NutrEval®

INTERPRETIVE GUIDE

Contents

INTRODUCTION

A shortage of any nutrient can lead to biochemical disturbances that affect healthy cellular and tissue function leading to disease. Nutrient shortages are traditionally the result of increased utilization (i.e. athletes and pregnancy), impaired digestion and absorption, as well as decreased dietary intake. The human body is adaptive. It can sometimes function for long periods of time even if important nutrients are lacking. However, eventually it can impact a person's overall quality of life.

Metabolism is a complex process revealing how vitamins and minerals (micronutrients) plus proteins, fats, and carbohydrates (macronutrients) are used to perform thousands of necessary biochemical reactions. The NutrEval profile evaluates several important biochemical pathways to help determine nutrient recommendations for vitamins, minerals, amino acids, digestive support, and essential fatty acids. The results of the NutrEval are entered into a complex algorithm based on functional markers associated with particular nutrients needs in the literature.

Because no two people are exactly alike, functional nutrition testing can help identify specific nutrient shortages. An individual's distinct nutrient needs are dependent on several factors, including genetic and environmental influences.

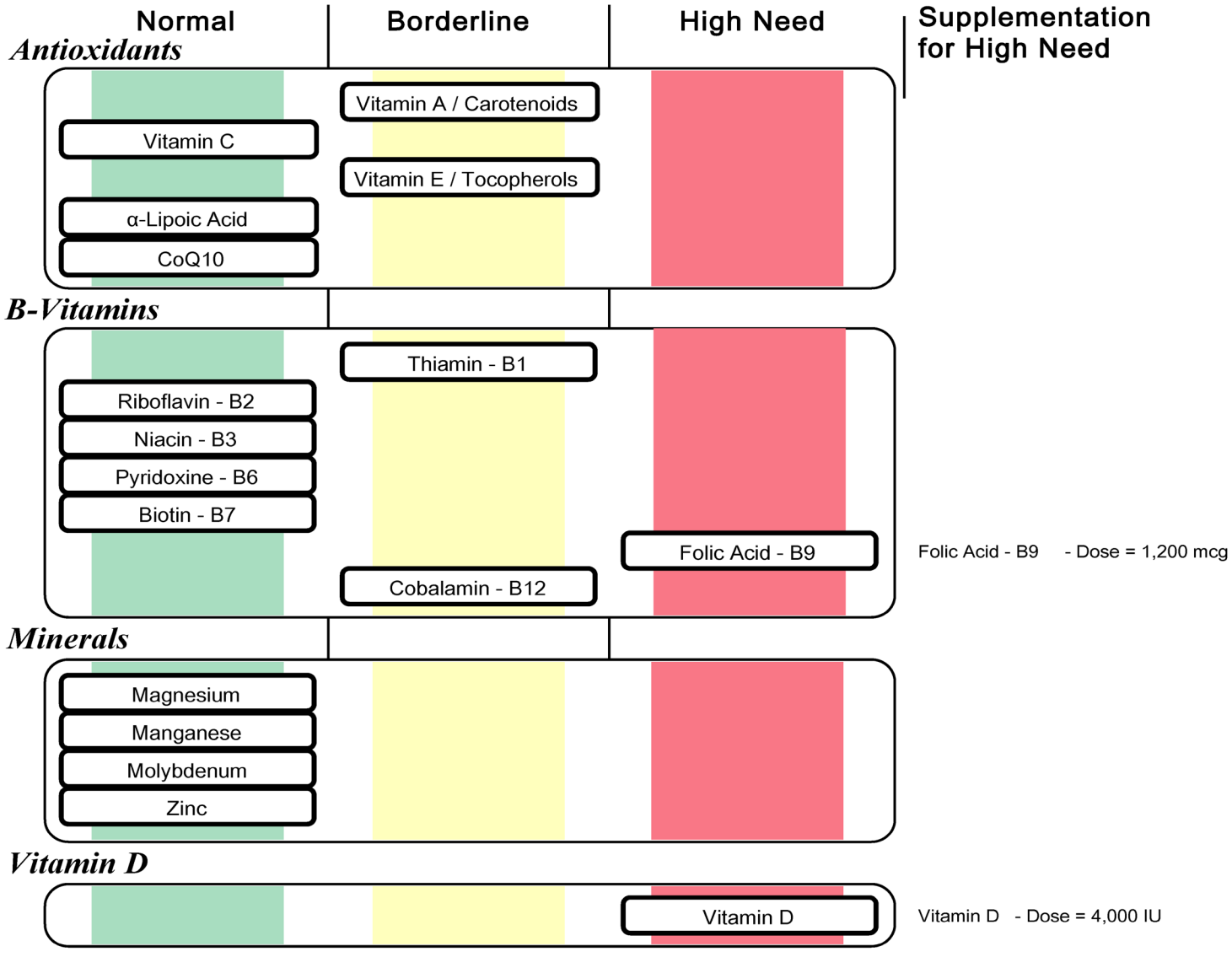
The laboratory tests performed include:

- Metabolic Analysis Markers
- Amino Acids
- Essential and Metabolic Fatty Acids Markers
- Oxidative Stress Markers
- Elemental Markers (add-on)

To help understand how the recommendations were created, this booklet is organized by category to show how each component of the NutrEval Profile relates to nutrient status. Specific needs for vitamins, minerals, amino acids, fatty acids, and antioxidants are determined by grouping together all of the test results that indicate the need for nutritional support. The Interpretation-At-A-Glance key can be found at the end of this booklet, and it includes biomarker associations that generate each nutrient need. The recommendations are adjusted according to the significance of biomarker results. With full knowledge of an individual's medical history, this information can be used to assist in providing an optimal nutritional support program.

The first five pages of the NutrEval report include personalized nutritional recommendations; the pages to follow include the biomarker results that drive those recommendations. The report begins with a high-level overview of the key nutrients where additional support is indicated, separating the individual nutrients into normal (green), borderline (yellow), and high (red) need columns.

NutrEval Results Overview



The **Suggested Supplement Schedule** provides initial suggested dosages that are meant to be adjusted by the clinician, depending on each patient's clinical history. All supplementation decisions are at the discretion of the treating clinician.

SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	5,000 IU	
Vitamin C	75 mg	250 mg	
Vitamin E / Tocopherols	22 IU	200 IU	
α-Lipoic Acid		50 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	25 mg	
Riboflavin - B2	1.1 mg	10 mg	
Niacin - B3	14 mg	20 mg	
Pyridoxine - B6	1.5 mg	10 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	320 mg	400 mg	
Manganese	1.8 mg	3.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	8 mg	10 mg	
Essential Fatty Acids			
Omega-3 Oils	500 mg	1,000 mg	
Digestive Support			
Probiotics		50 billion CFU	
Pancreatic Enzymes		10,000 IU	
Other Vitamins			
Vitamin D	800 IU	4,000 IU	

DRI is a reference value determined by nutritional boards to plan and assess nutrient intakes of healthy people.

The recommendations in this column represent the functional nutrient need determined by the algorithmic calculation involving the patient's test results. Recommendations for age and gender-specific supplementation were set by an in-depth analysis of many sources including: peer reviewed literature; US Institute of Medicine (IOM) toxicity research; Lyle Mac William's Comparative Guide to Nutritional Supplements and Comparative Guide to Children's Nutritionals; Alan Gaby's Nutritional Medicine; and additional published data from PubMed.

This column is for the clinician to make appropriate adjustments to the suggested dosages based on the patient's clinical history and therapeutic need for certain nutrients.

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	0
Asparagine	0	Phenylalanine	0
Cysteine	0	Serine	0
Glutamine	334	Taurine	0
Glycine	327	Threonine	0
Histidine	0	Tryptophan	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		

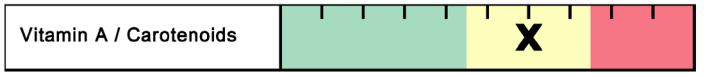
Amino acid dosage recommendations are based on the individual measurement of each amino acid.

Recommendations for age and gender-specific supplementation are set by comparing levels of nutrient functional need to optimal levels as described in the peer-reviewed literature. They are provided as guidance for short-term support of nutritional deficiencies only.

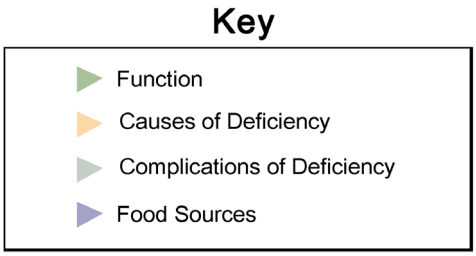
The Suggested Supplemental Schedule is provided at the request of the ordering practitioner. Any application of it as a therapeutic intervention is to be determined by the ordering practitioner.

Key: Normal | Borderline | High Need

Pages 3-5 of the report provide additional information about each nutrient. Each nutrient is accompanied by a description of function, causes of deficiency, complications of deficiency and food sources for practitioner and patient education. Additionally, the 'X' indicates where the patients' results flagged along the spectrum of nutrient need and gives more insight into whether the supplement schedule may be adjusted to a lower or higher dosage accordingly.



- 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.

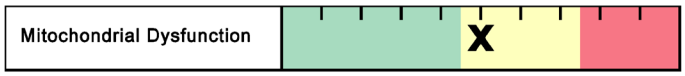


The Functional Imbalances page is optional, and provides information on mitochondrial dysfunction, need for methylation, and toxic exposure. Imbalances in these categories signal the need to focus on a particular functional process.

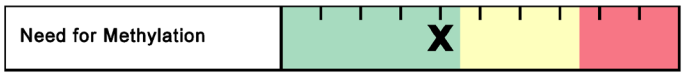
NutrEval FMV amino acids

Interpretation At-A-Glance

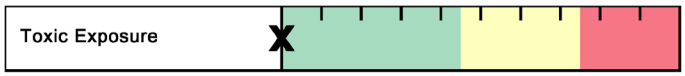
Functional Imbalances



- Mitochondria are a primary site of generation of reactive oxygen species. Oxidative damage is considered an important factor in decline of physiologic function that occurs with aging and stress.
- Mitochondrial defects have been identified in cardiovascular disease, fatigue syndromes, neurologic disorders such as Parkinson's and Alzheimer's disease, as well as a variety of genetic conditions. Common nutritional deficiencies can impair mitochondrial efficiency.



- Methylation is an enzymatic process that is critical for both synthesis and inactivation. DNA, estrogen and neurotransmitter metabolism are all dependent on appropriate methylation activity.
- B vitamins and other nutrients (methionine, magnesium, selenium) functionally support catechol-O-methyltransferase (COMT), the enzyme responsible for methylation.



- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal studies suggest that drinking MTBE may cause gastrointestinal irritation, liver and kidney damage and nervous system effects.
- Styrene is classified by the US EPA as a "potential human carcinogen," and is found widely distributed in commercial products such as rubber, plastic, insulation, fiberglass, pipes, food containers and carpet backing.

Metabolic Analysis Markers

The **Metabolic Analysis Markers** are organic acids, which refers to a broad class of compounds formed during fundamental metabolic processes of the body. Metabolic reactions produce carboxylic acid compounds derived from the digestion of dietary protein, fat, and carbohydrates. The resulting organic acids are used by the body to generate cellular energy and provide many of the building blocks necessary for cell function.

The quantitative measurement of specific organic acids in urine allows the simultaneous assessment of mitochondrial function, potential nutritional inadequacies, neurotransmitter metabolism, potential microflora imbalances in the gut, and concerns regarding environmental exposures.

While the metabolic analysis markers provide an abundance of data, the interpretation can be simplified by addressing four basic questions of clinical relevance:

1. Are symptoms related to excessive growth of bacteria and fungi in the gut?
2. Is mitochondrial energy production adversely affected?
3. Are functional nutrient needs present?
4. Is there an undue toxic load, and if so, is it adversely affecting detoxification capacity?

Malabsorption and Dysbiosis Markers[1-7]

The compounds of bacterial and yeast origin are byproducts of bacterial and fungal activity in the GI tract. They are usually evaluated as a group for overall trends versus individually. When multiple markers are elevated, a stool test may provide further information regarding dysbiosis or other GI dysfunction. These markers are not recommended for use as a direct GI evaluation.

SUMMARY OF ABNORMALITIES FOR ORGANIC ACIDS IN URINE			
Name		**Potential Intervention**	**Metabolic Pathway**
Malabsorption Markers			
Indoleacetic Acid (IAA)	H	These compounds may reflect maldigestion/malabsorption. Take appropriate steps to ensure favorable digestion and absorption of macronutrients. Consider follow-up stool testing.	Malabsorption/maldigestion
Phenylacetic Acid (PAA)	H		
Bacterial Dysbiosis Markers			
Dihydroxyphenylpropionic Acid (DHPPA)	H	These compounds may reflect intestinal overgrowth. Take appropriate steps to ensure favorable gut microflora population. Consider follow-up stool testing.	Intestinal bacterial dysbiosis
3-Hydroxyphenylacetic Acid	H		
4-Hydroxyphenylacetic Acid	H		
Benzoic Acid	H		
Hippuric Acid	H		
Yeast/Fungal Dysbiosis Markers			
Arabinose	H	These compounds may reflect intestinal overgrowth. Take appropriate steps to ensure favorable gut microflora population. Consider follow-up stool testing	Fungal dysbiosis
Citramalic Acid	H		
Tartaric Acid	H		

The malabsorption and dysbiosis markers can also be influenced by common foods, supplements, or preservatives; correlation with the patient's dietary intake is encouraged.[8-33]

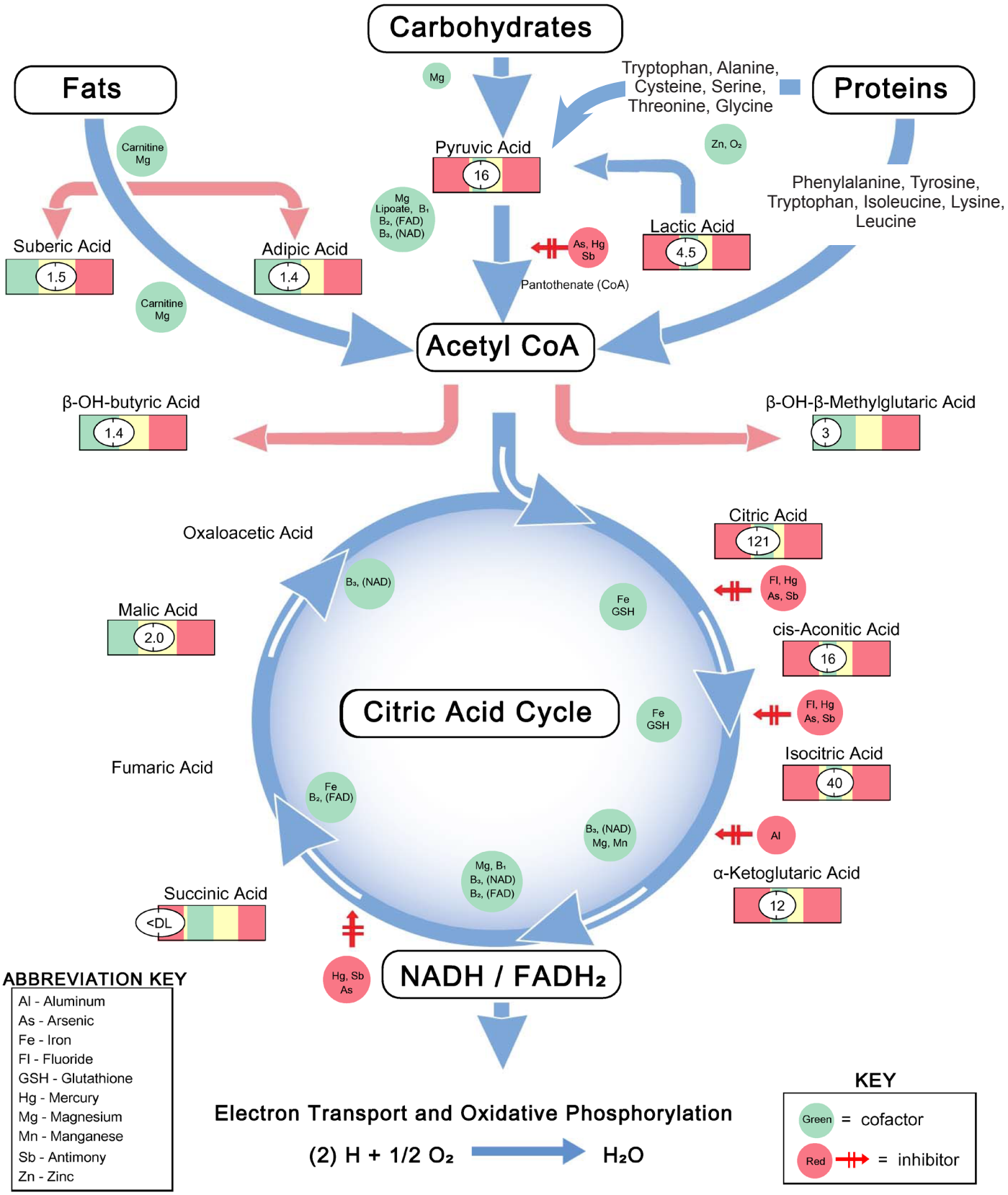
Urinary Metabolite	Common Dietary Sources
Indoleacetic Acid	High tryptophan intake, green/black tea
Phenylacetic Acid	Wine/grapes
Dihydroxyphenylpropionic Acid	Whole-grains, chocolate, coffee, green/black tea, olives/olive oil, citrus fruits (animal studies)
3-Hydroxyphenylacetic Acid & 4-Hydroxyphenylacetic Acid	Wine/grapes, cranberries, green/black tea, berries, orange juice, grape seed extract
Benzoic Acid/Hippuric Acid	Orange juice, elderberry, huckleberry, food preservative, berries, other flavonoids
Arabinose	Widely distributed, grains, commercial sweetener
Citramalic Acid	Apples, cranberries, sugar beets
Tartaric Acid	Wine/grapes, chocolate, food additive/preservative

Cellular Energy & Mitochondrial Metabolites[34-44]

The cellular energy and mitochondrial metabolites are biomarkers that reflect cellular energy production and mitochondrial function. Elevated fatty acid metabolism markers suggest poor beta-oxidation, whereby patients may benefit from carnitine and magnesium. Abnormal carbohydrate metabolism is often seen in dysglycemia and metabolic syndrome. Strenuous exercise can also affect these markers. The energy production markers may reflect the need for B-vitamin support. They may also indicate mitochondrial dysfunction.

SUMMARY OF ABNORMALITIES FOR ORGANIC ACIDS IN URINE			
Name		**Potential Intervention**	**Metabolic Pathway**
Carbohydrate Metabolism			
Lactic Acid	H	Zn O_2	Aerobic/anaerobic energy production
Pyruvic Acid	H	Mg Lipoate B1 B2 B3	
β-OH-Butyric Acid	H		Balance of fat and CHO metabolism; ketone body
Energy Metabolism			
Citric Acid	H	Iron Glutathione	Citric acid cycle intermediates
Cis-Aconitic Acid	H		
Isocitric Acid	H	B3 Mg Mn	
α-Ketoglutaric Acid	H	Mg B1 B2 B3	
Succinic Acid	H	Iron B2	
Malic Acid	H	B3	
β-OH-β-Methylglutaric Acid	H	CoQ10	HMG-CoA reductase inhibition; note levels may be impacted by statin use
Fatty Acid Metabolism			
Adipic Acid	H	Carnitine Mg	Fatty acid oxidation
Suberic Acid	H		

Krebs Cycle At-A-Glance



ABBREVIATION KEY

Al - Aluminum
As - Arsenic
Fe - Iron
Fl - Fluoride
GSH - Glutathione
Hg - Mercury
Mg - Magnesium
Mn - Manganese
Sb - Antimony
Zn - Zinc

KEY

Green = cofactor
Red = inhibitor

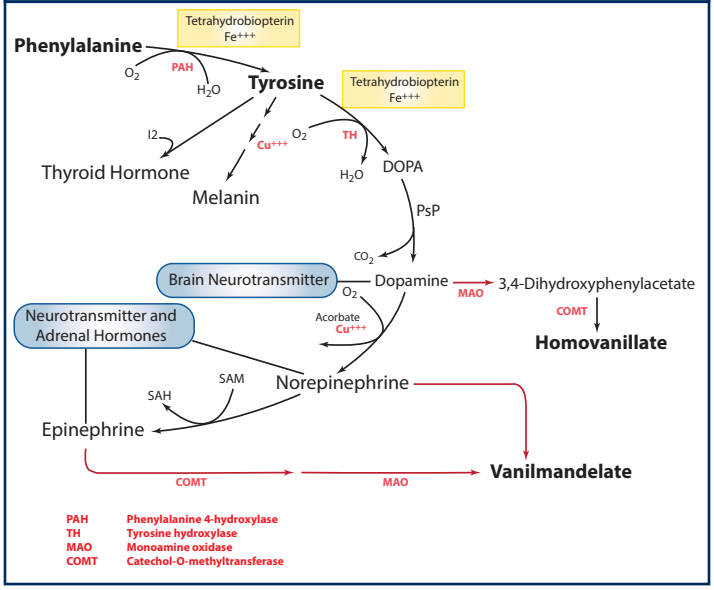
Neurotransmitter Metabolites[45-50]

The neurotransmitter metabolites can reflect the turnover of neurotransmitters, as seen in acute and chronic stress.

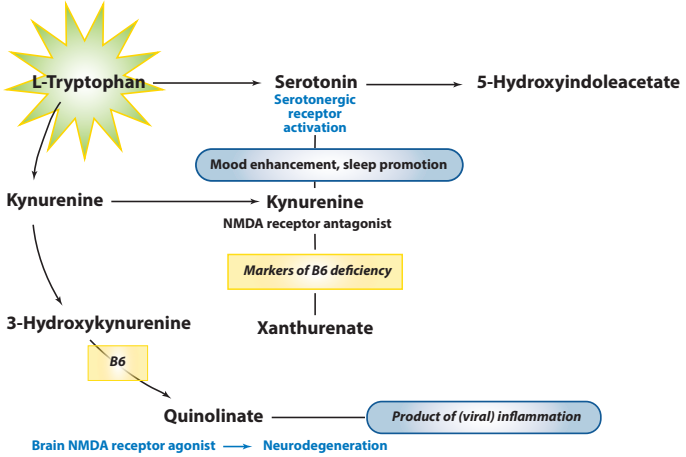
- **High**: They may also reflect the need for B-vitamin or methylation support. In addition, medications that impact certain neurotransmitter pathways may also influence levels. Other common medications, including acetaminophen, aspirin, and guaifenesin may also impact levels.
- **Low**: This may reflect the need to evaluate amino acid precursors of neurotransmitters and cofactors to help with conversion. Note, corticosteroids may lower inflammation resulting in lower quinolinic acid levels.

SUMMARY OF ABNORMALITIES FOR ORGANIC ACIDS IN URINE			
Name		**Potential Intervention**	**Metabolic Pathway**
Neurotransmitter Metabolites			
Vanilmandelic Acid (VMA)	L,H	Tyrosine B-vitamins	Epi/Norepinephrine metabolite Dopamine metabolite
Homovanillic Acid (HVA)	L,H		
5-OH-indoleacetic Acid (5-HIAA)	L,H	Tryptophan B-vitamins Mg Mn	Serotonin metabolite
3-Methyl-4-OH-phenylglycol (MHPG)	H		Epi/Norepinephrine metabolite
Kynurenic Acid	H	B2 B3 B6	Inflammation and/or oxidative stress Tryptophan metabolite
Quinolinic Acid	H	B3 B6	
Kynurenic / Quinolinic Ratio	L		

NEUROTRANSMITTERS FROM AMINO ACIDS



TRYPTOPHAN PATHWAYS IN VITAMIN B6 DEFICIENCY AND INFLAMMATION



Vitamin Markers[51-58]

The vitamin markers can suggest the need for specific B-vitamin support.

SUMMARY OF ABNORMALITIES FOR ORGANIC ACIDS IN URINE			
Name		**Potential Intervention**	**Metabolic Pathway**
Vitamin Markers			
α-Ketoadipic Acid	H	B1	Lysine and tryptophan catabolism
α-Ketoisovaleric Acid	H	B-complex	Valine catabolism
α-Ketoisocaproic Acid	H		Leucine catabolism
α-Keto-β-methylvaleric Acid	H		Isoleucine catabolism
Formiminoglutamic Acid	H	B9 (Folate) B12	Histidine catabolism
Glutaric Acid	H	B2	Lysine catabolism
Isovalerylglycine	H	B2	Leucine catabolism
Methylmalonic Acid	H	B9 (Folate) B12	Methionine catabolism
Xanthurenic Acid	H	B3 B6	Tryptophan catabolism
3-Hydroxypropionic Acid	H	B7	Branched chain amino acid catabolism
3-Hydroxyisovaleric Acid	H	B7	Leucine catabolism

Toxin & Detoxification Markers[59-63]

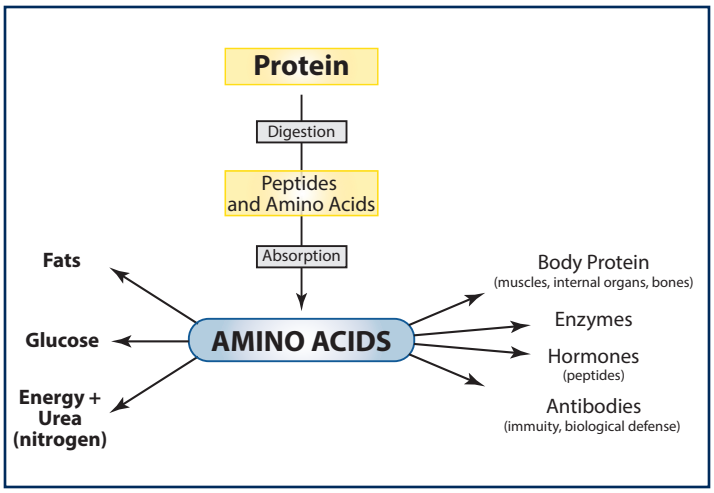
The detoxification markers reflect increased exposure to environmental toxins, or up-regulation of detoxification pathways in response to stress. Collectively, when these markers are elevated:

1. Identify the source of toxin exposure.
2. Minimize or reduce exposure.
3. Consider the use of antioxidants, like glutathione, plus other nutrients and botanicals to support detoxification.
4. Helpful websites:
   a. **Tox Town** https://toxtown.nlm.nih.gov
   b. **Environmental Working Group** https://www.ewg.org
   c. **Agency for Toxic Substances and Disease Registry** https://www.atsdr.cdc.gov

SUMMARY OF ABNORMALITIES FOR TOXIN & DETOXIFICATION MARKERS			
Name		**Potential Intervention**	**Clinical Relevance**
Toxin and Detoxification Markers			
α-Ketophenylacetic Acid (from Styrene)	H	Avoidance of styrene Hydration Antioxidants	Environmental exposure
α-Hydroxyisobutyric Acid (from MTBE)	H	Avoidance of MTBE Carbon-water filter Hydration Antioxidants	
Orotic Acid	H	B-vitamins Antioxidants	
Pyroglutamic Acid	L,H	Glutamine Glycine Cysteine B6 Mg Antioxidants	Detoxification

Amino Acids

Amino acids are the building blocks that make up proteins in tissues (i.e. bone, muscles, ligaments, tendons, nails, hair, glands and organs) and the basic constituent of hormones, enzymes, and neurotransmitters. Since amino acids are involved in every body system, deficiencies or imbalances in these compounds can lead to disorders of behavior and mood, digestion and absorption, hormone balance, cardiovascular function, detoxification, oxidative stress, pH regulation, and the musculoskeletal system.



Amino acid assessment can help to identify contributors to chronic disease and allow for precise replacement of deficient amino acids. Because various vitamins and minerals are used as cofactors in amino acid metabolism, imbalances in amino acids noted on the test report can also point to insufficiencies of some of these nutrient cofactors including B-vitamins and minerals. Supplementing essential amino acids can greatly benefit people who have low protein diets, have trouble adequately digesting protein, or who have increased demand for specific amino acids. Between meals, amino acids also supply energy to keep cells functioning.

High-protein foods vary in their amino acid composition and concentration. In general amino acid containing foods include poultry, meats, eggs, fish, milk, cheese, beans and legumes, vegetables (spirulina, seaweed, mushrooms, peppers, potato, spinach, broccoli, Brussels sprouts, corn, artichoke, cauliflower), fruits (Gogi berries, apricots, bananas, prunes, guava, blueberries, dates, avocados, pears, plantains, blackberries), nuts, seeds, grains, tempeh, and nutritional yeast (in descending order of protein concentration).[64,65]

The complete **Amino Acid Analysis** assesses nutritionally essential amino acids, non-essential amino acids, and intermediary metabolites that provide insight into B-vitamin, amino acid, and digestive support needs.

Commonly observed amino acid patterns include:

1. The majority of essential and non-essential amino acids shifting to the left (low) indicating
   a. inadequate intake of protein
   b. maldigestion/malabsorption (especially with elevated dietary peptide related markers)
   c. increased demand (i.e. pregnancy or athletes)
2. The majority of essential and non-essential amino acids shifting to the right (elevated) indicating
   a. increased dietary intake of protein and/or supplementation (urea cycle markers may also be elevated)
   b. potential need need for vitamins and minerals (B6, magnesium) for utilization
3. Low non-essential amino acids may indicate inadequate vitamins and minerals to convert essential into non-essential amino acids.

SUMMARY OF ABNORMALITIES FOR AMINO ACIDS[64-73]		
Name	**Potential Intervention**	**Clinical Relevance**
Nutritionally Essential Amino Acids		
Arginine	Mn, B6	Urea cycle and ammonia disposal Immune function Stimulates insulin release Creatine/creatinine precursor (muscle metabolism) Forms NO, glutamic acid, proline Conversion into glucose/glycogen if needed Stimulates release of GH and prolactin
Histidine	B1, B2, B6, B9, B12, Mo	Histamine biosynthesis (inflammatory response, gastric secretions) Antioxidant, anti-inflammatory Forms carnosine and glutamic acid
Isoleucine	B1, B3, B6, B12, Zn	Branched-chain amino acid (BCAA) for collagen/elastin (ligaments), skeletal muscle catabolism Metabolized to carbohydrate and fat Forms hemoglobin
Leucine	B1, B3, B6, B12, Zn	BCAA for collagen/elastin (ligaments), skeletal muscle catabolism Metabolized to fat
Lysine	B1, B3	Immune function Collagen formation Arginine antagonizes lysine Carnitine precursor
Methionine	B3, B6, B9, B12, Mo, lipoic acid	Methylation Cysteine and carnitine precursor
Phenylalanine	Assess intake of artificial sweeteners (aspartame) B1, B3, B7, B9, B12, Mg	Tyrosine precursor
Taurine	Assess oxidative stress/ antioxidant status B1, B6, Mg, Mo	Bile acid synthesis Cellular transport of electrolytes Neurotransmitter activities Cardiac muscle function Antioxidant Synthesized from cysteine
Threonine	B3, B6	Collagen, elastin, tooth enamel formation Serine and glycine precursor
Tryptophan	B3, B6	Serotonin, melatonin, niacin and picolinic acid precursor
Valine	B1, B3, B6, B12, Zn	BCAA for collagen/elastin (ligaments), skeletal muscle catabolism

SUMMARY OF ABNORMALITIES FOR AMINO ACIDS[64-73]		
Name	**Potential Intervention**	**Clinical Relevance**
Nonessential Protein Amino Acids		
Alanine	B1, B3, B6, B7	Glucose-alanine cycle for energy Inhibitory neurotransmitter action Immune function Formed from valine, leucine, isoleucine, carnosine, anserine, and pyruvate
Asparagine	Assess precursors	Incorporated into cellular proteins Formed from glutamine and aspartic acid
Aspartic Acid	Assess intake of artificial sweeteners (aspartame) Assess precursors B6	Citric acid cycle Excitatory neurotransmitter activity Pyrimidine and purine synthesis Urea synthesis Asparagine, arginine, lysine, methionine, isoleucine synthesis Formed from glutamic acid and oxaloacetatic acid
Cysteine	Assess oxidative stress/ antioxidant status B6, B12, Mo	Glutathione precursor Sulfation (detoxification) High affinity for mercury, lead, cadmium Antioxidant properties Collagen production Taurine precursor Sulfur-containing amino acid Formed from serine and methionine (sulfur donor)
Cystine	Assess oxidative stress/ antioxidant status	Oxidized form of cysteine Glutathione precursor (immune cells) Found in digestive enzymes, immune cells, skeletal tissues, and skin
Gamma-Aminobutyric Acid	Assess dysbiosis B6, Mn	Decarboxylation of glutamic acid Does not reflect CNS levels of inhibitory neurotransmitter GABA
Glutamic Acid	Assess intake of MSG B1, B3, B6, Mn	Formed from alpha-ketoglutarate and multiple amino acids Does not reflect CNS levels of excitatory neuro-transmitter glutamate; free glutamic acid cannot cross the BBB in appreciable quantities, and instead is converted to glutamine, which the brain uses for fuel and protein synthesis
Glutamine	B1	Most abundant AA in blood Glutathione precursor Intestinal mucosal integrity Immune function Niacin conversion to nicotinamide for NADH, NADP, NADPH Nitrogen (ammonia) detoxification Pyrimidine and purine synthesis Formed from glutamic acid and NH4
Proline	B1	Collagen/elastin (skin, bone, cartilage, ligaments) Formed from glutamic acid and ornithine
Tyrosine	B1, B3, B6	Thyroid (T3), catecholamine (dopamine, epi/norepinephrine), melanin precursor Formed from phenylalanine

SUMMARY OF ABNORMALITIES FOR AMINO ACID INTERMEDIARY METABOLITES[75-77]			
Name		**Potential Intervention**	**Metabolic Pathway**
B Vitamin Markers			
α-Aminoadipic Acid	H	B-complex	Tryptophan and lysine catabolism
α-Amino-N-butyric Acid	H		Methionine and threonine catabolism
β-Aminoisobutyric Acid	H		Valine catabolism
Cystathionine	H		Methionine catabolism
3-Methylhistidine	H		Methylated form of histidine
Urea Cycle Markers			
Citrulline	H	B1	Urea cycle marker intermediates
Ornithine	H	B1 B6 Magnesium	
Urea	H	Magnesium B6	
Glycine/Serine Metabolites			
Glycine	H	B-complex	Choline production and catabolism
Serine	H		
Ethanolamine	H	Mg	
Phosphoethanolamine	H	Zn	
Phosphoserine	H	B1 Magnesium	
Sarcosine	H	B-complex	
Dietary Peptide Related Markers			
Anserine	H	Maldigestion/absorption Imbalanced gut flora	Digestion/absorption
Carnosine	H		
1-Methylhistidine	H		
β-Alanine	H		

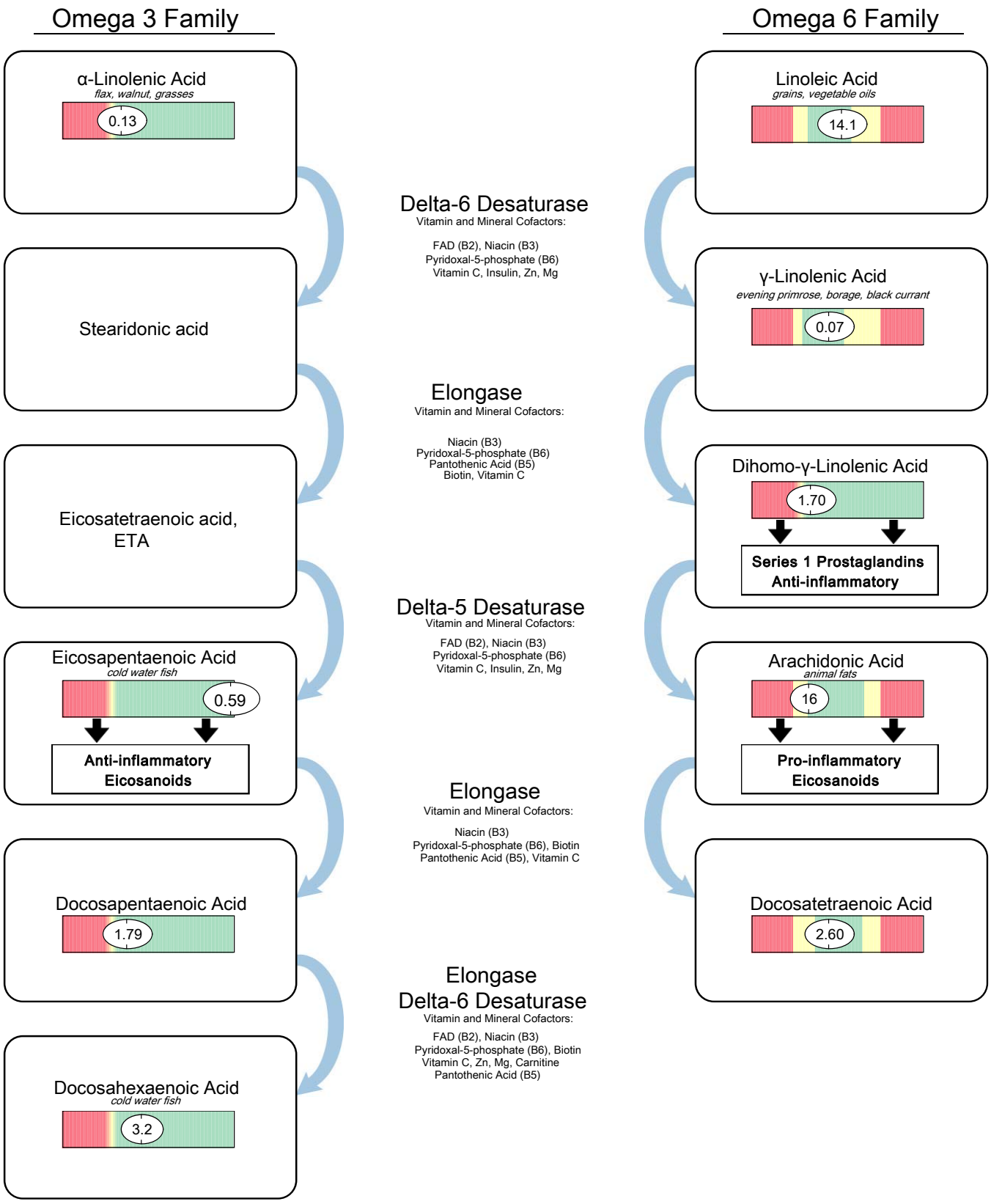
Essential and Metabolic Fatty Acids

Essential fatty acids (EFAs) exercise a powerful influence on overall health due to their pivotal role in cell membrane function. EFAs are transformed by the body into critical local hormones, called eicosanoids, that regulate all stages of the inflammatory process. EFAs control initiation, propagation, and termination of inflammation, vital to the body's ability to repair and protect itself immunologically.[78] EFAs can impact the clinical course of several diseases including inflammatory disorders, cardiovascular disease, hormonal disorders, auto-immune, arthritis, mental and behavioral disorders, and neurological degeneration.[78-80]

Fatty acids derived from digestion and absorption or endogenous production are either converted into energy, stored as triglycerides, incorporated into cellular membranes in the form of phospholipids, or they give rise to longer fatty acids.[81] Fatty acids are traditionally classified into two main systems: 1) type of saturation (saturated, monounsaturated, polyunsaturated, and trans fats) and 2) families of fats, based on physical structure (omega-3, omega-6, omega-9, etc.).[82,83]

The Essential and Metabolic Fatty Acids (EMFA) markers give an overall sense of the relationship of the different families of EMFAs to each other and their degree of balance or imbalance. Measured fatty acids include the polyunsaturated Omega-3, Omega-6 and Omega-9 fatty acids; monounsaturated fats (Omega-7 fats and Trans fat); and saturated fatty acids. This assessment provides a snapshot of dietary intake, as well as support, for clinicians regarding patient education around dietary changes.

Essential Fatty Acid Metabolism



Polyunsaturated Omega-3 Fatty Acids: Alpha Linolenic Acid (ALA; 18:3n3), an essential omega fatty acid, is used to generate energy. It gives rise to Eicosapentaenoic Acid (EPA; 20:5n3) and Docosahexaenoic Acid (DHA 22:6n3). These enzymes require vitamin and mineral cofactors. Omega-3 fatty acids have many physiologic functions: they are the precursors for eicosanoids that exert anti-inflammatory and immune effects; they regulate smooth muscle contraction and relaxation; and they are critical cell membrane components. [78-80,84]

Polyunsaturated Omega-6 Fatty Acids: Linoleic acid (LA 18:2n6), an essential omega fatty acid, gives rise to anti-inflammatory Dihomo-gamma-linolenic acid (DGLA; 20:3n6) and pro-inflammatory Arachidonic acid (AA; 20:4n6). Like omega-3 fatty acids, omega-6 fatty acids also play a physiologic role as core constituents of cellular membranes as well as precursor compounds for the production of eicosanoids. However, the compounds derived from omega-6 fatty acids are generally more inflammatory compared to those of the omega-3 family. [78-80,84]

Polyunsaturated Omega-9 Fatty Acids: Like omega-3 and omega-6 fatty acids, omega-9 fatty acids are polyunsaturated fatty acids present in the human diet. Omega-9 fatty acids are found in both animal and vegetable sources. One commonly known omega-9 fatty acid is oleic acid which is present in olive oil and other monounsaturated fats.[85]

Saturated Fatty Acids: Saturated fatty acids have no double bonds between the individual carbon atoms of the fatty acid chain - the chain of carbon atoms is fully "saturated" with hydrogen atoms.[83] While most fat sources contain a mixture of unsaturated and saturated fatty acids, some foods are higher in saturated fatty acids than others. These include animal products such as dairy products, lard, and fatty meats. Vegetable sources include coconut, cottonseed and palm kernel oil, as well as chocolate.[83,86] Nutritional recommendations are typically against substantive intake of saturated fatty acids in the diet given their association with increased risk for cardiovascular disease and numerous cancers (colorectal, prostate, breast, and ovarian).[79,87]

Monounsaturated Fatty Acids: Monounsaturated fatty acids (MUFAs) have one double bond in a fatty acid chain composed of single-bonded carbon atoms. The health effects of MUFAs appear to depend on the particular monounsaturated acid being examined. Research suggests that some monounsaturated fatty acids (in the same way as saturated fats) may promote insulin resistance; however, other studies suggest this may not be the case. Healthier lipid profiles have been associated with MUFA consumption in children.

Dietary sources of monounsaturated fats include: red meat, whole milk products, whole grain wheat, oatmeal, nuts (cashews) and high-fat fruits such as olives and avocados. Other sources include oils derived from macadamia nut, grapeseed, peanut, sesame, safflower, and sunflower.[83,88]

Trans Fat: Trans fats are monounsaturated or polyunsaturated fats. They are primarily obtained in the diet via consumption of foods produced using the industrial partial hydrogenation of vegetable oils.[86] However, certain trans fats (vaccenyl and conjugated linoleyl) occur naturally in trace amounts in meat and dairy products from ruminants.[89] Consumption of trans fats has been implicated in a variety of health risks, including increased risk of cardiovascular disease by raising levels of LDL cholesterol and lowering levels of HDL cholesterol. Health authorities worldwide recommend minimal to zero consumption of trans fat in the diet.[86]

Cardiovascular Risk

Omega 6/Omega 3: Studies examining the evolutionary composition of the human diet suggest that major shifts have occurred, particularly in relation to fatty acids. An intake ratio of omega-6 to omega-3 essential fatty acids (EFA) of approximately 1 has been suggested for Paleolithic man. Current estimates for the standard Western diet suggest that the ratio is likely15-20:1 or higher, given the vast overconsumption of omega-6 fatty acids compared to omega-3 fatty acids.[90] This imbalance has been implicated in many chronic diseases, including cardiovascular disease, cancer, and inflammatory and autoimmune diseases.[90,91]

AA/EPA: The Arachidonic/Eicosapentaenoic acid ratio [AA/EPA] has been utilized in research to assess systemic inflammation – particularly the influences of pro-inflammatory eicosanoids and cytokines.[92,93] An elevated finding raises concern regarding inflammation.

Omega-3 Index: Research suggests that the Omega-3 Index may be utilized to provide additional information on mortality risk for both coronary heart disease (CHD) and sudden cardiac death (SCD). This index is based on determinations that red blood cell (RBC) membranes reflect cardiac membrane omega-3 fatty acid (EPA + DHA) content. Evidence from secondary prevention trials suggests that supplementation with roughly 1g of omega-3 fatty acids daily – primarily in the form of EPA and DHA - can reduce CHD and SCD mortality risk.[94,95]

Oxidative Stress Markers

Oxidative stress occurs when the production of reactive oxygen species (ROS) outweighs the body's ability to remove them, thus shifting this equilibrium in the direction of oxidation. The instability of free radicals and other ROS causes them to extract electrons from neighboring molecules in a chain reaction, resulting in cellular damage. Reducing agents, including dietary antioxidants, nutritional supplements, and antioxidant enzymes provide protection against free radical damage.

Oxidative stress has an integral relationship with the inflammatory cascade, which produces ROS, and is considered a driving force in the aging process. Oxidative stress has been implicated in a growing list of disorders, including cancer, arthritis, cardiovascular disease, inflammation, diabetes, autoimmune diseases, and neurodegenerative diseases.[96]

Antioxidant needs vary significantly between individuals. Therefore, evaluating one's reduction/oxidation ("redox") balance can help pinpoint imbalances that may contribute to chronic illness. The evaluation includes markers of antioxidant RESERVES and the presence of tissue DAMAGE. Any imbalances are then addressed specifically.

RESERVE AND DAMAGE BALANCE		
Low antioxidant reserve and/or increased oxidative stress damage		
Low Reserve - glutathione and/or CoQ10 • Reduced antioxidant capacity, increased risk of oxidative damage and chronic illness • Reduced ability to detoxify environmental toxins and metabolic byproducts **Elevated Damage – 8-OHdG (DNA) and/or Lipid peroxides (lipid membranes)** • Oxidative damage/stress and a need for greater antioxidant protection • Important to identify source of oxidative stress – Inflammation or infection, environmental toxicity, impaired glucose tolerance, alcoholism, homocysteinemia		
Dietary Adjustments	**Supplementation consideration**	**Further evaluation**
Increase: • Antioxidant rich foods • Omega-3 rich foods **Eliminate**: • Free-radical promoting foods (i.e. poor quality fats, fried foods, and artificial sweeteners and food colors)	**Antioxidants:** • n-Acetylcysteine (NAC) • Glutathione support • Vitamins A, C, and E • Alpha-lipoic acid (ALA) • CoQ10 • B-vitamins **Herbal Antioxidants:** • Garlic • ECGC • Curcumin • Resveratrol • *Ginkgo biloba*	**Environmental Testing:** • Heavy metal testing • Toxic Effects CORE **Detoxification**: • DetoxiGenomic Profile

Elemental Markers[73,74,97-100,102]

Nutrient Markers		
Nutrient	**Function**	**Food Sources**
Copper (plasma)	Copper is an important enzymatic cofactor for cellular energy production, iron metabolism, connective tissue formation, antioxidant functions, and neurotransmitter synthesis.	Organ meats, shellfish, nuts and seeds, lentils, mushrooms, wheat cereal, and semisweet chocolate
Magnesium (RBC)	Magnesium is involved in hundreds of metabolic reactions. Key areas include energy production, bone density, ATP formation, muscle & nerve conduction and cell signaling.	Dark leafy greens, oatmeal, buckwheat, unpolished grains, chocolate, milk, nuts & seeds, lima beans, and molasses
Manganese (whole blood)	Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production, and digestion.	Whole grains, legumes, dried fruits, nuts, dark green leafy vegetables, liver, kidney, and tea
Potassium (RBC)	Potassium plays a role in maintaining fluid and electrolyte balance important for nerve conduction, muscle contraction, and blood pressure.	Fruits, vegetables, and nuts
Selenium (whole blood)	Selenium functions as an antioxidant. It plays a role in thyroid hormone synthesis, enhancing immune function and anti-viral activity.	Meat, fish, whole grains, legumes, brazil nuts, and mushrooms
Zinc (plasma)	Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion, and antioxidant function.	Oysters, organ meats, soybean, wheat germ, seeds, nuts, red meat, chicken, herring, milk, yeast, leafy, and root vegetables

Toxic Elements[102-109]

Toxic heavy metals measured in whole blood indicate recent exposure (within a time-frame of a few months). It is unknown whether the patient is storing the metal in their tissues or detoxifying it appropriately. Identify the source of exposure and avoid or minimize exposure if possible. Assess other markers of detoxification and oxidative stress, and address if warranted.

Toxic Element	Source of Exposure	Health Effects
Lead – Pb (whole blood)	Ingestion of contaminated foods (improperly glazed pottery or ceramic dishes) and drinking water (lead soldered pipes), ingestion of contaminated soil/dust or lead-based paint, non-Western supplements, some hair dyes and cosmetics, hobbies that use lead (casting ammunition and fishing weights, soldering with lead solder, stained glass), leaded gasoline (used in some race cars, airplanes, and off-road vehicles), occupation (lead smelting and refining industries, battery manufacturing plants, steel welding, construction, rubber and plastic industries, firing ranges, and radiator repair industries)	Hematological, gastrointestinal, cardiovascular (elevated blood pressure), renal (decreased GFR), neurological (encephalopathy, peripheral neuropathy, neurobehavioral, neuropsychological effects, and cognitive), and reproductive
Arsenic – As (whole blood)	Air (burning or sawing of arsenic-treated wood prior to 2015), drinking water, food (some areas in the US naturally contain higher levels of arsenic in soil and may be used as an herbicide and as antimicrobial additives for animal and poultry feed), occupation (smelting of copper or lead, pesticide production or application)	Skin hyperpigmentation, peripheral neuropathy, carcinogen (lung, skin, and bladder), respiratory irritation, nausea, cardiovascular effects, kidney and bladder effects
Mercury – Hg (whole blood)	Air (breathing vapors from spills, incinerators, hazardous waste sites, and industries that burn mercury-containing fossil fuels), water, food (eating fish or shellfish contaminated with Hg), dental work with Hg-amalgams, religious practices containing Hg, herbal remedies that contain Hg, damaged or broken Hg-containing products (thermostats, fluorescent light bulbs, barometers, glass thermometers, and some blood pressure devices)	Weakness, fatigue, anorexia, insomnia, weight loss, gastrointestinal distress, reduced visual acuity, delayed reaction time, ataxia, skin rashes, deficits in mental concentration, and a possible human carcinogen
Cadmium – Cd (whole blood)	Food (agriculture soil naturally containing Cd, equipment in food processing and preparation, enamel and pottery glazes with Cd based pigments, and some plastics) – highest levels typically found in leafy vegetables, potatoes, grains, peanuts, and organ meats (liver and kidney), cigarette smoking, drinking water, air, and occupation (heating Cd-containing products, battery production, pigment production and use, plastics production, and smelting refining)	Kidney (renal damage, glomerular damage), bone (decreased mineralization, increased risk fractures), decreased lung function and emphysema, and probable human carcinogen
Tin – Sn (whole blood)	Toothpastes, perfumes, soaps, food additives and dyes, plastics, food packages, plastic pipes, pesticides, paints, and pest repellents; air, water, and soil near places where naturally present in rocks	Stomach ache, anemia, liver and kidney problems, reproduction, skin and eye irritation, affects brain and nervous system

1.

Interpretation At-A-Glance **Key**

NutrEval *Interpretation At-A-Glance*

Nutritional Needs

Vitamin A / Carotenoids

Biomarkers Evaluated:

β-Alanine
Cysteine
Cystine
Glycine
Taurine
8-OHdG
Lipid Peroxides

Vitamin C

Biomarkers Evaluated:

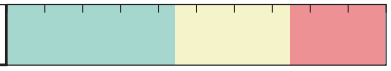
Cysteine
Cystine
Glutathione
8-OHdG

Vitamin E / Tocopherols

Biomarkers Evaluated:

β-Alanine
Cysteine
Cystine
Glycine
Taurine
8-OHdG
Lipid Peroxides

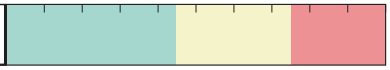
α-Lipoic Acid



Biomarkers Evaluated:

Glutathione
Pyroglutamic Acid
Methionine
Taurine
8-OHdG
Lipid Peroxides

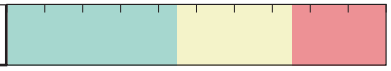
CoQ10



Biomarkers Evaluated:

β-OH-β-Methylglutaric Acid
CoQ10
Lactic Acid
Succinic Acid

Glutathione



Biomarkers Evaluated:

8-OHdG
Citric Acid
Cis-Aconitic Acid
Glutathione
Lipid Peroxides
Pyroglutamic Acid

Plant-based Antioxidants

Biomarkers Evaluated:

8-OHdG
Cis-Aconitic Acid
Citric Acid
Cysteine
Cystine
Glutathione
Lipid Peroxides
Taurine

Nutritional Needs

Thiamin - B1

Biomarkers Evaluated:

5-OH-Indoleacetic Acid
Lactic Acid
Pyruvic Acid
α-Keto-β-Methylvaleric Acid
α-Ketoglutaric Acid
α-Ketoisocaproic Acid
α-Ketoisovaleric Acid
α-Ketoadipic Acid
Alanine
Citrulline
Glutamic Acid
Glutamine
Histidine
Isoleucine
Leucine
Lysine
Ornithine
Phenylalanine
Proline
Serine
Taurine
Tyrosine
Valine

Pyridoxine - B6

Biomarkers Evaluated:

Homovanillic Acid
5-OH-Indoleacetic Acid
Kynurenic Acid
Quinolinic Acid
Xanthurenic Acid
Alanine
α-Aminoadipic Acid
α-Amino-N-butyric Acid
Arginine
β-Alanine
β-Aminoisobutyric Acid
Cystathionine
Cysteine
γ-Aminobutyric Acid
Glutamic Acid
Glycine
Histidine
Isoleucine
Leucine
Methionine
Ornithine
Phosphoserine
Serine
Taurine
Threonine
Tryptophan
Tyrosine
Urea
Valine

Riboflavin - B2

Biomarkers Evaluated:

Succinic Acid
Pyruvic Acid
Adipic Acid
Suberic Acid
α-Keto-β-Methylvaleric Acid
α-Ketoglutaric Acid
α-Ketoisocaproic Acid
α-Ketoisovaleric Acid
Kynurenic Acid
Glutaric Acid
α-Aminoadipic Acid
Histidine
Sarcosine

Biotin - B7

Biomarkers Evaluated:

3-Hydroxyisovalerate
3-Hydroxypropionic Acid
Pyruvic Acid
Alanine
Glycine
Phenylalanine

Niacin - B3

Biomarkers Evaluated:

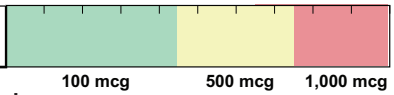
5-OH-Indoleacetic Acid
Pyruvic Acid
Isocitric Acid
α-Ketoglutaric Acid
Malic Acid
α-Keto-β-Methylvaleric Acid
α-Ketoisocaproic Acid
α-Ketoisovaleric Acid
Kynurenic Acid
Quinolinic Acid
Xanthurenic Acid
Alanine
Glutamic acid
Isoleucine
Leucine
Lysine
Methionine
Phenylalanine
Threonine
Tryptophan
Tyrosine
Valine

Folic Acid - B9

Biomarkers Evaluated:

3-Methyl-4-OH-phenylglycol
5-OH-Indoleacetic Acid
Formiminoglutamic Acid
Methylmalonic acid
α-Aminoadipic Acid
β-Aminoisobutyric Acid
Cystathionine
Glycine
Histidine
Methionine
Phenylalanine
Sarcosine
Serine
Valine

Cobalamin - B12



Biomarkers Evaluated:

Succinic Acid
5-OH-Indoleacetic Acid
Lactic Acid
Formiminoglutamic Acid
Methylmalonic Acid
α-Aminoadipic Acid
Cystathionine
Cysteine
Glycine
Histidine
Isoleucine
Leucine
Methionine
Phenylalanine
Sarcosine
Valine

Nutritional Needs

Manganese

Biomarkers Evaluated:

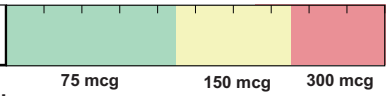
5-OH-Indoleacetic Acid
Homovanillic Acid
Vanilmandelic Acid
Arginine
γ-Aminobutyric Acid
Glutamic Acid
Manganese

Magnesium

Biomarkers Evaluated:

5-HIAA
Citric Acid
Ethanolamine
Isocitric Acid
Lactic Acid
Magnesium
Ornithine
Phenylalanine
Phosphoethanolamine
Taurine
Urea

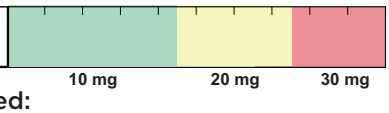
Molybdenum



Biomarkers Evaluated:

Cysteine
Histidine
Methionine
Taurine

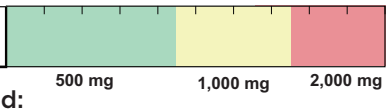
Zinc



Biomarkers Evaluated:

Lactic Acid
Anserine
Carnosine
Isoleucine
Leucine
Valine
Phosphoethanolamine
Zinc

Need for Essential Fatty Acids

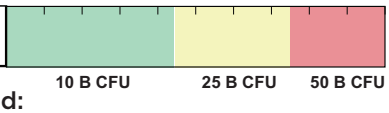


Biomarkers Evaluated:

Omega 3 Index (DHA+EPA)
Omega 3 DHA
Omega 3 EPA
Omega 3 ALA
Omega 6 AA
Omega 6 GLA
Omega 6 DGLA
Omega 6 LA
Omega 3/6 Ratio

Digestive Support

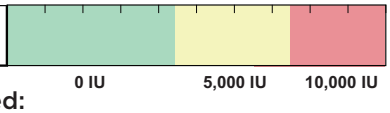
Need for Probiotics



Biomarkers Evaluated:

3-Hydroxyphenylacetic Acid
4-Hydroxyphenylacetic Acid
Benzoic Acid
β-Alanine
Citramalic Acid
Dihydroxyphenylpropionic Acid
Ethanolamine
γ-Aminobutyric Acid
Hippuric Acid
Indoleacetic Acid
Phenylacetic Acid
Phosphoethanolamine
Succinic Acid

Need for Pancreatic Enzymes



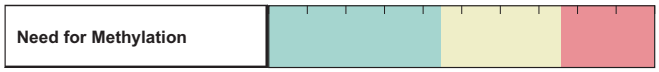
Biomarkers Evaluated:

1-Methylhistidine
Dihydroxyphenylpropionic Acid
Histidine
Indoleacetic Acid
Isoleucine
Leucine
Lysine
Methionine
Phenylacetic Acid
Phenylalanine
Succinic Acid
Threonine
Tryptophan
Tyrosine
Valine

Functional Imbalances

Biomarkers Evaluated:

Adipic Acid
a-Ketoglutaric Acid
Cis-Aconitic Acid
Citric Acid
CoQ10
Formiminoglutamic Acid
Glutaric Acid
Glutathione
Isocitric Acid
Lactic Acid
Magnesium
Malic Acid
Manganese
Methylmalonic Acid
Pyruvic Acid
Suberic Acid
Succinic Acid



Biomarkers Evaluated:

Arginine
Creatinine
Formiminoglutamic Acid
Glutathione
Glycine
Methionine
Methylmalonic Acid
Sarcosine
Serine
Vanilmandelic Acid

Biomarkers Evaluated:

Mercury
Lead
Antimony
Cadmium
Arsenic
Cis-Aconitic Acid
Citric Acid
Glutaric Acid
Isocitric Acid
Orotic Acid
a-Ketophenylacetic Acid
a-Hydroxyisobutryic Acid
Pyroglutamic Acid

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