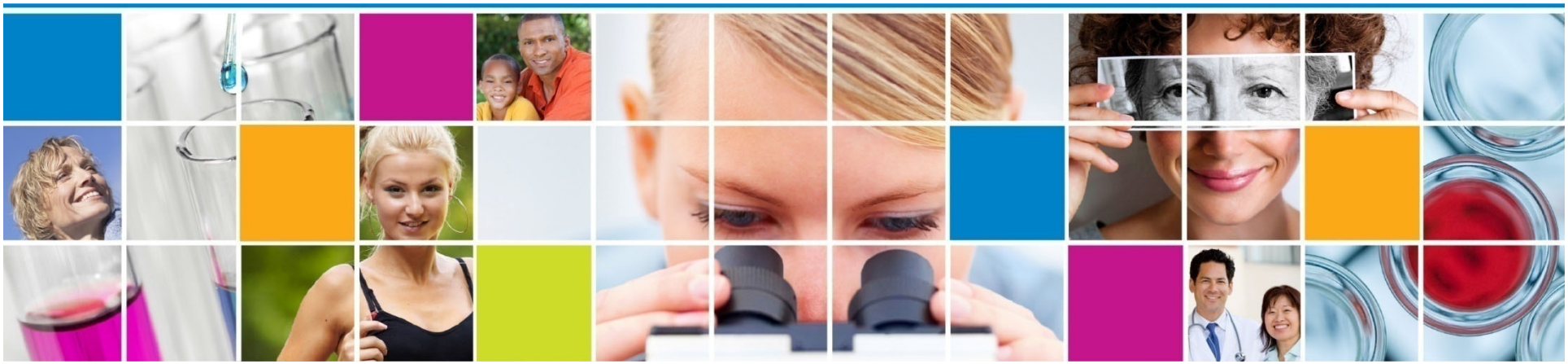
SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	3,000 IU	3,000 IU	
Vitamin C	90 mg	500 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		200 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.2 mg	25 mg	
Riboflavin - B2	1.3 mg	10 mg	
Niacin - B3	16 mg	20 mg	
Pyridoxine - B6	1.7 mg	10 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	800 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	420 mg	400 mg	
Manganese	2.3 mg	3.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	11 mg	10 mg	
Essential Fatty Acids			
Omega-3 Oils	500 mg	500 mg	
Digestive Support			
Probiotics		25 billion CFU	
Pancreatic Enzymes		10,000 IU	
Other Vitamins			
Vitamin D	600 IU	4,000 IU	

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	384
Asparagine	206	Phenylalanine	317
Cysteine	0	Serine	0
Glutamine	1,505	Taurine	7
Glycine	3,858	Threonine	0
Histidine	1,188	Tryptophan	0
Isoleucine	272	Tyrosine	799
Leucine	0	Valine	0
Lysine	1,480		

Summary

- There are many ways to evaluate a patient for fatigue in a personalized medicine approach to healthcare.
- All the methods are designed to lead the patient to not just a resolution of their symptoms, but to also find the etiology or causes of the problem.
- The science is now here to help our patients achieve the optimal health that they desire.
- Life is not about how to survive the storm, but how to dance in the rain!



Case Histories: Nutrients

Pamela W. Smith, M.D., MPH, MS

Reference

- Smith, P. What You Must Know About Vitamins, Minerals, Herbs, And So Much More. New York: Square One Publishing, 2020.
- Coombs, G. The Vitamins: Fundamental Aspects in Nutrition and Health, 3rd Ed. Burlington, MA: Elsevier Academic Press, 2008, 265-381.

Micronutrient Testing

B Vitamins

Are water soluble and need to be taken twice a day

SpectraCell Laboratories

LABORATORY REPORT

Account Number: 186506	Name: **Janet Doe**
	Gender: Female DOB: 04/21/1972
John Doe, M.D. 1234 Any Street Suite 244 Anytown, TX 77581-1234 USA	Accession Number: M00001 Requisition Number: 438507
	Date of Collection: 04/25/2014 Date Received: 04/26/2014 Date Reported: 05/13/2014

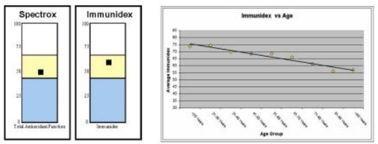
Summary of Deficient Test Results

Testing determined the following functional deficiencies:

Oleic Acid Glutathione Vitamin E

Borderline deficiencies include:

Vitamin B2	Vitamin B12	Pantothenate	Inositol
Vitamin D3	Manganese	Chromium	Magnesium
Coenzyme Q-10	Selenium	Vitamin K2	Vitamin C
Copper	Spectrox	Immunidex	



John F. Crawford, Ph.D.
Laboratory Director

CLIA# 45D0710715

OVERVIEW OF TEST PROCEDURE

1. A mixture of lymphocytes is isolated from the blood.
2. These cells are grown in a defined culture medium containing optimal levels of all essential. nutrients necessary to sustain their growth in cell culture.
3. The T-lymphocytes are stimulated to grow with a mitogen (phytohemagglutinin) and growth is measured by the incorporation of tritiated (radioactive) thymidine into the DNA of the cells.

The growth response under optimal conditions is defined as 100%, and all other growth rates are compared to this 100% level of growth.

For example – we remove vitamin B6 from the medium and stimulate the cells to grow by mitogen stimulation. Growth is measured by DNA synthesis and the rate of growth is dependent only upon the functional level of vitamin B6 available within the cells to support growth. For Vitamin B6 a growth rate of at least 55% of the growth rate observed in the optimal (100%) media is considered normal. Results less than 55% are considered to indicate a functional deficiency for Vitamin B6. Each nutrient has a different reference range that was established by assaying thousands of apparently healthy individuals.

BREAKING DOWN THE REPORT

1. TEST RESULT (% CONTROL)

This column represents the patient's growth response in the test media measured by DNA synthesis as compared to the optimal growth observed in the 100% media.

2. FUNCTIONAL ABNORMALS

An interpretation is provided for those nutrients found to be deficient.

3. REFERENCE RANGE

This column represents how this patient's result compares to thousands of patients previously tested. A patient's result is considered deficient when it is less than the reference range.

4. GRAPHS

The abnormal range of results is noted in the blue area. Abnormal results are indicated in red. The gray cross hatch area is a representation of the range of test results found in a random selection of subjects.

SPECTROX® – TOTAL ANTIOXIDANT FUNCTION

SPECTROX® is a measurement of overall antioxidant function. The patient's cells are grown in the optimal media, stimulated to grow, and then increasing amounts of a free radical generating system (H2O2) are added. The cell's ability to resist oxidative damage is determined. The increasing levels of peroxide will result in diminished growth rates in those patients with poor antioxidant function capacity.

INDIVIDUAL ANTIOXIDANT LEVELS

In the tests for individual antioxidants, it is determined which specific antioxidants may be deficient and thus affecting the SPECTROX® antioxidant function result. For these tests, the patient's cells are preincubated with one of the nutrient antioxidants, i.e. selenium, and then the Spectrox® test is repeated to determine if the addition of selenium improves the patient's antioxidant function. This process is repeated for each individual antioxidant.

Antioxidants tested with this process:
Glutathione, Cysteine, Coenzyme-Q10, Selenium, Vitamin E, and Alpha Lipoic Acid

Repletion Suggestions

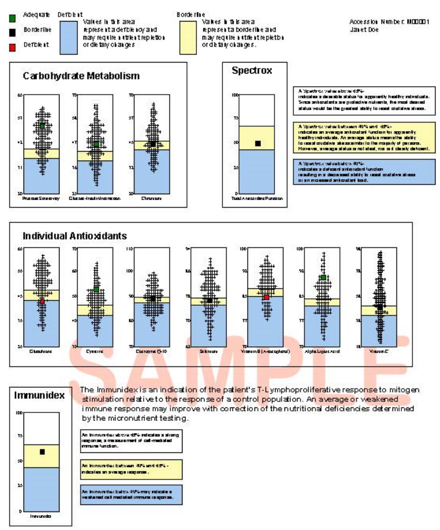
1. Oleic Acid	2-3 tbsp olive oil daily for repletion of Oleic Acid. Deficiency of Oleic Acid suggests impaired synthesis of unsaturated long chain fatty acids. Take 600 mg b.i.d. (1.2 grams daily) of EPA and DHA in Omega-3 Fatty Acids.
2. Glutathione	600 mg b.i.d. (1200 mg daily) of N-Acetylcysteine (NAC) Take each dose with a meal
3. Vitamin E (A-tocopherol)	400 IU daily of mixed tocopherols

Please note: Supplementation is usually required for four to six months to effect the repletion of a functional deficiency in lymphocytes

Suggestions for supplementation with specific micronutrients must be evaluated and approved by the attending physician. This decision should be based upon the clinical condition of the patient and the evaluation of the effects of supplementation on current treatment and medication of the patient.

Micronutrients	Patient Results (% Control)	Functional Abnormals	Reference Range (greater than)
B Complex Vitamins			
Vitamin B1 (Thiamin)	85		>78%
Vitamin B2 (Riboflavin)	56	Borderline	>53%
Vitamin B3 (Niacinamide)	87		>80%
Vitamin B6 (Pyridoxine)	63		>54%
Vitamin B12 (Cobalamin)	16	Borderline	>14%
Folate	38		>32%
Pantothenate	12	Borderline	>7%
Biotin	45		>34%
Amino Acids			
Serine	49		>30%
Glutamine	46		>37%
Asparagine	57		>39%
Metabolites			
Choline	26		>20%
Inositol	60	Borderline	>58%
Carnitine	55		>46%
Fatty Acids			
Oleic Acid	65	Deficient	>65%
Other Vitamins			
Vitamin D3 (Cholecalciferol)	51	Borderline	>50%
Vitamin A (Retinol)	77		>70%
Vitamin K2	34	Borderline	>30%
Minerals			
Calcium	48		>38%
Manganese	55	Borderline	>50%
Zinc	47		>37%
Copper	45	Borderline	>42%
Magnesium	41	Borderline	>37%
Carbohydrate Metabolism			
Glucose-Insulin Interaction	46		>38%
Fructose Sensitivity	49		>34%
Chromium	43	Borderline	>40%
Antioxidants			
Glutathione	42	Deficient	>42%
Cysteine	52		>41%
Coenzyme Q-10	88	Borderline	>86%
Selenium	76	Borderline	>74%
Vitamin E (A-tocopherol)	84	Deficient	>84%
Alpha Lipoic Acid	90		>81%
Vitamin C	47	Borderline	>40%
SPECTROX™			
Total Antioxidant Function	50	Borderline	>40%
Proliferation Index			
Immunidex	57	Borderline	>40%

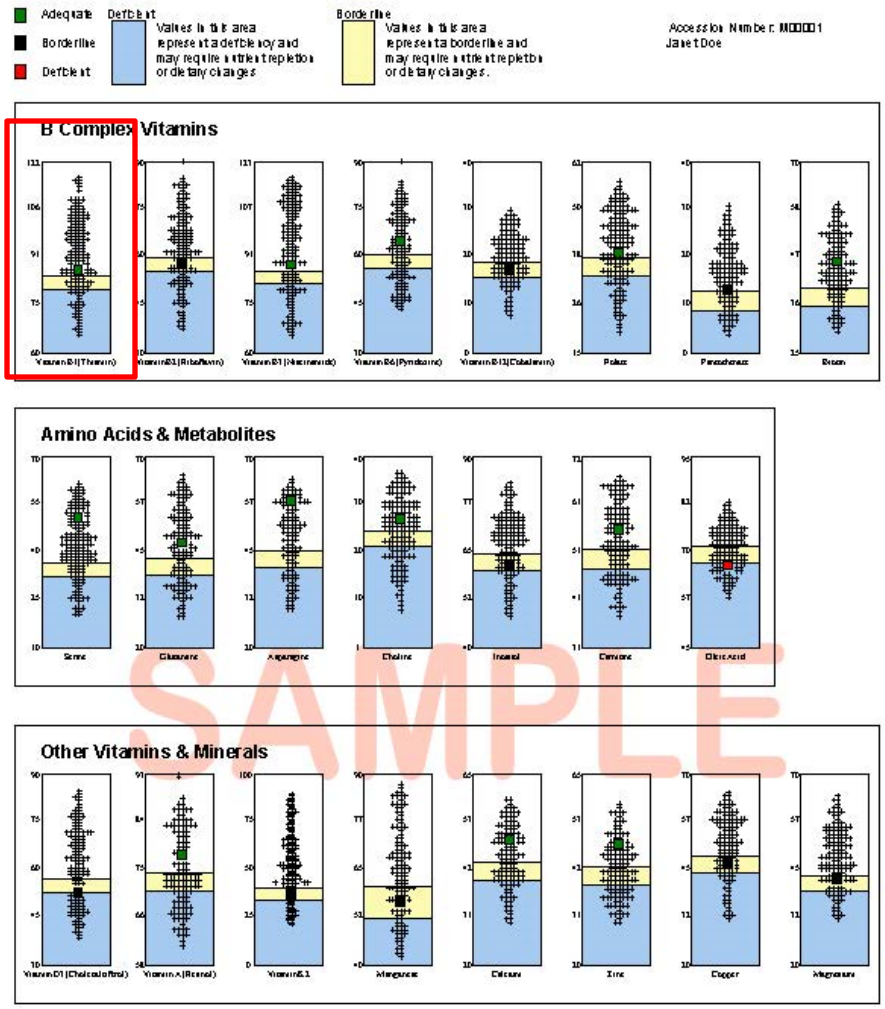
The reference ranges listed in the above table are valid for male and female patients 12 years of age or older.



Case History

- 55-year-old attorney who comes to see you because she says that her memory is not as sharp as it use to be. She is seeing a metabolic/anti-aging specialist who has her on natural hormones and the patient states that her memory has improved on them but her cognitive function is still not as sharp as it was when she was 30.
- PH: unremarkable
- Meds: none. Does take EPA/DHA 2,000 mg qd
- SH: She works 18 hours a day 6-7 days a week and she drinks two gin and tonics each night
- PE: is unremarkable

What Do You Want To Look At In This Patient?


Adequate
Borderline
Deficient
Deficient
Values in this area represent a deficiency and may require nutrient repletion or dietary changes.
Borderline
Values in this area represent a borderline and may require nutrient repletion or dietary changes.
Accession Number: MDDDD1
Janet Doe
B Complex Vitamins
Amino Acids & Metabolites
Other Vitamins & Minerals

Vitamin B1 (Thiamine)

- Functions in the body
  - Helps the body deal with stress
  - Needed for metabolism of thyroid hormones
  - Needed for synthesis of nucleic acids and coenzymes
  - Needed for making aldosterone
  - Required for energy production (Krebs cycle)
  - Required for proper nerve function
  - Used in the synthesis of acetylcholine

Symptoms of B1 Deficiency

- Appetite decreased
- Bradycardia
- Cardiomyopathy
- CHF
- Confusion
- Edema
- Fatigue
- Forgetfulness

Symptoms of B1 Deficiency

- General weakness
- GI disturbances
- Headaches
- Irritability
- Loss of appetite
- Mild depression
- Memory loss

Symptoms of B1 Deficiency (Cont.)

- Nervousness
- Peripheral neuropathy
- Poor memory
- Racing heart
- Sleep disturbance
- Vision problems

Causes of B1 Deficiency

- Alcohol
- Antibiotics
- Blueberries
- Brussels sprouts
- Coffee
- Diuretics
- Horseradish
- Oral contraceptives

Causes of B1 Deficiency (Cont.)

- Red beet root
- Seafood such as fish, shrimp, clams, and mussels
- Sugar
- Sulfa drugs
- Sulfites (as a food additive)
- Theophylline
- Tea

Vitamin B1

- Dosage: 10-100 mg
- High dosages of B1 may deplete the body of vitamin B6 or magnesium

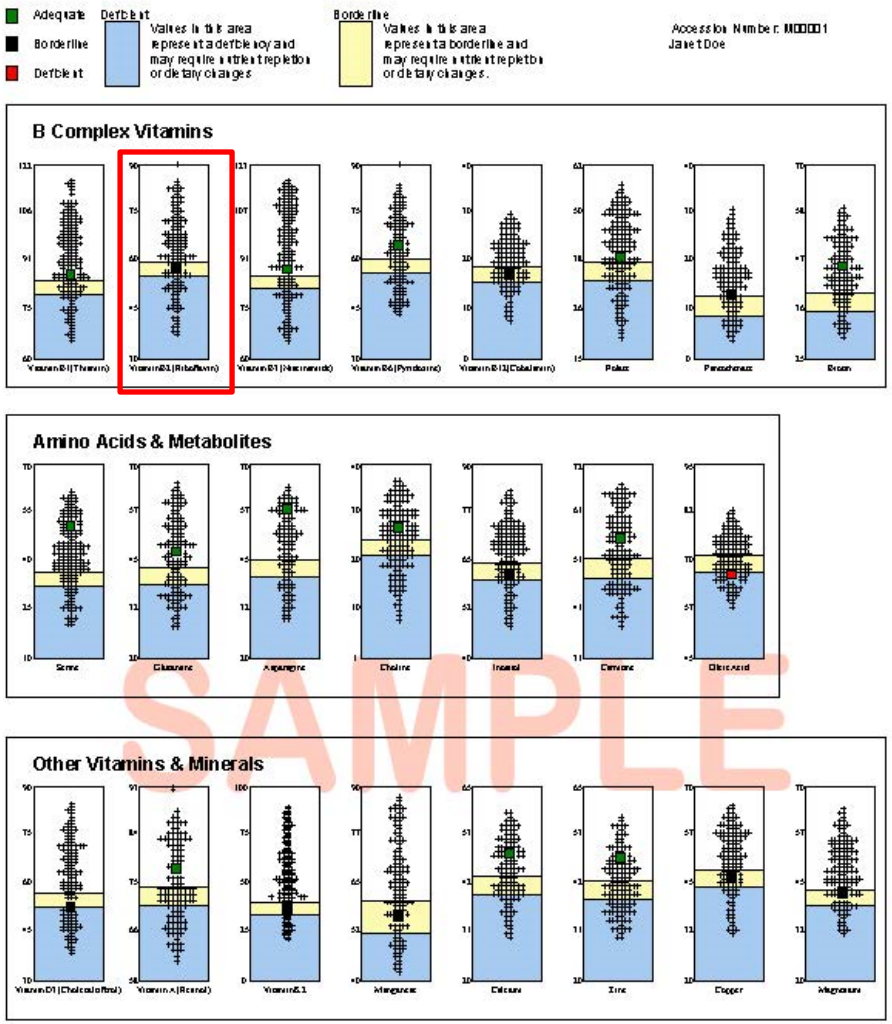
Diseases That Can Be Helped With Vitamin B1

- Alcoholism
- Confusion
- Dementia
- Depression
- Fatigue
- Memory loss
- Neuropathy
- Pain

Case History

- 34-year-old female who comes in to see you for dry, cracking skin. She has seen an endocrinologist and her thyroid function is optimal.
- She has also seen a dermatologist who gave her a "cream" to put on her skin but it has not helped. The dermatologist diagnosed her condition as seborrhic dermatitis.
- The remainder of her history and physical are unremarkable except for she heard that taking a lot of vitamin C was good for her so she takes as much as she can.

What Do You Want To Look At In This Patient?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Accession Number: M00001
Janet Doe
B Complex Vitamins
Amino Acids & Metabolites
Other Vitamins & Minerals

Vitamin B2 (Riboflavin)

- Functions of B2
  - Involved with energy production
  - Needed for healthy eyes
  - Used for the production of antibodies
  - Important for tissue repair
  - Catalyzes reactions that process CHO, fats, and proteins
  - Crucial to the cytochrome P450 system
  - Needed for proper thyroid function

Vitamin B2 (Riboflavin)

- Involved in the metabolism of vitamin K
- Needed for energy metabolism
- Needed in the regeneration of glutathione
- Needed to convert vitamin B6, folic acid, vitamin A, and niacin into their active forms
- Used in lipid metabolism
- Important for the formation of aldosterone

Signs and Symptoms of B2 Deficiency

- Angular stomatitis
- Cheilosis
- Depression
- Dry, cracking skin
- Glossitis
- Hyperemia and edema of the oral mucosa
- Light sensitivity

Signs and Symptoms of B2 Deficiency (Cont.)

- Normocytic, normochromic anemia with reticulocytopenia, leukopenia, and thrombocytopenia
- Peripheral neuropathy of the extremities characterized by hyperesthesia, coldness and pain, and also decreased sensitivity to touch, temperature, vibration, and position
- Seborrheic dermatitis around the nose, mouth, and scrotum/vulva

Substances That Reduce The Bioavailability of B2

- Adriamycin
- Alcohol
- Amitriptyline
- Antacids
- Caffeine
- Copper
- Imipramine
- Phenothiazines

Substances That Reduce The Bioavailability of B2 (Cont.)

- Phenytoin
- Saccharin
- Theophylline
- Tryptophan
- Vitamin B3
- Vitamin C
- Zinc

Vitamin B2

- Dosage: 10-100 mg
- Side effects: none

Diseases That Can Be Helped With B2

- Acne
- Alcoholism
- Arthritis
- Athlete's foot
- Baldness
- Cataracts
- Depression
- Diabetes

Diseases That Can Be Helped With B2 (Cont.)

- Diarrhea
- Failure to detoxify effectively
- Hysteria
- Indigestion
- Light sensitivity
- Migraines
- Nerve damage

Diseases That Can Be Helped With B2 (Cont.)

- Reddening of eyes
- Scrotal skin changes
- Seborrhic dermatitis
- Skin changes around the mouth
- Stress
- Visual changes

Case History

- 60-year-old male who comes into your office wanting to know what he can do to lower his cholesterol. He states that he has been on a statin drug, and that it has worked fine for him but now he has a high lipoprotein a level from the use of the statin drug.
- PH: unremarkable
- SH: owns a factory that he started with his brother
- FH: Father died of acute MI at the age of 62
- Meds: none. Takes a MVI
- P/E: per his cardiologist is unremarkable

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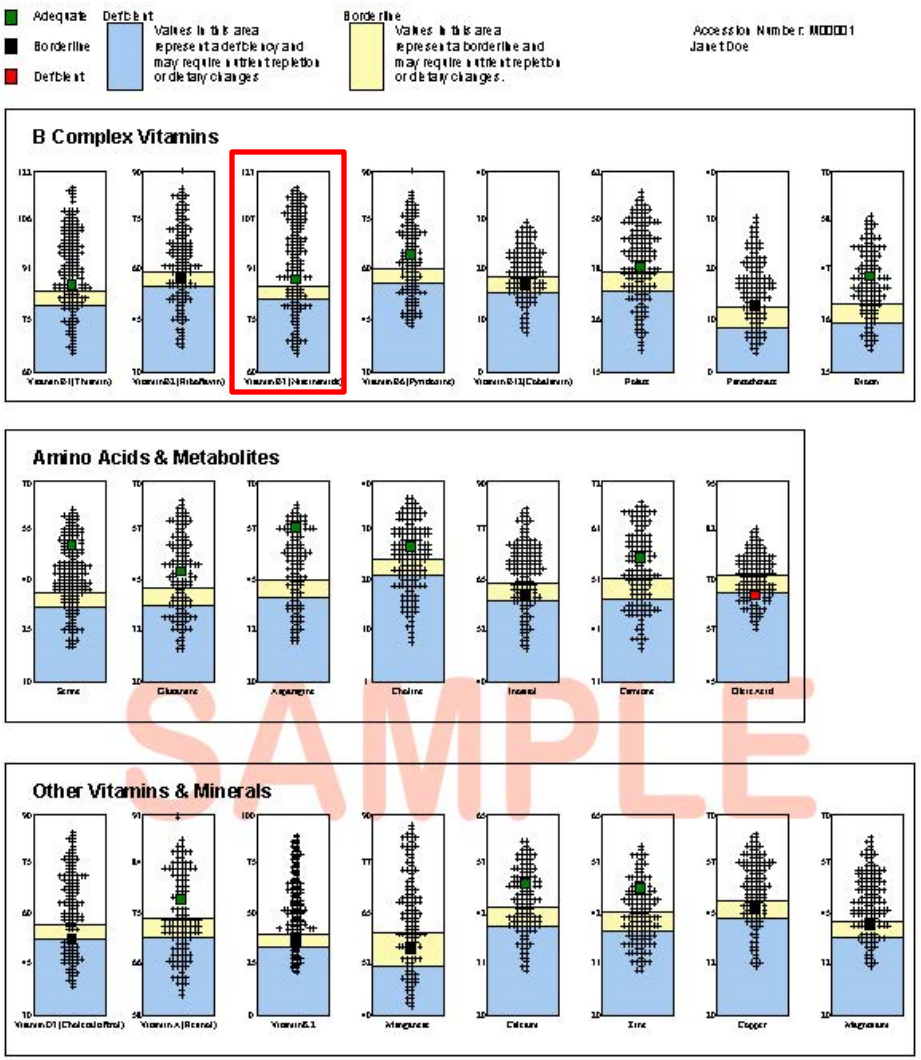
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Janet Doe
B Complex Vitamins
Amino Acids & Metabolites
Other Vitamins & Minerals

Vitamin B3

- Includes both niacin and its derivative niacinamide
- Is used in at least forty chemical reactions in the body
- Lowers cholesterol
- Taking niacin by itself may elevate homocysteine

Functions of Niacin In The Body

- Can decrease lipoprotein A
- Can lower LDL and raise HDL cholesterol
- Decreases fibrinogen
- Involved in energy production
- Lowers triglycerides
- Provides energy to convert cholesterol to pregnenolone

Functions of Niacin In The Body (Cont.)

- Needed for the proper function of the adrenal glands
- Used in the metabolism of CHO, proteins and fats
- Used in the metabolism of tryptophan and serotonin

Symptoms of Niacin Deficiency

- Anorexia
- Confusion
- Depression
- Dermatitis
- Fatigue
- Headaches
- Inability to detoxify
- Indigestion

Symptoms of Niacin Deficiency (Cont.)

- Insomnia
- Irritability
- Mouth ulcers
- Muscle weakness
- Nausea
- Pellagra
- Skin changes around the mouth

Niacin Status

- Supplies of tryptophan and pyridoxine are important determinants of niacin levels.
- Excess levels of leucine may antagonize niacin synthesis and/or utilization.
- Zinc may also play a role in the pyridoxine-dependent metabolic conversion of tryptophan to niacin.

Niacin

- Dosage: 50-3,000 mg
- Should be prescribed by physician to use if using more than 100 mg a day
- Side effects: niacin flush
- High dose or extended release can cause liver damage, peptic ulcers, high uric acid levels or glucose intolerance
- Do not take niacin with a statin drug—may cause rhabdiomyolysis

Niacin (Cont.)

- High chronic intake of nicotinamide may deplete methyl groups due to the elevated demand for methylation to excrete this vitamin.

Diseases That Can Be Helped With Niacin

- Acne
- Depression
- Diabetes
- Hypercholesterolemia
- Hypertriglyceridemia
- Intermittent claudication
- Low HDL

Diseases That Can Be Helped With Niacin (Cont.)

- Memory loss
- Osteoarthritis
- Dysmenorrhea
- Parkinson's disease
- Rheumatoid arthritis
- Lowers lipoprotein a

Case History

- 50-year-old female who presents to your office for "burning feet". Her PCP checked her for diabetes and her FBS, fasting insulin, HgBA1C and 2-hour GTT are all normal. She wants to know what else she can be done.
- Remainder of her history and physical are noncontributory except that she is currently using an estradiol patch. She had a hysterectomy 5 years ago.

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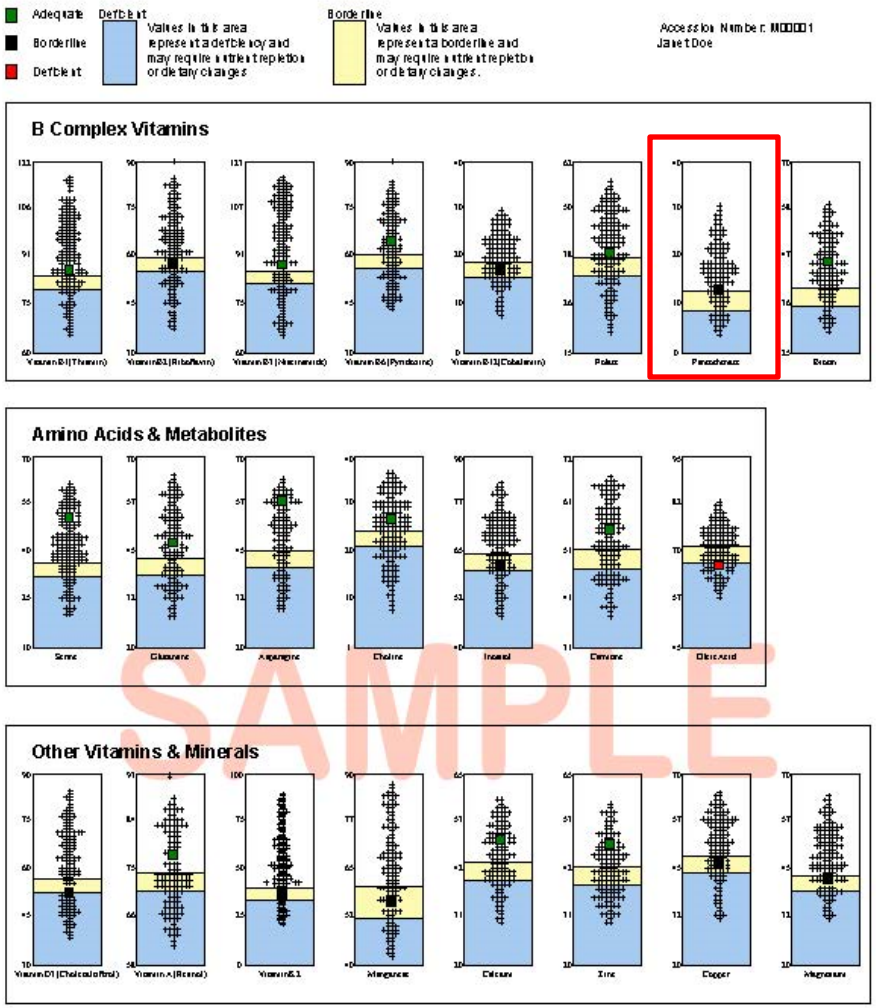
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Vitamin B2 (Riboflavin)
Vitamin B3 (Niacinamide)
Vitamin B6 (Pyridoxine)
Vitamin B12 (Cobalamin)
Folate
Pantothenic
Biotin
Amino Acids & Metabolites
Serine
Glutamine
Asparagine
Choline
Inositol
Carnitine
Citric Acid
Other Vitamins & Minerals
Vitamin D1 (Cholecalciferol)
Vitamin A (Retinol)
Vitamin E1
Manganese
Calcium
Zinc
Copper
Magnesium

Vitamin B5 (Pantothenic Acid)

- Functions in the body
  - Involved in the metabolism of CHO, fats and proteins
  - Aids in the formation of antibodies
  - Aids in wound healing
  - Helps with fatty acid transport
  - Helps the body use other vitamins
  - Needed for the synthesis of coenzyme A

Vitamin B5 (Pantothenic Acid) (Cont.)

- Stimulates adrenal glands
- Used in RBC production
- Used in the synthesis of amino acids
- Used to make vitamin D

Symptoms of B5 Deficiency

- Adrenal exhaustion
- Allergies
- Arthritis
- Burning sensation in feet
- Constipation
- Decreased antibody formation
- Decreased production of HCL in stomach
- Depression

Symptoms of B5 Deficiency (Cont.)

- Duodenal ulcers
- Eczema
- Enlarge, chunky, furrowed tongue
- Fatigue
- Gout
- Graying hair
- Headache

Symptoms of B5 Deficiency (Cont.)

- High blood pressure
- Insomnia
- Intestinal inflammation
- Muscle cramps
- Nerve degeneration
- Restlessness
- Upper respiratory tract infections
- Vomiting

Causes of B5 Deficiency

- Caffeine
- Estrogen supplementation
- Sleeping pills

Diseases That Can Be Helped With B5

- Acne
- Adrenal dysfunction
- Allergies
- Cold sores
- Detoxification
- Hypertriglyceridemia
- Genital herpes

Diseases That Can Be Helped With B5 (Cont.)

- Fatigue
- Infection
- Osteoarthritis
- Rheumatoid arthritis
- Shingles
- Ulcerative cholitis

Vitamin B5

- Dose: 25 to 50 mg BID

Case History

- 25-year-old female presents to your office with the chief complaint of bilateral carpal tunnel syndrome. Her internist ran thyroid studies and they are normal. She wants to know what else she can do to help the carpal tunnel syndrome besides wearing splints and having surgery.
- Meds: Tetracycline BID for acne

Case History (Cont.)

- SH: Pt. is a secretary and spends a lot of her day typing on a computer. Her employer has gotten her a better chair at the right height to try and egonomically help with her carpel tunnel syndrome.
- Remainder of history and physical are noncontributory.

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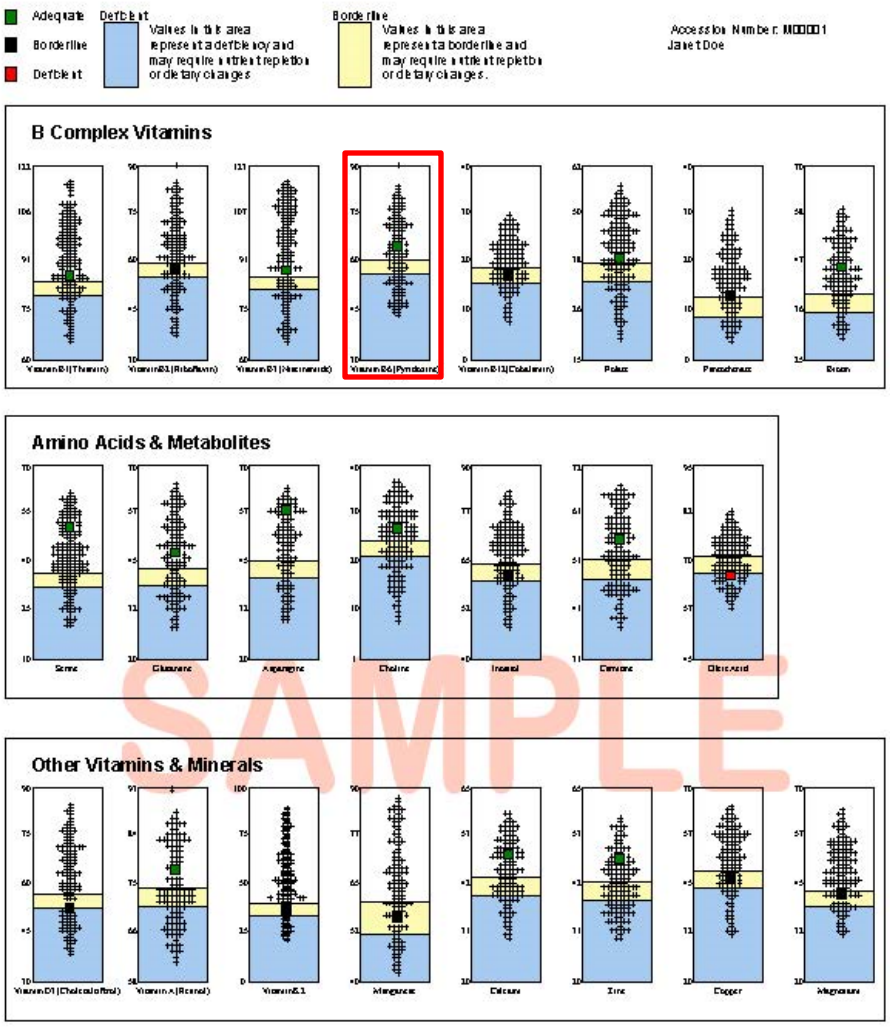
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Janet Doe
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Amino Acids & Metabolites
Other Vitamins & Minerals

Vitamin B6 (Pyridoxine)

- Is a cofactor for over 100 different enzymes
- As one ages the ability to utilize B6 declines

Vitamin B6 (Pyridoxine) (Cont.)

- Functions of B6 in the body
  - Detoxifies chemicals
  - Involved in strengthening connective tissue
  - Key to the synthesis of several neurotransmitters
  - Needed for the absorption of fats and proteins
  - Needed for the immune system
  - Essential for the production of HCL acid

Vitamin B6 (Pyridoxine) (Cont.)

- Functions (cont.)
  - Needed for the transfer of amino groups
  - Used in the metabolism of amino acids
  - Involved in the methylation process
  - Needed for REM sleep

Signs and Symptoms of B6 Deficiency

- Cheilosis
- Depression
- Fatigue
- Glossitis
- Hyperactivity
- Impaired cellular immunity
- Insomnia
- Irritability

Signs and Symptoms of B6 Deficiency (Cont.)

- Mental confusion
- Mouth ulcers
- Nervousness
- Numbness
- Peripheral neuropathies
- Skin lesions around the mouth
- Stomatitis
- Weakness

Causes of B6 Deficiency

- Aminoglycosides
- Amphetamines
- Antidepressants
- Bumetanide
- Cephalosporins
- Cigarette smoking
- Cortisone
- DES

Causes of B6 Deficiency (Cont.)

- Dopamine
- Estrogen supplementation
- Ethacrynic acid
- Excessive exercise
- Fluroquinolones
- Food additives (FDC yellow #5)
- Hydralazine
- Hydrochlorothiazide

Causes of B6 Deficiency (Cont.)

- Isoniazid
- Macrolides
- Oral contraceptives
- Penicillamine
- Penicillins
- Pesticides
- Phenelzine

Causes of B6 Deficiency (Cont.)

- Quinestrol
- Raloxifene
- Sulfonamides
- Tetracylcines
- Theophylline
- Torsemide
- Trimethoprim

Vitamin B6

- Dose: 30-500 mg
- Dosages higher than 500 mg/day can cause a neuropathy
- Do not use in patients taking levodopa unless also using a decarboxylase inhibitor since B6 can interfere with L-dopa.

Diseases That Can Be Helped With B6

- Asthma
- Artherosclerosis
- Autism
- Carpal tunnel syndrome
- Constipation
- Depression
- Diabetes

Diseases That Can Be Helped With B6 (Cont.)

- Eczema
- Epilepsy
- Infertility
- Irritability
- MSG sensitivity
- Nausea and vomiting related to pregnancy
- Nervous system dysfunction

Diseases That Can Be Helped With B6 (Cont.)

- Osteoporosis
- PMS
- Prevention of calcium oxalate kidney stones
- Schizophrenia
- Seborrheic dermatitis
- Sickle cell disease

Supranutritional Doses of B6 and Their Usages

- Chinese restaurant syndrome
  - Studies have shown that Chinese restaurant syndrome may respond to vitamin B6 (50 mg/day).
    - Ibid., Combs, p. 326.

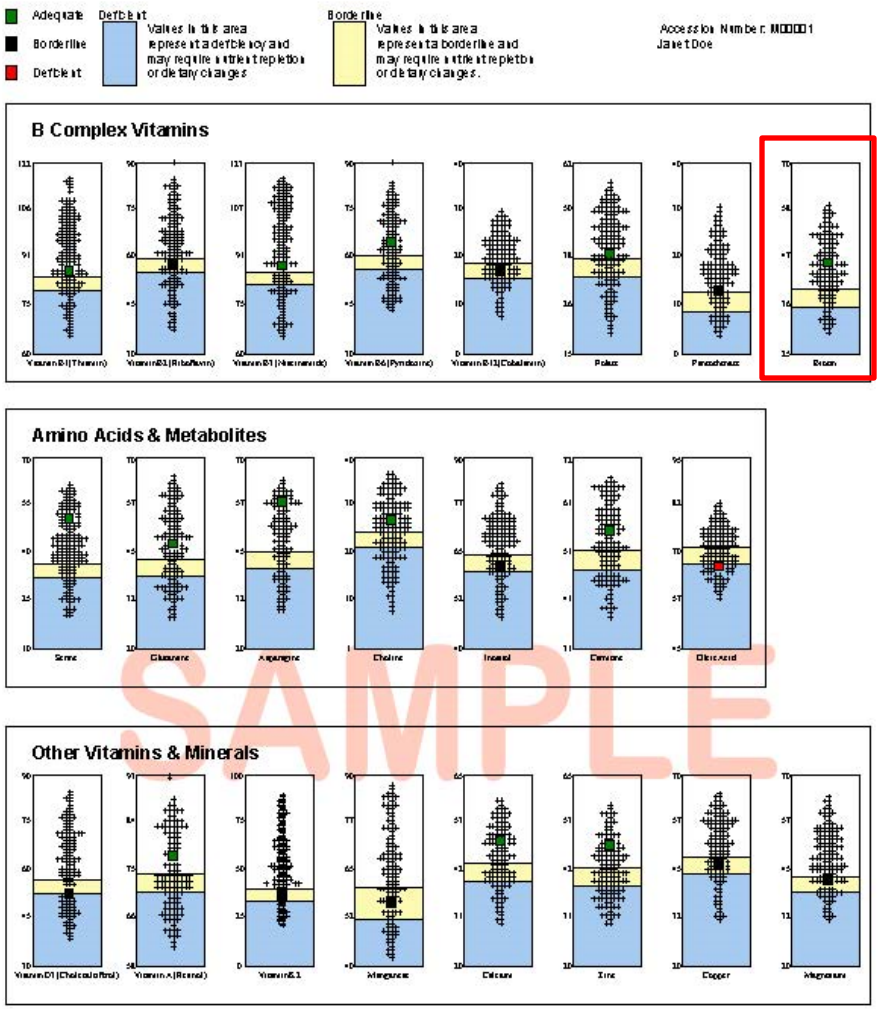
Case History

- 34-year-old female presents to your office for hair loss. She has seen a dermatologist who tested her DHT level and it is normal. She wants to know what else she can do. She brings in a bag with hair in it to show you how much hair she lost this morning in the shower.
- SH: She owns her own quilting shop and the struggling economy has caused her to lay off all of her employees and she is now working at her store 12 hours a day 6 days a week.

Case History (Cont.)

- Meds: Armour thyroid 60 mg qd
- ROS: Is unremarkable except she has brittle nails.
- Physical examination is negative except for her hair which has patchy spots of thinning hair.

What Do You Want To Look At In This Patient?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Inositol
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Other Vitamins & Minerals
Vitamin D1 (Cholecalciferol)
Vitamin A (Retinol)
Vitamin E
Manganese
Calcium
Zinc
Copper
Magnesium

Biotin (Vitamin B7)

- Is made in the GI tract
- Functions
  - Increases insulin sensitivity
  - Needed for fatty acid synthesis
  - Strengthens nails
  - Helps maintain healthy hair
  - Used in energy metabolism

Symptoms of Biotin Deficiency

- Cradle cap (in newborns)
- Dandruff
- Depression
- Hair loss
- Hallucinations
- Localized numbness and tingling
- Muscle pain

Signs and Symptoms of Biotin Deficiency

- Decreased appetite/anorexia
- Depression
- Dermatitis
- Glossitis
- Hepatic steatosis
- Hypercholesterolemia

Signs and Symptoms of Biotin Deficiency (Cont.)

- Nausea
- Reduced appetite
- Scaly dermatitis
- SIDS
  - Marginal biotin status may play a role in the development of SIDS.
  - Studies have shown that die of SIDS have a lower hepatic concentration of biotin.
    - Ibid., Combs, p. 340.

Causes of Biotin Deficiency

- Aging process
- Alcohol excess
- Anticonvulsants
- Athletic competition
- Patients that have suffered significant burns
- Partial gastrectomy or other causes of achlorhydria
- Raw egg white ingestion

Biotin

- Vegetarian diet increases biotin levels
- Dosage: 300-600 micrograms
  - May use up to 5 mg a day for improvement in hair and nails
- No C/I

Diseases That Can Be Helped With Biotin

- Brittle nails
- Diabetes
- Diabetic neuropathy
- Seborrheic dermatitis
- Hair loss

Case History

- 60-year-old male who presents to your office wanting to have his homocysteine level tested.
- FH: He states that his brother just found out that he had a high level and that their father had an MI at the age of 64 and then died of an MI at the age of 67. His mother died at the age of 78 of a CVA and she had dementia for 4 years before her death.
- PH: + rheumatoid arthritis
- Meds: Methotrexate. He could not tolerate other med
- SH: owns a bakery and starts work every day at 4am

Case History (Cont.)

- ROS: weight gain o 20 pounds over the last five years, also has fatigue and pain in his hands and right knee that is worse in the am
- P/E: BP 102/94. Patient appears older than stated age. Tenderness and swelling with joint deformity in hands bilaterally.

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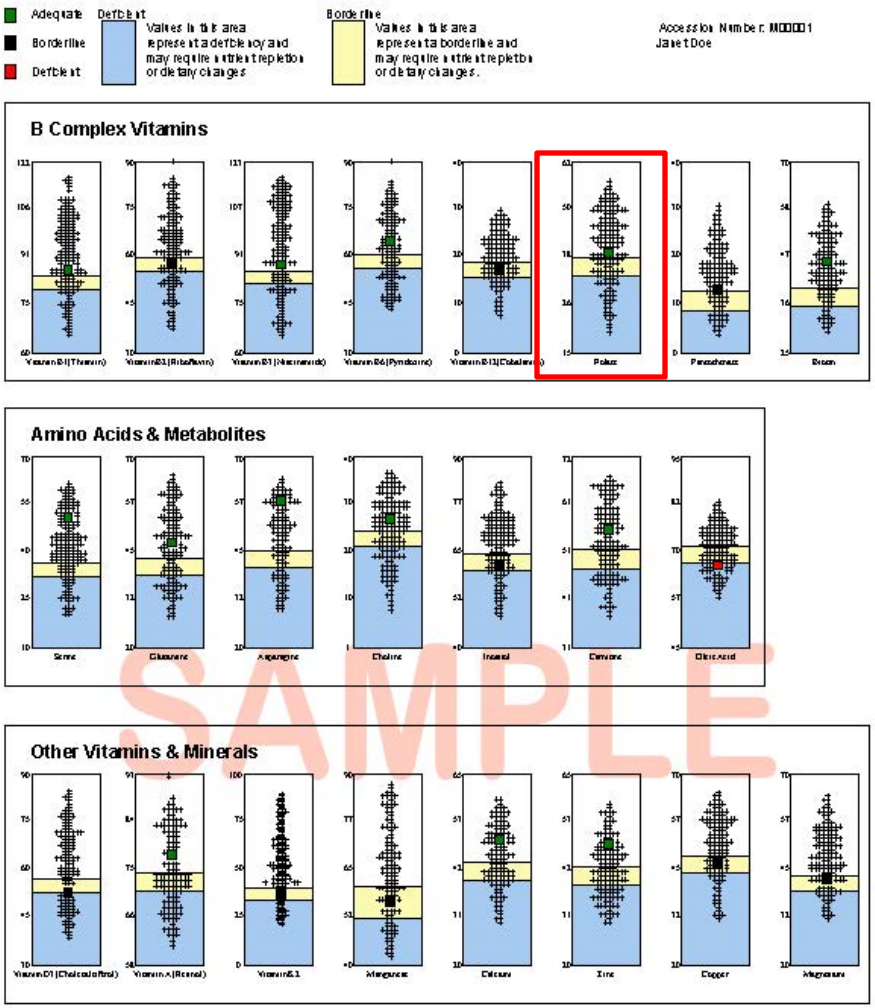
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Janet Doe
B Complex Vitamins
Folate
Amino Acids & Metabolites
Other Vitamins & Minerals
SAMPLE

Folic Acid (Vitamin B9)

- Functions of folic acid in the body
  - Detoxifies hormones such as estrogen
  - Detoxifies phenols
  - Essential for CNS function
  - Essential for DNA synthesis
  - Involved in methylation
  - Metabolic conversion of dopamine
  - Needed for the synthesis of hemoglobin

Folic Acid (Vitamin B9)

- Functions (cont.)
  - Needed for proper health of all tissues, especially mucous membranes
  - Produces complex phospholipids for neurological function
  - Produces SAMe
  - Protects babies from neural tube defects such as spina bifida

Symptoms of Folic Acid Deficiency

- Birth defects affecting the neural tube
- Decreased resistance to infection
- Depression
- Diarrhea
- Drowsiness
- Graying hair
- Indigestion
- Insomnia

Symptoms of Folic Acid Deficiency (Cont.)

- Inflamed tongue that is smooth and shiny
- Irritability
- Mental illness
- Numbness or tingling in hands and feet
- Slow, weakened pulse
- Toxemia
- Weakness
- Wound healing is impaired

Problems Associated With Folic Acid Deficiency

- Adrenal dysfunction
- Anemia
- Depression
- Impaired synthesis of estrogen and progesterone
- Increased number of ovarian cysts
- Increased risk of cervical cancer
- High homocysteine
- Low vitamin C levels

Causes of Folic Acid Deficiency

- Atrophic gastitis
- Alcohol
- ASA
- Barbiturates
- BCP
- Carbamazepine
- Celecoxib
- Celiac disease

Causes of Folic Acid Deficiency (Cont.)

- Cholestyramine
- Cimetidine and other gastric acid suppressants
- Colestipol
- Corticosteroids
- Ethosuximide
- Famlotidine
- Fosphenytoin
- 5-Fluorouracil

Causes of Folic Acid Deficiency (Cont.)

- Genetic disorders
- Hydrochlorothiazide
- Indomethacin
- Lactation
- Metformin
- Methotrexate
- NSAIDs
- Phenobarbital

Causes of Folic Acid Deficiency (Cont.)

- Phenytoin
- Pregnancy
- Primidone
- Rantidine
- Salsalate
- Sulfasalazine
- Tobacco

Causes of Folic Acid Deficiency (Cont.)

- Triamterene
- Trimethoprim
- Tropical sprue
- Valproic acid

Folic Acid

- Always check B12 since supplementation of folic acid may mask a B12 deficiency.
- Side effects of large doses of folic acid
  - Insomnia, irritability, GI symptoms
- Do not use high doses of folic acid if the patient is taking phenytoin
- Folic acid supplementation can interfere with seizure medications such as valproic acid, carbamazepine, and primidone.

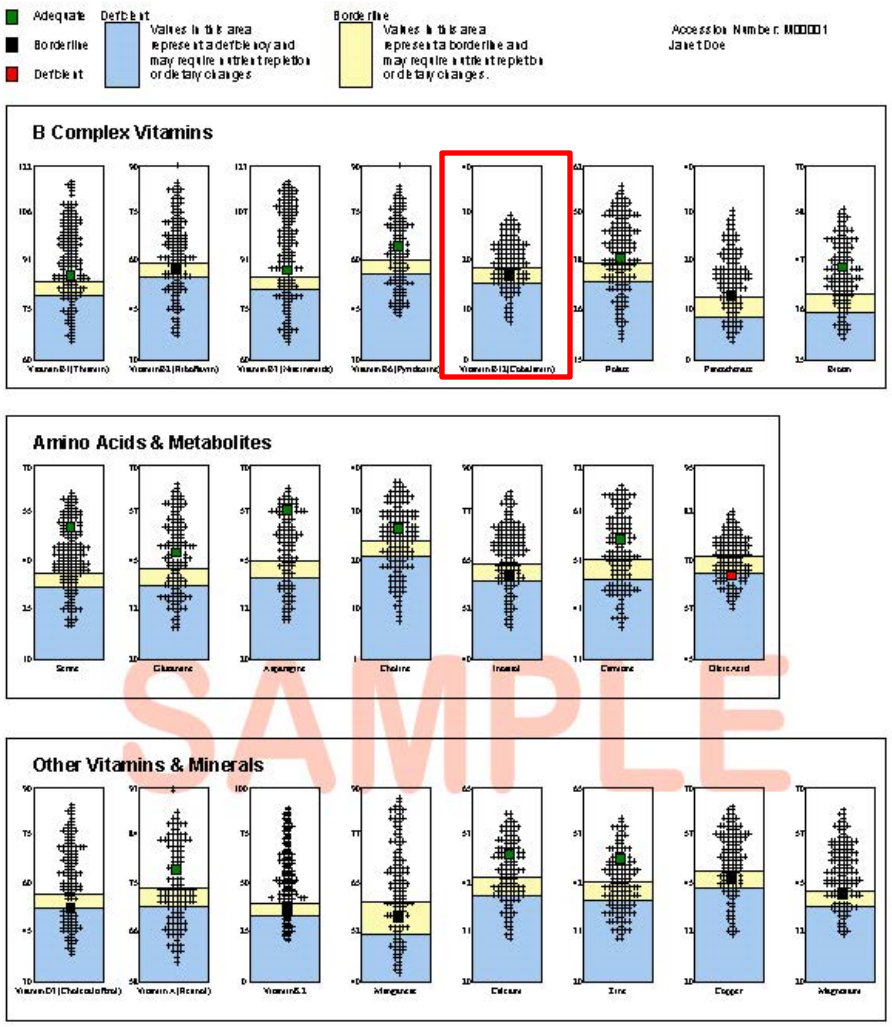
Diseases That Can Be Helped With Folic Acid

- Prevention of neural tube defects and cleft palate
- Cancer prevention
- Cervical dysplasia
- Depression
- Gingivitis
- Gout
- Lowers homocysteine
- Psoriasis
- Restless leg syndrome

Case History

- 57-year-old male who goes into to see you for "ringing in his ears". He states that his doctor put him on Lasix and it has helped somewhat but his still has some ringing. He wants to know if there is any other medication or anything else that will take away this symptom.
- SH: works as a CPA
- FH: + mother hypertension and father has diabetes
- Remainder of history and physical are unremarkable except for he takes a lot of antacids

What Do You Want To Look At In This Patient?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Biotin
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Glutamine
Arginine
Choline
Inositol
Carnitine
Citric Acid
Other Vitamins & Minerals
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Vitamin A (Retinol)
Vitamin E
Manganese
Calcium
Zinc
Copper
Magnesium

Vitamin B12 (Cobalamin)

- Functions of B12
  - Essential for DNA synthesis
  - Facilitates the metabolism of folic acid
  - Functions as a methyl donor
  - Helps synthesize proteins
  - Involved in the neurotransmitter production
  - Needed for carnitine metabolism

Vitamin B12 (Cobalamin) (Cont.)

- Functions
  - Used for nervous system function
  - Needed for RBC metabolism
  - Required for proper digestion

Symptoms of B12 Deficiency

- Confusion
- Constipation
- Decreased estrogen in women
- Decreased progesterone in women
- Depression
- Diarrhea
- Dizziness
- Drowsiness

Symptoms of B12 Deficiency (Cont.)

- Elevated levels of homocysteine
- Fatigue
- Hallucinations
- Increased cortisol levels
- Insomnia
- Irritability
- Memory loss
- Moodiness

Symptoms of B12 Deficiency (Cont.)

- Numbness and tingling of extremities
- Poor appetite
- Ringing in ears
- Sore tongue
- Stiffness
- Weakness

Causes of B12 Deficiency

- Antacids
- Digestive disorders
- Nitrous oxide
- Potassium citrate and choloride
- Medications

Medications That Deplete B12 From The Body

- Aminoglycosides
- Cephalosporins
- Cholesterol lowering medications
- Cholestyramine
- Cimetidine
- Colchicine
- Cotrimoxazole

Medications That Deplete B12 From The Body (Cont.)

- Famotidine
- Fluoroquinolones
- Histamine blockers
- Lansoprazole
- Macrolides
- Metformin
- Neomycin
- Nizatidine

Medications That Deplete B12 From The Body (Cont.)

- Omeprazole
- Oral contraceptive
- Penicillin
- Phenytoin
- Ranitidine
- Sulfonamides
- Tetracylines
- Trimethoprim
- Zidovudine

Diseases That Can Be Helped With B12

- AIDS
- Anemia
- Anxiety
- Asthma
- Ataxia
- Bell's palsy
- Dementia

Diseases That Can Be Helped With B12 (Cont.)

- Depression
- Epilepsy
- Fatigue
- Hepatitis
- Infertility
- Insomnia
- Irritability

Diseases That Can Be Helped With B12 (Cont.)

- RLS
- MS
- Neuropathy
- Numbness
- Psychosis
- Retinopathy
- Sciatica

Diseases That Can Be Helped With B12 (Cont.)

- Seborrheic dermatitis
- Tingling
- Tinnitus
- Trigeminal neuralgia
- Vitiligo
- Xanthelasma

Case History

- 47-year-old female with the chief complaint of insomnia. She has been taking sleeping pills for the last 10 years. She states that she saw an anti-aging physician that gave her progesterone and it has helped the insomnia somewhat but she is still having problems getting to sleep because she is very anxious.
- Remainder of history and physical are noncontributory.

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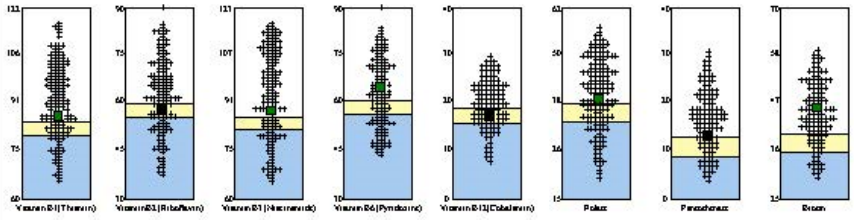
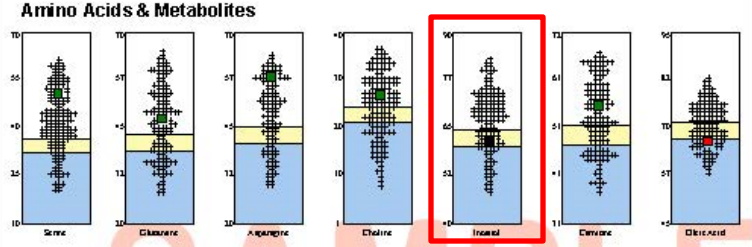
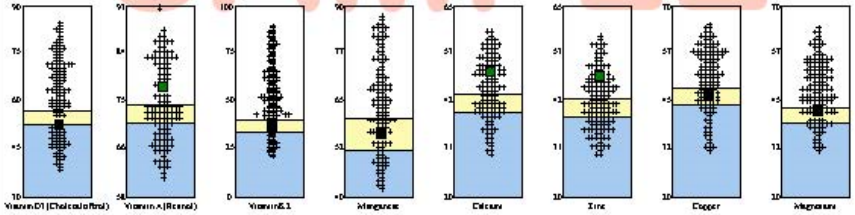
B Complex Vitamins



Amino Acids & Metabolites



Other Vitamins & Minerals



Inositol

- Inositol is part of the vitamin B complex
- Functions of inositiol
  - Can reduce LDL
  - Has a calming effect
  - Helps form lecithin
  - Aids in the prevention of atherosclerosis
  - Involved in augmenting effects of neurotransmitter release

Inositol

- Functions (cont.)
  - Improves quality of sleep
  - Involved with metabolizing fats and cholesterol
  - Supports the metabolism of estrogen and progesterone
  - Used to treat depression and panic disorders

Symptoms of Inositol Deficiency

- Anxiety
- Depression
- Difficulty falling asleep
- Fibroids
- PMS

Causes of Inositol Deficiency

- CAFFEINE!!!!

Inositol

- Dosage: 200 mg to 12 grams qd
- Dosages larger than 200 mg should be supervised by a health care practitioner
- C/I: Not to be used in patients with renal failure

Diseases That Can Be Helped With Inositol

- Depression
- Fibroids
- Liver disease
- Neuropathy
- Panic attacks
- PMS
- Premature infants
- Psoriasis

Conclusion

Nutritional depletions are a common issue with patients that can cause significant symptoms and/or disease states.

It is important to measure levels of vitamins, minerals, and amino acids to help prevent and treat disease and to aid the patient in keeping their health as optimal as possible.

Conclusion (Cont.)

Medicine now has reached a crossroads. We have the capability to individualize and customize care for each patient.

One size does not fit all.

Customized care requires the measurement of nutrients.