GENOVA DIAGNOSTICS

63 Zillicoa Street
Asheville, NC 28801

ONE FMV®
OPTIMAL NUTRITION EVALUATION

Patient: **FINN SCHUREMAN**
DOB: September 14, 2012
Sex: M
MRN: 1232649532

Order Number: L7180516
Completed: January 24, 2018
Received: January 18, 2018
Collected: January 16, 2018

Innovative Hyperbaric Solutions
Patrick Elliott DO
3744 W Chester Pike
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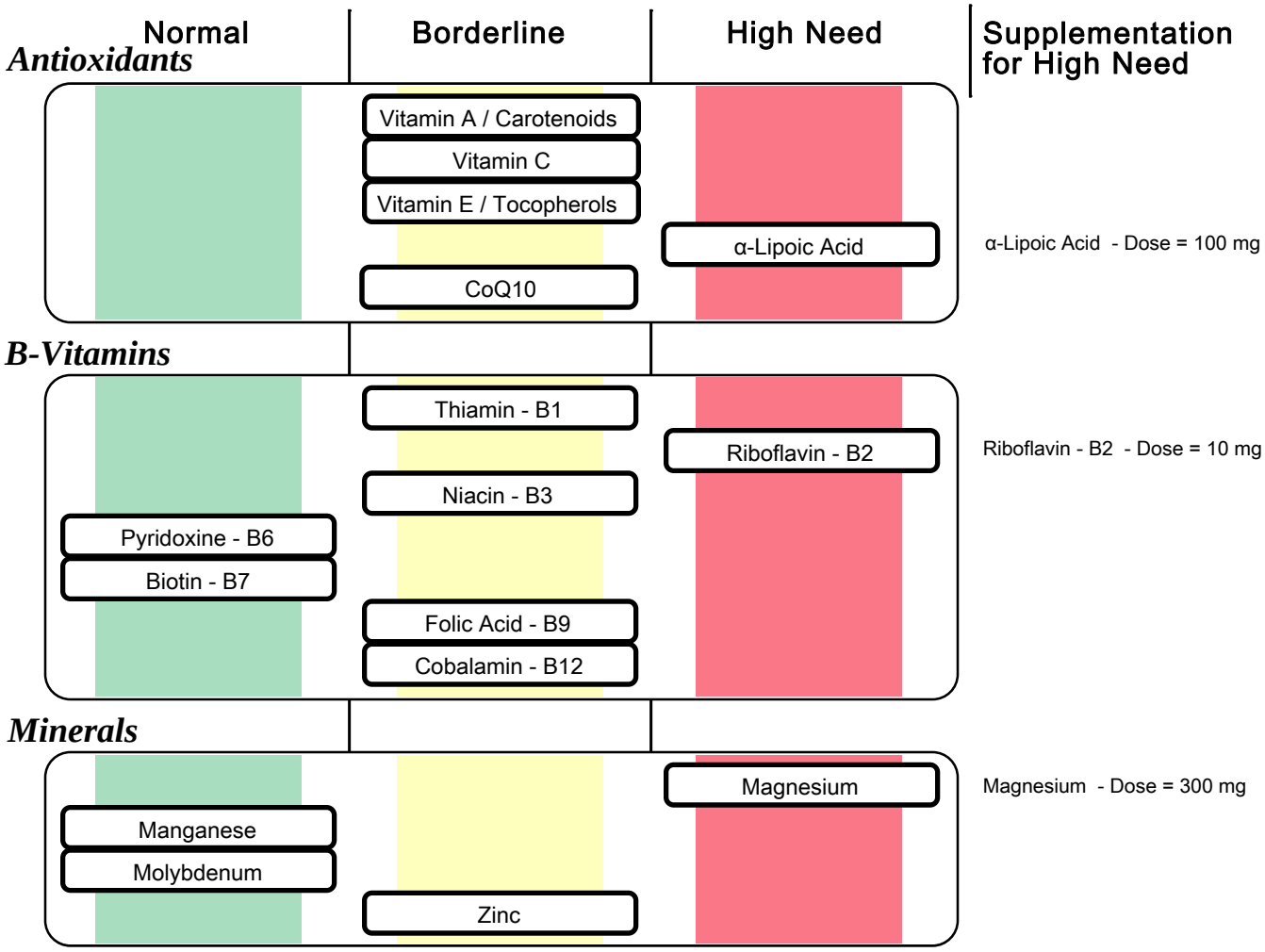
ONE Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	1,333 IU	2,500 IU	
Vitamin C	25 mg	100 mg	
Vitamin E / Tocopherols	10 IU	100 IU	
α-Lipoic Acid		100 mg	
CoQ10		40 mg	
B-Vitamins			
Thiamin - B1	0.6 mg	5 mg	
Riboflavin - B2	0.6 mg	10 mg	
Niacin - B3	8 mg	20 mg	
Pyridoxine - B6	0.6 mg	2 mg	
Biotin - B7	12 mcg	50 mcg	
Folic Acid - B9	200 mcg	300 mcg	
Cobalamin - B12	1.2 mcg	50 mcg	
Minerals			
Magnesium	130 mg	300 mg	
Manganese	1.5 mg	1.5 mg	
Molybdenum	22 mcg	25 mcg	
Zinc	5 mg	10 mg	
Digestive Support			
Probiotics		25 billion CFU	
Pancreatic Enzymes		5,000 IU	
Other Vitamins			
Vitamin D	600 IU		

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	0
Asparagine	0	Phenylalanine	0
Cysteine	0	Serine	0
Glutamine	0	Taurine	0
Glycine	45	Threonine	0
Histidine	0	Tryptophan	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		

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.

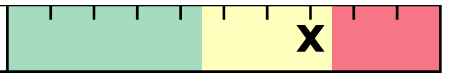
Key Normal | Borderline | High Need

Interpretation At-A-Glance

Nutritional Needs

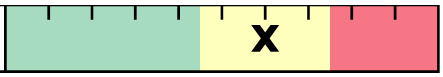
Antioxidants

Vitamin A / Carotenoids



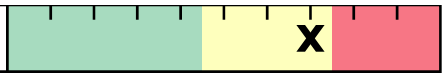
- Beta-carotene & other carotenoids are converted to vitamin A (retinol), involved in vision, antioxidant & immune function, gene expression & cell growth.
- Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, or oral contraceptives containing estrogen & progestin.
- 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



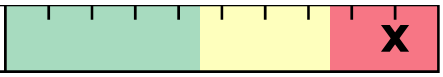
- Vitamin C is an antioxidant (also used in the regeneration of other antioxidants). It is involved in cholesterol metabolism, the production & function of WBCs and antibodies, and the synthesis of collagen, norepinephrine and carnitine.
- Deficiency may occur with oral contraceptives, aspirin, diuretics or NSAIDs.
- Deficiency can result in scurvy, swollen gingiva, periodontal destruction, loose teeth, sore mouth, soft tissue ulcerations, or increased risk of infection.
- Food sources include oranges, grapefruit, strawberries, tomato, sweet red pepper, broccoli and potato.

Vitamin E / Tocopherols



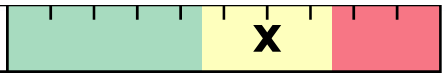
- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital, 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



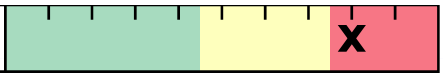
- Lipoic acid plays an important role in energy production, antioxidant activity (including the regeneration of vitamin C and glutathione), insulin signaling, cell signaling and the catabolism of α-keto acids and amino acids.
- High biotin intake can compete with lipoic acid for cell membrane entry.
- Optimal levels of lipoic acid may improve glucose utilization and protect against diabetic neuropathy, vascular disease and age-related cognitive decline.
- Main food sources include organ meats, spinach and broccoli. Lesser sources include tomato, peas, Brussels sprouts and brewer's yeast.

CoQ10



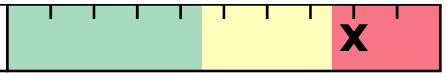
- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) 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) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.

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 nutriceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).

Key

- Function
- Causes of Deficiency
- Complications of Deficiency
- Food Sources

Interpretation At-A-Glance

Nutritional Needs

B-Vitamins

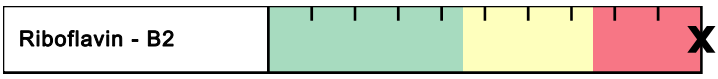
Thiamin - B1

- 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

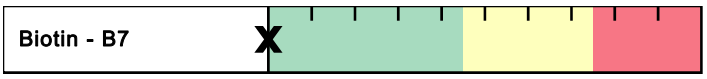
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or digoxin.
- B6 deficiency may result in neurologic symptoms (e.g., irritability, depression, seizures), oral inflammation, impaired immunity or increased homocysteine.
- Food sources include poultry, beef, beef liver, fish, whole grains, wheat germ, soybean, lentils, nuts & seeds, potato, spinach and carrots.

Riboflavin - B2



- 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 for enzymes involved in functions such as fatty acid (FA) synthesis, mitochondrial FA oxidation, gluconeogenesis, and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN use, anticonvulsants, high-dose B5, sulfa drugs & other antibiotics.
- Low levels may result in neurologic symptoms (e.g., paresthesias, depression), hair loss, scaly rash on face or genitals or impaired immunity.
- Food sources include yeast, whole grains, wheat germ, eggs, cheese, liver, meats, fish, wheat, nuts & seeds, avocado, raspberries, sweet potato and cauliflower.

Niacin - B3

- 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 key role in coenzymes involved in DNA and SAMe synthesis, methylation, nucleic acids & amino acid metabolism and RBC production.
- Low folate may result from alcoholism, high-dose NSAIDs, diabetic meds, H2 blockers, some diuretics and anti-convulsants, SSRIs, methotrexate, trimethoprim, pyrimethamine, triamterene, sulfasalazine or cholestyramine.
- Folate deficiency can result in anemia, fatigue, low methionine, increased homocysteine, impaired immunity, heart disease, birth defects and CA risk.
- Food sources include fortified grains, green vegetables, beans & legumes.

Cobalamin - B12

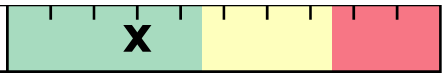
- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 blockers, PPIs), vegan diets, diabetic meds, cholestyramine, chloramphenicol, neomycin or colchicine.
- B12 deficiency can lead to anemia, fatigue, neurologic symptoms (e.g., paresthesias, memory loss, depression, dementia), methylation defects or chromosome breaks.
- Food sources include shellfish, red meat poultry, fish, eggs, milk and cheese.

Interpretation At-A-Glance

Nutritional Needs

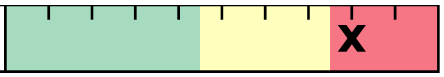
Minerals

Manganese



- 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

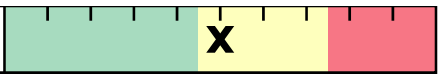


- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses 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

- 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).

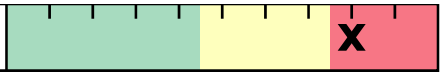
Zinc



- 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.

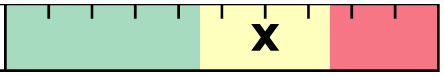
Digestive Support

Need for Probiotics



- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhancement of digestion & absorption; decreasing severity of diarrheal illness; modulation 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



- 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.

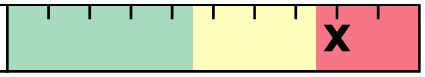
Interpretation At-A-Glance

Functional Imbalances

Mitochondrial Dysfunction

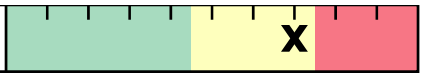
- Mitochondria are a primary site of generation of reactive oxygen species. Oxidative damage is considered an important factor in decline of physiologic function that occurs with aging and stress.
- Mitochondrial defects have been identified in cardiovascular disease, fatigue syndromes, neurologic disorders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

Toxic Exposure



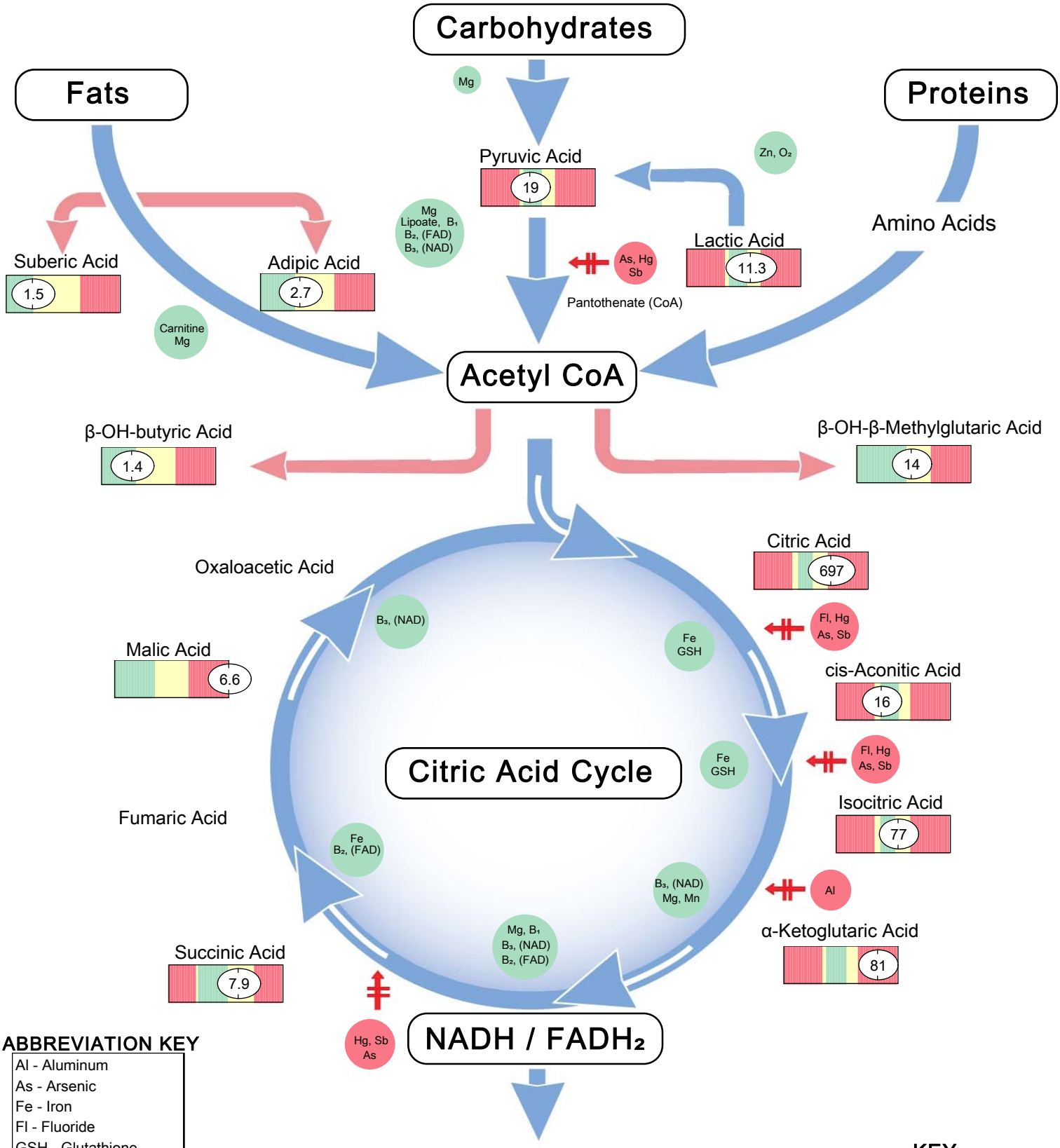
- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal 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.
- Levels of these toxic substances should be examined within the context of the body's functional capacity for methylation and need for glutathione.

Need for Methylation



- 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.

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

Metabolic Analysis Markers (Urine)

All biomarkers reported in mmol/mol creatinine unless otherwise noted.

Malabsorption and Dysbiosis Markers

Malabsorption Markers

		Reference Range
Indoleacetic Acid (IAA)	1.9	<= 4.2
Phenylacetic Acid (PAA)	0.11	<= 0.15

Bacterial Dysbiosis Markers

		Reference Range
Dihydroxyphenylpropionic Acid (DHPPA)	>14.8	<= 7.0
3-Hydroxyphenylacetic Acid	<dl	<= 9.2
4-Hydroxyphenylacetic Acid	18	<= 37
Benzoic Acid	0.21	<= 0.10
Hippuric Acid	369	<= 921

Yeast / Fungal Dysbiosis Markers

		Reference Range
Arabinose	120	<= 132
Citramalic Acid	7.6	<= 5.3
Tartaric Acid	19	<= 20

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism

		Reference Range
Lactic Acid	11.3	3.7-14.6
Pyruvic Acid	19	12-39
β-OH-Butyric Acid (BHBA)	1.4	<= 3.4

Energy Metabolism

		Reference Range
Citric Acid	697	62-648
Cis-Aconitic Acid	16	13-33
Isocitric Acid	77	38-97
α-Ketoglutaric Acid (AKG)	81	12-55
Succinic Acid	7.9	0.8-10.4
Malic Acid	6.6	<= 2.7
β-OH-β-Methylglutaric Acid (HMG)	14	<= 19

Fatty Acid Metabolism

		Reference Range
Adipic Acid	2.7	<= 5.0
Suberic Acid	1.5	<= 4.2

Creatinine Concentration

		Reference Range
Creatinine ◆	7.4	3.1-19.5 mmol/L

Methodology: GCMS, LC/MS/MS, Alkaline Picrate

Neurotransmitter Metabolites

		Reference Range
Vanilmandelic Acid	2.8	1.5-5.0
Homovanillic Acid	7.3	1.8-8.6
5-OH-indoleacetic Acid	21.5	6.4-24.3
3-Methyl-4-OH-phenylglycol	0.32	0.07-0.41
Kynurenic Acid	3.8	<= 9.2
Quinolinic Acid	4.5	<= 11.6
Kynurenic / Quinolinic Ratio	0.84	>= 0.46

Vitamin Markers

		Reference Range
α-Ketoadipic Acid	1.5	<= 2.1
α-Ketoisovaleric Acid	0.48	<= 0.85
α-Ketoisocaproic Acid	0.56	<= 0.91
α-Keto-β-Methylvaleric Acid	1.0	<= 2.3
Formiminoglutamic Acid (FIGlu)	0.4	<= 2.7
Glutaric Acid	1.14	<= 0.92
Isovalerylglycine	2.4	<= 5.4
Methylmalonic Acid	2.0	<= 2.2
Xanthurenic Acid	0.24	<= 1.07
3-Hydroxypropionic Acid	10	6-23
3-Hydroxyisovaleric Acid	19	<= 38

Toxin & Detoxification Markers

		Reference Range
α-Ketophenylacetic Acid (from Styrene)	0.53	<= 0.50
α-Hydroxyisobutyric Acid (from MTBE)	13.8	<= 8.7
Orotic Acid	0.74	0.38-0.91
Pyroglutamic Acid	47	22-64

Tyrosine Metabolism

		Reference Range
Homogentisic Acid	27	<= 33
2-Hydroxyphenylacetic Acid	0.77	<= 0.99

Metabolic Analysis Reference Ranges are Age Specific

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

Amino Acids (Urine FMV)

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

Nutritionally Essential Amino Acids

Amino Acid		Reference Range
Arginine	29	8-59
Histidine	1,346	218-2,114
Isoleucine	18	10-44
Leucine	40	26-109
Lysine	138	25-320
Methionine	17	7-39
Phenylalanine	85	33-188
Taurine	1,141	80-1,560
Threonine	175	31-246
Tryptophan	67	24-113
Valine	58	26-88

Nonessential Protein Amino Acids

Amino Acid		Reference Range
Alanine	460	78-560
Asparagine	223	44-360
Aspartic Acid	56	<= 19
Cysteine (FMV urine)	38	12-98
Cystine (FMV Urine)	60	27-148
γ-Aminobutyric Acid	5	<= 5
Glutamic Acid	20	10-36
Glutamine	724	162-1,290
Proline	10	3-24
Tyrosine	153	61-410

Creatinine Concentration

		Reference Range
Creatinine ◆	6.1	3.1-19.5 mmol/L

Amino Acid reference ranges are age specific.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assays have not been cleared by the U.S. Food and Drug Administration.

Methodology: LC/MS/MS, Alkaline Picrate

Intermediary Metabolites

B Vitamin Markers		Reference Range
α-Aminoadipic	26	13-87
α-Amino-N-butyric Acid	20	6-49
β-Aminoisobutyric Acid	213	5-284
Cystathionine	43	4-106
3-Methylhistidine	141	75-456

Urea Cycle Markers

Citrulline	4.7	0.6-8.5
Ornithine	16	5-21
Urea ◆	272	196-711 mmol/g creatinine

Glycine/Serine Metabolites

Glycine	236	118-907
Serine	373	61-295
Ethanolamine	300	74-286
Phosphoethanolamine	10	4-27
Phosphoserine	7	3-23
Sarcosine	1.2	<= 0.9

Dietary Peptide Related Markers

		Reference Range
Anserine (dipeptide)	42.9	1.0-268.1
Carnosine (dipeptide)	118	7-318
1-Methylhistidine	280	28-1,985
β-Alanine	4	<= 29

Oxidative Stress Markers

Oxidative Stress Markers

Reference Range

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

Lipid Peroxides (urine)	11.3	<=10.0 micromol/g Creat.
8-OHdG (urine)	12	<=15 mcg/g Creat.

Lab Comments

Please note the reference range for 8-OHdG (urine) has been updated.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

Interpretation At-A-Glance Details

Antioxidants

Vitamin A / Carotenoids

Contributing Biomarkers:
8-OHdG
Cystine
Cysteine
Lipid Peroxides

Vitamin C

Contributing Biomarkers:
8-OHdG
Cystine
Cysteine

Vitamin E / Tocopherols

Contributing Biomarkers:
8-OHdG
Cystine
Cysteine
Lipid Peroxides

α-Lipoic Acid

Contributing Biomarkers:
Lipid Peroxides
Pyroglutamic Acid
8-OHdG

CoQ10

Contributing Biomarkers:
Lactic Acid
β-OH-β-Methylglutaric Acid
Succinic Acid

Glutathione

Contributing Biomarkers:
8-OHdG
Citric Acid
Lipid Peroxides

Interpretation At-A-Glance Details

Plant-based Antioxidants

Contributing Biomarkers:
8-OHdG
Citric Acid
Cystine
Cysteine
Lipid Peroxides

B-Vitamins

Thiamin - B1

Contributing Biomarkers:
5-OH-Indoleacetic Acid
α-Ketoglutaric Acid
Lactic Acid
Serine

Riboflavin - B2

Contributing Biomarkers:
Adipic Acid
α-Ketoglutaric Acid
Glutaric Acid
Sarcosine

Niacin - B3

Contributing Biomarkers:
α-Ketoglutaric Acid
Malic Acid

Folic Acid - B9

Contributing Biomarkers:
Methylmalonic Acid
Sarcosine
Serine

Cobalamin - B12

Contributing Biomarkers:
Methylmalonic Acid
Sarcosine

Minerals

Interpretation At-A-Glance Details

Manganese	**Contributing Biomarkers:** 5-OH-Indoleacetic Acid
Molybdenum	**Contributing Biomarkers:** Taurine
Magnesium	**Contributing Biomarkers:** Citric Acid Ethanolamine Phosphoethanolamine Isocitric Acid Lactic Acid
Zinc	**Contributing Biomarkers:** Lactic Acid

Digestive Support

Need for Probiotics	**Contributing Biomarkers:** Benzoic Acid Citramalic Acid Dihydroxyphenylpropionic Acid Ethanolamine
Need for Pancreatic Enzymes	**Contributing Biomarkers:** Dihydroxyphenylpropionic Acid

Interpretation At-A-Glance Details

Functional Imbalances

Mitochondrial Dysfunction

Contributing Biomarkers:
α-Ketoglutaric Acid
Citric Acid
Glutaric Acid
Malic Acid

Need for Methylation

Contributing Biomarkers:
Methylmalonic Acid
Sarcosine

Toxic Exposure

Contributing Biomarkers:
α-Hydroxyisobutyric Acid
α-Ketophenylacetic Acid
Citric Acid
Glutaric Acid

Metabolic Analysis Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

2,3 Dihydroxyphenylpropionic acid (DHPPA) is elevated. This organic acid is a byproduct of the bacterial metabolism of phenylalanine, tyrosine, and/or tryptophan. Research has identified various species of Clostridia in the *in-vitro* production of this compound. Other research on quinoline demonstrates production of DHPPA by Pseudomonas species. Presence of elevated levels of DHPPA in the urine may thus suggest overgrowth of Clostridia and/or Pseudomonas, as well as a degree of malabsorption of aromatic amino acids. A comprehensive stool analysis is suggested.

Benzoic acid is a common food component, especially in fruits and in particular berries/cranberries. It is also a common food additive/preservative. Benzoic acid is also formed by gut microflora metabolism of phenylalanine and dietary polyphenols. Elevated levels may thus reflect dietary intake (for example strawberries), imbalanced gut flora or a high intake of polyphenols or phenylalanine. Older studies note a relationship between decreased cognitive function and increased BA in the urine.

Citramalic Acid is elevated. With a chemical structure very similar to that of malic acid, citramalate may cause metabolic interference with malate. This is of concern because malic acid has extra-mitochondrial functions, as with the "malate shuttle" for carrying reducing equivalents (protons) into the mitochondria. While the metabolic interference aspect is uncertain, the presence of citramalate in the urine indicates intestinal dysbiosis. Not formed in human tissues, citramalate may be formed by anaerobic bacteria such as clostridia, as well as by yeast/fungi. A stool analysis with bacteriology or microbiology is suggested.

Citric Acid , or citrate, is measured to be high. Citric acid is a key component of the citric acid cycle and is formed inside the mitochondria from acetyl coenzyme A and oxaloacetic acid.

Citric acid is essential in the production of bicarbonate, a compound that helps to maintain proper pH in the body. Elevated urinary citrate may be a sign of a metabolic pH imbalance (metabolic acidosis), possibly due to damaged proximal tubular function in the kidney that results in urinary wasting of citrate. Another possible cause of elevated urine citrate is pancreatic dysfunction, as bicarbonate production would be reduced, leading to less utilization of citric acid. In this situation, cis-aconitic and isocitric acids may be also elevated.

However, if cis-aconitic or isocitric acids are low, this may be indicative of impaired enzymatic conversion within the citric acid cycle. The enzyme cis-aconitase converts citric acid into cis-aconitic acid. This enzyme requires the presence of a sulfhydryl (-SH) group from cysteine or glutathione and it is activated by ferrous iron (Fe+2). Deficiencies of methionine, cysteine, glutathione, or iron, would result in sub-optimal enzyme efficiency. In addition, toxic elements with high sulfur affinity, like arsenic, antimony and mercury, may impair cis-aconitase activity. Also, xenobiotic toxicity, if it depletes glutathione, or increased oxidative stress from any cause may lead to elevated citrate. Excess fluorine can combine with acetate and, as fluoroacetate, can also inhibit the cis-aconitase enzyme. Any of the above situations may result in increased urinary citrate.

Alpha-ketoglutaric Acid (alpha-ketoglutarate or AKG) is measured to be elevated. Alpha-ketoglutaric acid is formed from isocitrate or from the deamination or transamination of glutamate (a process requiring vitamin B6). Metabolism of alpha-ketoglutaric acid then leads to the formation of succinyl CoA.

Commentary

Elevated alpha-ketoglutaric acid can be due to specific weakness in the alpha-ketoglutaric acid dehydrogenase complex that converts alpha-ketoglutarate to is downstream citric acid cycle metabolite, succinic acid. Dehydrogenase enzymes require vitamin B1 as thiamin pyrophosphate, vitamin B2 as FAD, vitamin B3 as NAD, and lipoic acid. Phosphorylation requiring magnesium is also involved, and coenzyme A is needed. Coenzyme A is formed from the nutrients pantothenic acid, cysteine, and magnesium, and requires phosphorylation and energy from CTP and ATP. Insufficiencies of these nutrients or cofactors may cause elevated alpha-ketoglutaric acid. Arsenic can also inhibit the dehydrogenase enzyme.

Elevated alpha-ketoglutaric acid also may be accompanied by elevated glyoxylate and oxalate. If there is weakness in the decarboxylation of glyoxylate and alpha-ketoglutarate, renal stone (calcium oxalate) formation is possible. This is not a common condition, and its diagnosis should be made from urine levels of oxalate and glyoxylate. In this case, supplements of vitamin B6 or pyridoxal 5-phosphate may be beneficial. (B6 aids the transformation of glyoxylate to glycine and thus decreases oxalate formation.)

Moderate increase in urinary alpha-ketoglutaric acid may occur, without clinical significance, with low-carbohydrate or high-protein diets (where metabolic need is increased).

Malic Acid (malate) is measured to be elevated. An important intermediate of the citric acid cycle in cell mitochondria, malic acid or malate is formed from fumaric acid (fumarate), and it becomes oxaloacetic acid. Malic acid also participates in the malate-aspartate shuttle, a cellular process in which malate and a proton (H+) can enter the mitochondrion from the cytosol. This brings a chemical reducing equivalent, H+, inside the mitochondrial membrane. This is the mechanism whereby the NADH produced in glycolysis can enter the mitochondria to participate in oxidative phosphorylation.

Malic acid can be elevated if its dehydrogenation to oxaloacetic acid is reduced; this dehydrogenase enzyme requires vitamin B3 as NAD. Malate can also be high if oxaloacetic acid is high. Use of D-malic acid (or D,L-malate) as a nutritional supplement, instead of L-malic acid will also cause elevated urine levels, since this compound will interfere with its metabolism. Only L-malic acid can be utilized properly.

Impairments in pyruvate metabolism with elevated pyruvate and lactate usually result in elevated malate, as well. (Refer to commentary for these analytes.)

Glutaric Acid is measured to be high. This organic acid is formed from the essential amino acids lysine (primarily) and tryptophan, via alpha ketoadipic acid (AKAA) and glutaryl-CoA. Glutaric acid is elevated when glutaryl CoA metabolism is impaired, such as when needed nutrient cofactors are missing. Glutaryl-CoA is dehydrogenated to form glutaconyl-CoA and then crotonyl-CoA using a FAD-dependent dehydrogenase enzyme; the FAD (from riboflavin) becomes FADH2.

Glutaric aciduria may have negligible manifestations if mild, but if the dehydrogenase is notably weak, then severe symptoms can be experienced beginning in infancy and childhood with general neurological deterioration, spasticity and mental retardation. Glutaric acid can be very elevated in the rare case of multiple acyl-CoA dehydrogenase dysfunction. The resulting glutaric aciduria type II can lead to metabolic acidosis, hypoglycemia, hypotonia, nausea and diarrhea, and frequently the individual has a "sweaty feet" or foul odor. Poor weight gain and frequent regurgitation of food are seen in children. In glutaric aciduria type II, adipic, lactic, and beta-hydroxybutyric (BHBA) acids are also elevated. This more general enzyme impairment is postulated to be a weakness in mitochondrial electron transfer. Glutaric acid excess may or may not be helped by supplementation of riboflavin, mitochondrial support nutrients, or CoQ10.

Alpha hydroxyisobutyric acid (2-HIBA): This compound is a major urinary metabolite of the gasoline additive

Commentary

MTBE (methyl-tert-butyl ether). It is a potential toxicant for refinery workers, gasoline handlers and in water supplies where underground tanks have leaked into the groundwater aquifers. The elimination half-life of 2-HIBA varies from 7-18 hours at low levels of exposure. Reputed health effects of MTBE exposure include nephropathy, neoplasms and potential for genetic damage. MTBE has been controversially designated as "non-carcinogenic" by the National Toxicology Program.

Alpha keto-phenylacetic acid (phenylglyoxylic acid/PGA) is high. Alpha keto-phenylacetic acid [also known as phynelglyoxylic acid or PGA] is a major urinary metabolite of styrene, toluene, xylenes and ethylbenzene. PGA is a proven means to monitor exposure of workers using these solvents, particularly common in varnishing and reinforced fiberglass industries. Clinical signs of such exposure include diminished threshold for vibratory sense and impaired visual contrast sensitivity.&bnsp; Glutathione-processing deficient individuals exposed to these solvents are likely to have higher quantities of excreted PGA. PGA is a dependable biomarker which, if elevated, likely indicates exposure to solvent compounds with significant health risks.

Amino Acid Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

Ethanolamine is an intermediary metabolite of the serine-to-choline sequence. Ethanolamine is elevated in the urine. Two possibilities should be considered: excess microbial production of ethanolamine in the intestines and rate-limited formation of phosphoethanolamine from ethanolamine. A stool analysis can be used to rule out or confirm intestinal dysbiosis.

Formation of phosphoethanolamine from ethanolamine is a magnesium-dependent phosphorylation.

Magnesium deficiency is frequently observed to coincide with elevated ethanolamine and normal or reduced levels of phosphoethanolamine. Other possibilities involve impaired phosphorylation for reasons such as excessive body burden of aluminum or cell mitochondrial damage or dysfunction.

Elevated **serine** is measured; **glycine** is within normal limits. Metabolic disorders of genetic origin affecting only serine are not documented. Mildly elevated serine can be a sign of vitamin B6 insufficiency or pyridoxal 5-phosphate coenzyme dysfunction.

Sarcosine , or N-methylglycine, is an intermediate of the choline-to-serine catabolism sequence. It is formed by oxidative demethylation of dimethylglycine and it is then catabolized by further demethylation. Sarcosine is elevated in this individual's urine which suggests three possibilities.

1. Recent dietary supplementation of dimethylglycine, "DMG".
2. Deficiencies of the cofactors associated with sarcosine catabolism. These are folic acid as tetrahydrofolate, THF, and Vitamin B2, riboflavin, bound to the sarcosine dehydrogenase enzyme as FAD. The methyl group fragment removed from sarcosine is at the oxidative level of CHO and can form formaldehyde if tetrahydrofolate is insufficient. This would slow down sarcosine's catabolism while making it somewhat toxic.
3. Genetic weakness in sarcosine dehydrogenase with metabolic hypersarcosinuria and possibly hypersarcosinemia. Hereditary (severe) hypersarcosinuria is rare with an incidence of less than 1 in 40,000 newborns.

Unpublished clinical observations associate some cases of acquired, mild sarcosinuria (below 500 micromoles/24 hour) with past exposures to organic chemical solvent and petrochemicals. At such levels sarcosine itself is not known to be toxic. However, folic acid supplementation is suggested whenever sarcosine is elevated.

Oxidative Stress Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

Oxidation of DNA is caused by chemical exposure, inflammation, irradiation, iron overload, smoking. Accumulation of 8-OHdG occurs in chronic inflammatory states. Consider Vitamins A, C & E, beta carotene. Botanicals that reduce 8-OHdG include curcumin, grape seed, green tea. GSH, NAC and omega-3 fatty acid also help repair damaged DNA.

Patient Copy

GENOVA DIAGNOSTICS

63 Zillicoa Street
Asheville, NC 28801
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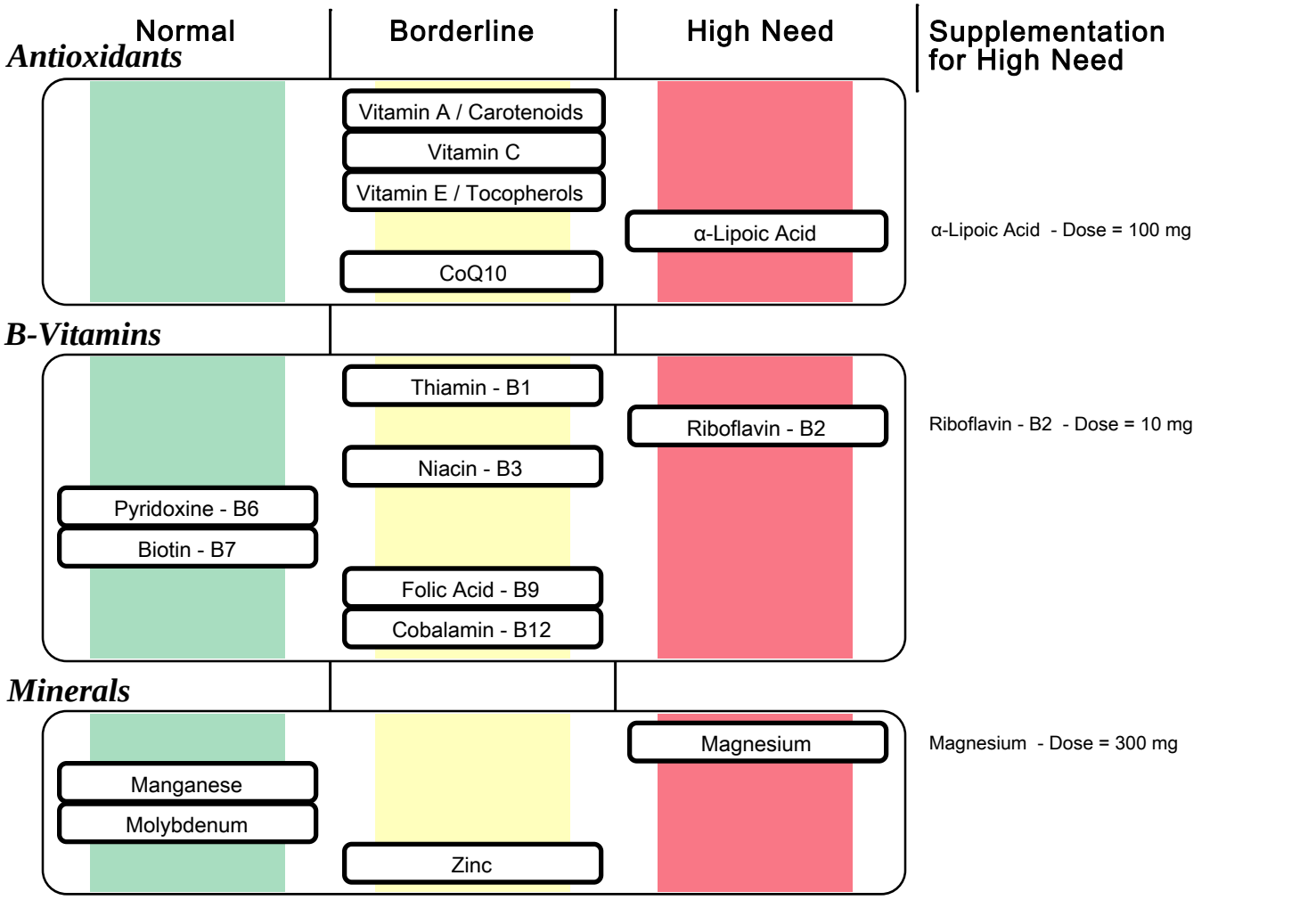
ONE FMV®
OPTIMAL NUTRITION EVALUATION

Patient: **FINN SCHUREMAN**
DOB: September 14, 2012
Sex: M
MRN: 1232649532

Order Number: L7180516
Completed: January 24, 2018
Received: January 18, 2018
Collected: January 16, 2018

Innovative Hyperbaric Solutions
Patrick Elliott DO
3744 W Chester Pike
Newtown Square, PA 19073-3224

ONE Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	1,333 IU	2,500 IU	
Vitamin C	25 mg	100 mg	
Vitamin E / Tocopherols	10 IU	100 IU	
α-Lipoic Acid		100 mg	
CoQ10		40 mg	
B-Vitamins			
Thiamin - B1	0.6 mg	5 mg	
Riboflavin - B2	0.6 mg	10 mg	
Niacin - B3	8 mg	20 mg	
Pyridoxine - B6	0.6 mg	2 mg	
Biotin - B7	12 mcg	50 mcg	
Folic Acid - B9	200 mcg	300 mcg	
Cobalamin - B12	1.2 mcg	50 mcg	
Minerals			
Magnesium	130 mg	300 mg	
Manganese	1.5 mg	1.5 mg	
Molybdenum	22 mcg	25 mcg	
Zinc	5 mg	10 mg	
Digestive Support			
Probiotics		25 billion CFU	
Pancreatic Enzymes		5,000 IU	
Other Vitamins			
Vitamin D	600 IU		

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	0
Asparagine	0	Phenylalanine	0
Cysteine	0	Serine	0
Glutamine	0	Taurine	0
Glycine	45	Threonine	0
Histidine	0	Tryptophan	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		

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.

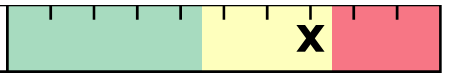
Key Normal | Borderline | High Need

Interpretation At-A-Glance

Nutritional Needs

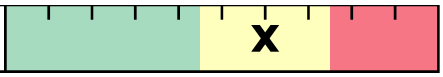
Antioxidants

Vitamin A / Carotenoids



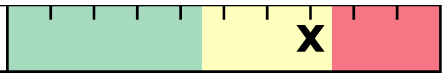
- Beta-carotene & other carotenoids are converted to vitamin A (retinol), involved in vision, antioxidant & immune function, gene expression & cell growth.
- Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, or oral contraceptives containing estrogen & progestin.
- 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



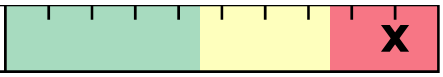
- Vitamin C is an antioxidant (also used in the regeneration of other antioxidants). It is involved in cholesterol metabolism, the production & function of WBCs and antibodies, and the synthesis of collagen, norepinephrine and carnitine.
- Deficiency may occur with oral contraceptives, aspirin, diuretics or NSAIDs.
- Deficiency can result in scurvy, swollen gingiva, periodontal destruction, loose teeth, sore mouth, soft tissue ulcerations, or increased risk of infection.
- Food sources include oranges, grapefruit, strawberries, tomato, sweet red pepper, broccoli and potato.

Vitamin E / Tocopherols



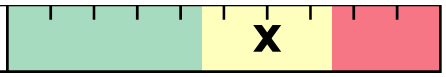
- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital, 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



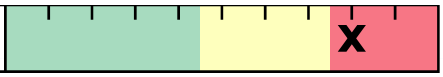
- Lipoic acid plays an important role in energy production, antioxidant activity (including the regeneration of vitamin C and glutathione), insulin signaling, cell signaling and the catabolism of α-keto acids and amino acids.
- High biotin intake can compete with lipoic acid for cell membrane entry.
- Optimal levels of lipoic acid may improve glucose utilization and protect against diabetic neuropathy, vascular disease and age-related cognitive decline.
- Main food sources include organ meats, spinach and broccoli. Lesser sources include tomato, peas, Brussels sprouts and brewer's yeast.

CoQ10



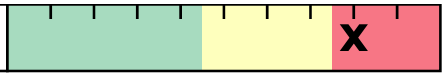
- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) 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) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.

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 nutriceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).

Key

- Function
- Causes of Deficiency
- Complications of Deficiency
- Food Sources

Interpretation At-A-Glance

Nutritional Needs

B-Vitamins

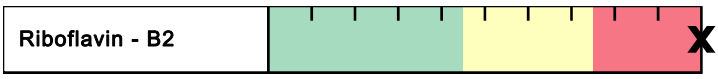
Thiamin - B1

- 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

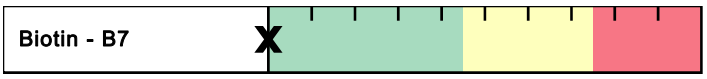
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or digoxin.
- B6 deficiency may result in neurologic symptoms (e.g., irritability, depression, seizures), oral inflammation, impaired immunity or increased homocysteine.
- Food sources include poultry, beef, beef liver, fish, whole grains, wheat germ, soybean, lentils, nuts & seeds, potato, spinach and carrots.

Riboflavin - B2



- 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 for enzymes involved in functions such as fatty acid (FA) synthesis, mitochondrial FA oxidation, gluconeogenesis, and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN use, anticonvulsants, high-dose B5, sulfa drugs & other antibiotics.
- Low levels may result in neurologic symptoms (e.g., paresthesias, depression), hair loss, scaly rash on face or genitals or impaired immunity.
- Food sources include yeast, whole grains, wheat germ, eggs, cheese, liver, meats, fish, wheat, nuts & seeds, avocado, raspberries, sweet potato and cauliflower.

Niacin - B3

- 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 key role in coenzymes involved in DNA and SAMe synthesis, methylation, nucleic acids & amino acid metabolism and RBC production.
- Low folate may result from alcoholism, high-dose NSAIDs, diabetic meds, H2 blockers, some diuretics and anti-convulsants, SSRIs, methotrexate, trimethoprim, pyrimethamine, triamterene, sulfasalazine or cholestyramine.
- Folate deficiency can result in anemia, fatigue, low methionine, increased homocysteine, impaired immunity, heart disease, birth defects and CA risk.
- Food sources include fortified grains, green vegetables, beans & legumes.

Cobalamin - B12

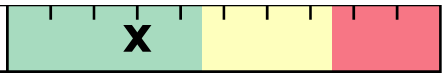
- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 blockers, PPIs), vegan diets, diabetic meds, cholestyramine, chloramphenicol, neomycin or colchicine.
- B12 deficiency can lead to anemia, fatigue, neurologic symptoms (e.g., paresthesias, memory loss, depression, dementia), methylation defects or chromosome breaks.
- Food sources include shellfish, red meat poultry, fish, eggs, milk and cheese.

Interpretation At-A-Glance

Nutritional Needs

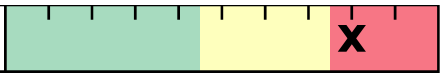
Minerals

Manganese



- 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

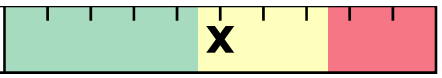


- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses 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

- 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).

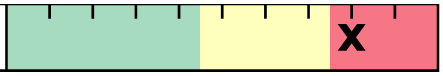
Zinc



- 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.

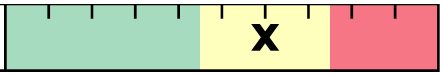
Digestive Support

Need for Probiotics



- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhancement of digestion & absorption; decreasing severity of diarrheal illness; modulation 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



- 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.

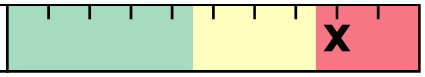
Interpretation At-A-Glance

Functional Imbalances

Mitochondrial Dysfunction

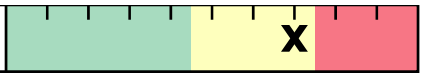
- Mitochondria are a primary site of generation of reactive oxygen species. Oxidative damage is considered an important factor in decline of physiologic function that occurs with aging and stress.
- Mitochondrial defects have been identified in cardiovascular disease, fatigue syndromes, neurologic disorders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

Toxic Exposure



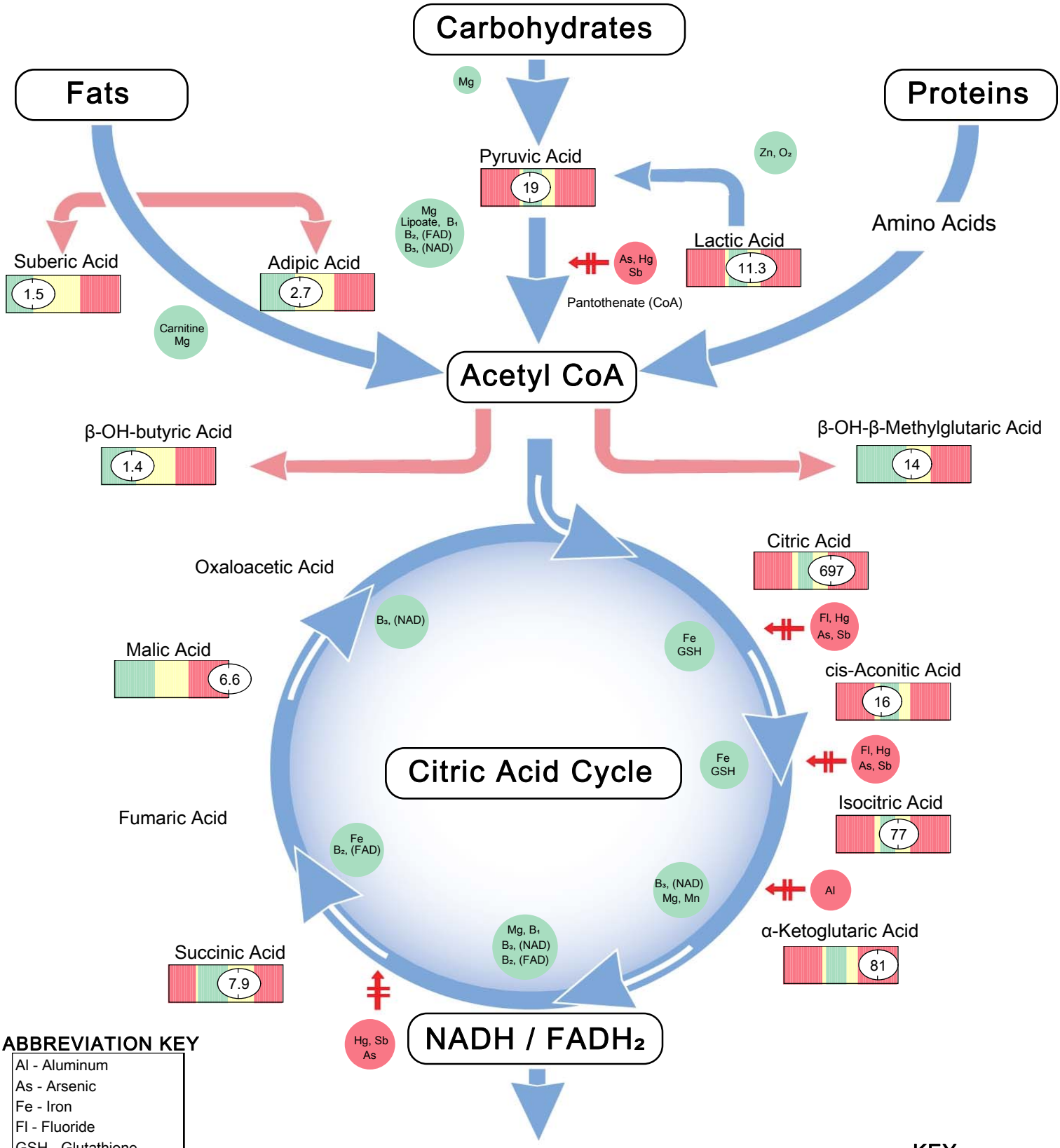
- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal 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.
- Levels of these toxic substances should be examined within the context of the body's functional capacity for methylation and need for glutathione.

Need for Methylation



- 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.

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

Metabolic Analysis Markers (Urine)

All biomarkers reported in mmol/mol creatinine unless otherwise noted.

Malabsorption and Dysbiosis Markers

Malabsorption Markers

		Reference Range
Indoleacetic Acid (IAA)	1.9	<= 4.2
Phenylacetic Acid (PAA)	0.11	<= 0.15

Bacterial Dysbiosis Markers

		Reference Range
Dihydroxyphenylpropionic Acid (DHPPA)	>14.8	<= 7.0
3-Hydroxyphenylacetic Acid	<dl	<= 9.2
4-Hydroxyphenylacetic Acid	18	<= 37
Benzoic Acid	0.21	<= 0.10
Hippuric Acid	369	<= 921

Yeast / Fungal Dysbiosis Markers

		Reference Range
Arabinose	120	<= 132
Citramalic Acid	7.6	<= 5.3
Tartaric Acid	19	<= 20

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism

		Reference Range
Lactic Acid	11.3	3.7-14.6
Pyruvic Acid	19	12-39
β-OH-Butyric Acid (BHBA)	1.4	<= 3.4

Energy Metabolism

		Reference Range
Citric Acid	697	62-648
Cis-Aconitic Acid	16	13-33
Isocitric Acid	77	38-97
α-Ketoglutaric Acid (AKG)	81	12-55
Succinic Acid	7.9	0.8-10.4
Malic Acid	6.6	<= 2.7
β-OH-β-Methylglutaric Acid (HMG)	14	<= 19

Fatty Acid Metabolism

		Reference Range
Adipic Acid	2.7	<= 5.0
Suberic Acid	1.5	<= 4.2

Creatinine Concentration

		Reference Range
Creatinine ◆	7.4	3.1-19.5 mmol/L

Methodology: GCMS, LC/MS/MS, Alkaline Picrate

Neurotransmitter Metabolites

		Reference Range
Vanilmandelic Acid	2.8	1.5-5.0
Homovanillic Acid	7.3	1.8-8.6
5-OH-indoleacetic Acid	21.5	6.4-24.3
3-Methyl-4-OH-phenylglycol	0.32	0.07-0.41
Kynurenic Acid	3.8	<= 9.2
Quinolinic Acid	4.5	<= 11.6
Kynurenic / Quinolinic Ratio	0.84	>= 0.46

Vitamin Markers

		Reference Range
α-Ketoadipic Acid	1.5	<= 2.1
α-Ketoisovaleric Acid	0.48	<= 0.85
α-Ketoisocaproic Acid	0.56	<= 0.91
α-Keto-β-Methylvaleric Acid	1.0	<= 2.3
Formiminoglutamic Acid (FIGlu)	0.4	<= 2.7
Glutaric Acid	1.14	<= 0.92
Isovalerylglycine	2.4	<= 5.4
Methylmalonic Acid	2.0	<= 2.2
Xanthurenic Acid	0.24	<= 1.07
3-Hydroxypropionic Acid	10	6-23
3-Hydroxyisovaleric Acid	19	<= 38

Toxin & Detoxification Markers

		Reference Range
α-Ketophenylacetic Acid (from Styrene)	0.53	<= 0.50
α-Hydroxyisobutyric Acid (from MTBE)	13.8	<= 8.7
Orotic Acid	0.74	0.38-0.91
Pyroglutamic Acid	47	22-64

Tyrosine Metabolism

		Reference Range
Homogentisic Acid	27	<= 33
2-Hydroxyphenylacetic Acid	0.77	<= 0.99

Metabolic Analysis Reference Ranges are Age Specific

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

Amino Acids (Urine FMV)

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

Nutritionally Essential Amino Acids

Amino Acid		Reference Range
Arginine	29	8-59
Histidine	1,346	218-2,114
Isoleucine	18	10-44
Leucine	40	26-109
Lysine	138	25-320
Methionine	17	7-39
Phenylalanine	85	33-188
Taurine	1,141	80-1,560
Threonine	175	31-246
Tryptophan	67	24-113
Valine	58	26-88

Nonessential Protein Amino Acids

Amino Acid		Reference Range
Alanine	460	78-560
Asparagine	223	44-360
Aspartic Acid	56	<= 19
Cysteine (FMV urine)	38	12-98
Cystine (FMV Urine)	60	27-148
γ-Aminobutyric Acid	5	<= 5
Glutamic Acid	20	10-36
Glutamine	724	162-1,290
Proline	10	3-24
Tyrosine	153	61-410

Creatinine Concentration

		Reference Range
Creatinine ◆	6.1	3.1-19.5 mmol/L

Amino Acid reference ranges are age specific.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assays have not been cleared by the U.S. Food and Drug Administration.

Methodology: LC/MS/MS, Alkaline Picrate

Intermediary Metabolites

B Vitamin Markers		Reference Range
α-Aminoadipic	26	13-87
α-Amino-N-butyric Acid	20	6-49
β-Aminoisobutyric Acid	213	5-284
Cystathionine	43	4-106
3-Methylhistidine	141	75-456

Urea Cycle Markers

Citrulline	4.7	0.6-8.5
Ornithine	16	5-21
Urea ◆	272	196-711 mmol/g creatinine

Glycine/Serine Metabolites

Glycine	236	118-907
Serine	373	61-295
Ethanolamine	300	74-286
Phosphoethanolamine	10	4-27
Phosphoserine	7	3-23
Sarcosine	1.2	<= 0.9

Dietary Peptide Related Markers

		Reference Range
Anserine (dipeptide)	42.9	1.0-268.1
Carnosine (dipeptide)	118	7-318
1-Methylhistidine	280	28-1,985
β-Alanine	4	<= 29

Oxidative Stress Markers

Oxidative Stress Markers

Reference Range

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

Lipid Peroxides (urine)	11.3	<=10.0 micromol/g Creat.
8-OHdG (urine)	12	<=15 mcg/g Creat.

Lab Comments

Please note the reference range for 8-OHdG (urine) has been updated.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assay has not been cleared by the U.S. Food and Drug Administration.

Metabolic Analysis Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

2,3 Dihydroxyphenylpropionic acid (DHPPA) is elevated. This organic acid is a byproduct of the bacterial metabolism of phenylalanine, tyrosine, and/or tryptophan. Research has identified various species of Clostridia in the *in-vitro* production of this compound. Other research on quinoline demonstrates production of DHPPA by Pseudomonas species. Presence of elevated levels of DHPPA in the urine may thus suggest overgrowth of Clostridia and/or Pseudomonas, as well as a degree of malabsorption of aromatic amino acids. A comprehensive stool analysis is suggested.

Benzoic acid is a common food component, especially in fruits and in particular berries/cranberries. It is also a common food additive/preservative. Benzoic acid is also formed by gut microflora metabolism of phenylalanine and dietary polyphenols. Elevated levels may thus reflect dietary intake (for example strawberries), imbalanced gut flora or a high intake of polyphenols or phenylalanine. Older studies note a relationship between decreased cognitive function and increased BA in the urine.

Citramalic Acid is elevated. With a chemical structure very similar to that of malic acid, citramalate may cause metabolic interference with malate. This is of concern because malic acid has extra-mitochondrial functions, as with the "malate shuttle" for carrying reducing equivalents (protons) into the mitochondria. While the metabolic interference aspect is uncertain, the presence of citramalate in the urine indicates intestinal dysbiosis. Not formed in human tissues, citramalate may be formed by anaerobic bacteria such as clostridia, as well as by yeast/fungi. A stool analysis with bacteriology or microbiology is suggested.

Citric Acid , or citrate, is measured to be high. Citric acid is a key component of the citric acid cycle and is formed inside the mitochondria from acetyl coenzyme A and oxaloacetic acid.

Citric acid is essential in the production of bicarbonate, a compound that helps to maintain proper pH in the body. Elevated urinary citrate may be a sign of a metabolic pH imbalance (metabolic acidosis), possibly due to damaged proximal tubular function in the kidney that results in urinary wasting of citrate. Another possible cause of elevated urine citrate is pancreatic dysfunction, as bicarbonate production would be reduced, leading to less utilization of citric acid. In this situation, cis-aconitic and isocitric acids may be also elevated.

However, if cis-aconitic or isocitric acids are low, this may be indicative of impaired enzymatic conversion within the citric acid cycle. The enzyme cis-aconitase converts citric acid into cis-aconitic acid. This enzyme requires the presence of a sulfhydryl (-SH) group from cysteine or glutathione and it is activated by ferrous iron (Fe+2). Deficiencies of methionine, cysteine, glutathione, or iron, would result in sub-optimal enzyme efficiency. In addition, toxic elements with high sulfur affinity, like arsenic, antimony and mercury, may impair cis-aconitase activity. Also, xenobiotic toxicity, if it depletes glutathione, or increased oxidative stress from any cause may lead to elevated citrate. Excess fluorine can combine with acetate and, as fluoroacetate, can also inhibit the cis-aconitase enzyme. Any of the above situations may result in increased urinary citrate.

Alpha-ketoglutaric Acid (alpha-ketoglutarate or AKG) is measured to be elevated. Alpha-ketoglutaric acid is formed from isocitrate or from the deamination or transamination of glutamate (a process requiring vitamin B6). Metabolism of alpha-ketoglutaric acid then leads to the formation of succinyl CoA.

Elevated alpha-ketoglutaric acid can be due to specific weakness in the alpha-ketoglutaric acid dehydrogenase

Commentary

complex that converts alpha-ketoglutarate to is downstream citric acid cycle metabolite, succinic acid. Dehydrogenase enzymes require vitamin B1 as thiamin pyrophosphate, vitamin B2 as FAD, vitamin B3 as NAD, and lipoic acid. Phosphorylation requiring magnesium is also involved, and coenzyme A is needed. Coenzyme A is formed from the nutrients pantothenic acid, cysteine, and magnesium, and requires phosphorylation and energy from CTP and ATP. Insufficiencies of these nutrients or cofactors may cause elevated alpha-ketoglutaric acid. Arsenic can also inhibit the dehydrogenase enzyme.

Elevated alpha-ketoglutaric acid also may be accompanied by elevated glyoxylate and oxalate. If there is weakness in the decarboxylation of glyoxylate and alpha-ketoglutarate, renal stone (calcium oxalate) formation is possible. This is not a common condition, and its diagnosis should be made from urine levels of oxalate and glyoxylate. In this case, supplements of vitamin B6 or pyridoxal 5-phosphate may be beneficial. (B6 aids the transformation of glyoxylate to glycine and thus decreases oxalate formation.)

Moderate increase in urinary alpha-ketoglutaric acid may occur, without clinical significance, with low-carbohydrate or high-protein diets (where metabolic need is increased).

Malic Acid (malate) is measured to be elevated. An important intermediate of the citric acid cycle in cell mitochondria, malic acid or malate is formed from fumaric acid (fumarate), and it becomes oxaloacetic acid. Malic acid also participates in the malate-aspartate shuttle, a cellular process in which malate and a proton (H+) can enter the mitochondrion from the cytosol. This brings a chemical reducing equivalent, H+, inside the mitochondrial membrane. This is the mechanism whereby the NADH produced in glycolysis can enter the mitochondria to participate in oxidative phosphorylation.

Malic acid can be elevated if its dehydrogenation to oxaloacetic acid is reduced; this dehydrogenase enzyme requires vitamin B3 as NAD. Malate can also be high if oxaloacetic acid is high. Use of D-malic acid (or D,L-malate) as a nutritional supplement, instead of L-malic acid will also cause elevated urine levels, since this compound will interfere with its metabolism. Only L-malic acid can be utilized properly.

Impairments in pyruvate metabolism with elevated pyruvate and lactate usually result in elevated malate, as well. (Refer to commentary for these analytes.)

Glutaric Acid is measured to be high. This organic acid is formed from the essential amino acids lysine (primarily) and tryptophan, via alpha ketoadipic acid (AKAA) and glutaryl-CoA. Glutaric acid is elevated when glutaryl CoA metabolism is impaired, such as when needed nutrient cofactors are missing. Glutaryl-CoA is dehydrogenated to form glutaconyl-CoA and then crotonyl-CoA using a FAD-dependent dehydrogenase enzyme; the FAD (from riboflavin) becomes FADH2.

Glutaric aciduria may have negligible manifestations if mild, but if the dehydrogenase is notably weak, then severe symptoms can be experienced beginning in infancy and childhood with general neurological deterioration, spasticity and mental retardation. Glutaric acid can be very elevated in the rare case of multiple acyl-CoA dehydrogenase dysfunction. The resulting glutaric aciduria type II can lead to metabolic acidosis, hypoglycemia, hypotonia, nausea and diarrhea, and frequently the individual has a "sweaty feet" or foul odor. Poor weight gain and frequent regurgitation of food are seen in children. In glutaric aciduria type II, adipic, lactic, and beta-hydroxybutyric (BHBA) acids are also elevated. This more general enzyme impairment is postulated to be a weakness in mitochondrial electron transfer. Glutaric acid excess may or may not be helped by supplementation of riboflavin, mitochondrial support nutrients, or CoQ10.

Alpha hydroxyisobutyric acid (2-HIBA): This compound is a major urinary metabolite of the gasoline additive MTBE (methyl-tert-butyl ether). It is a potential toxicant for refinery workers, gasoline handlers and in water supplies

Commentary

where underground tanks have leaked into the groundwater aquifers. The elimination half-life of 2-HIBA varies from 7-18 hours at low levels of exposure. Reputed health effects of MTBE exposure include nephropathy, neoplasms and potential for genetic damage. MTBE has been controversially designated as "non-carcinogenic" by the National Toxicology Program.

Alpha keto-phenylacetic acid (phenylglyoxylic acid/PGA) is high. Alpha keto-phenylacetic acid [also known as phynelglyoxylic acid or PGA] is a major urinary metabolite of styrene, toluene, xylenes and ethylbenzene. PGA is a proven means to monitor exposure of workers using these solvents, particularly common in varnishing and reinforced fiberglass industries. Clinical signs of such exposure include diminished threshold for vibratory sense and impaired visual contrast sensitivity.&bnsp; Glutathione-processing deficient individuals exposed to these solvents are likely to have higher quantities of excreted PGA. PGA is a dependable biomarker which, if elevated, likely indicates exposure to solvent compounds with significant health risks.

Amino Acid Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

Ethanolamine is an intermediary metabolite of the serine-to-choline sequence. Ethanolamine is elevated in the urine. Two possibilities should be considered: excess microbial production of ethanolamine in the intestines and rate-limited formation of phosphoethanolamine from ethanolamine. A stool analysis can be used to rule out or confirm intestinal dysbiosis.

Formation of phosphoethanolamine from ethanolamine is a magnesium-dependent phosphorylation.

Magnesium deficiency is frequently observed to coincide with elevated ethanolamine and normal or reduced levels of phosphoethanolamine. Other possibilities involve impaired phosphorylation for reasons such as excessive body burden of aluminum or cell mitochondrial damage or dysfunction.

Elevated **serine** is measured; **glycine** is within normal limits. Metabolic disorders of genetic origin affecting only serine are not documented. Mildly elevated serine can be a sign of vitamin B6 insufficiency or pyridoxal 5-phosphate coenzyme dysfunction.

Sarcosine , or N-methylglycine, is an intermediate of the choline-to-serine catabolism sequence. It is formed by oxidative demethylation of dimethylglycine and it is then catabolized by further demethylation. Sarcosine is elevated in this individual's urine which suggests three possibilities.

1. Recent dietary supplementation of dimethylglycine, "DMG".
2. Deficiencies of the cofactors associated with sarcosine catabolism. These are folic acid as tetrahydrofolate, THF, and Vitamin B2, riboflavin, bound to the sarcosine dehydrogenase enzyme as FAD. The methyl group fragment removed from sarcosine is at the oxidative level of CHO and can form formaldehyde if tetrahydrofolate is insufficient. This would slow down sarcosine's catabolism while making it somewhat toxic.
3. Genetic weakness in sarcosine dehydrogenase with metabolic hypersarcosinuria and possibly hypersarcosinemia. Hereditary (severe) hypersarcosinuria is rare with an incidence of less than 1 in 40,000 newborns.

Unpublished clinical observations associate some cases of acquired, mild sarcosinuria (below 500 micromoles/24 hour) with past exposures to organic chemical solvent and petrochemicals. At such levels sarcosine itself is not known to be toxic. However, folic acid supplementation is suggested whenever sarcosine is elevated.

Oxidative Stress Commentary

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

Oxidation of DNA is caused by chemical exposure, inflammation, irradiation, iron overload, smoking. Accumulation of 8-OHdG occurs in chronic inflammatory states. Consider Vitamins A, C & E, beta carotene. Botanicals that reduce 8-OHdG include curcumin, grape seed, green tea. GSH, NAC and omega-3 fatty acid also help repair damaged DNA.