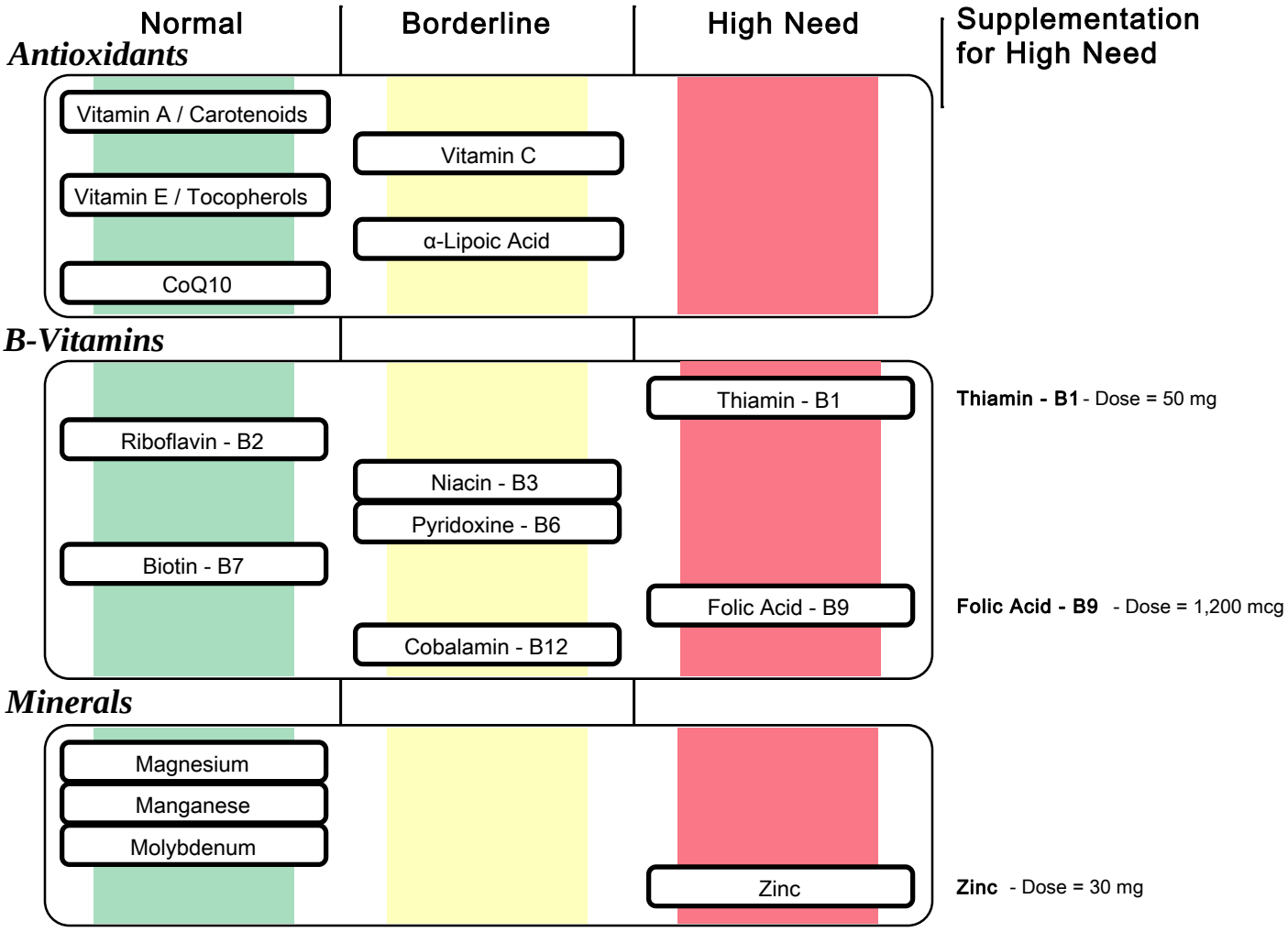
GENOVA DIAGNOSTICS

63 Zillicoa Street
Asheville, NC 28801

NutrEval™ Plasma amino acids

NutrEval Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	3,000 IU	3,000 IU	
Vitamin C	90 mg	500 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		100 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.2 mg	50 mg	
Riboflavin - B2	1.3 mg	10 mg	
Niacin - B3	16 mg	30 mg	
Pyridoxine - B6	1.3 mg	25 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	420 mg	400 mg	
Manganese	2.3 mg	3.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	11 mg	30 mg	
Essential Fatty Acids			
Omega-3 Oils	500 mg	500 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	0	Threonine	0
Histidine	0	Tryptophan	23
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

NutrEval® Plasma amino acids

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.

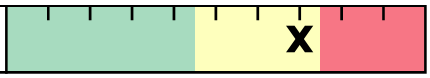
Vitamin C

- 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

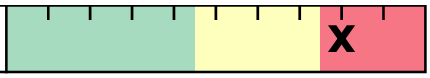


- α-Lipoic acid plays an important role in energy production, antioxidant activity (including the regeneration of vitamin C and glutathione), insulin signaling, cell signaling and the catabolism of α-keto acids and amino acids.
- High biotin intake can compete with lipoic acid for cell membrane entry.
- Optimal levels of α-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

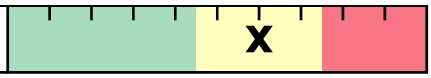
- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) 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 nutraceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).

Key

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

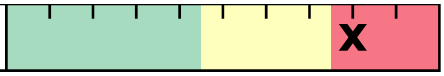
NutrEval Plasma amino acids

Interpretation At-A-Glance

Nutritional Needs

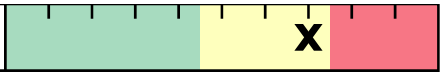
B-Vitamins

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

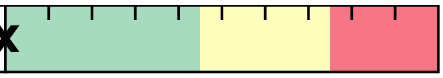


- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or 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

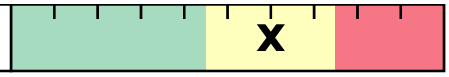
- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.
- 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



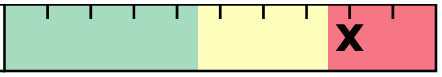
- Biotin is a cofactor for enzymes involved in functions such as fatty acid synthesis, mitochondrial FA oxidation, gluconeogenesis and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN, anticonvulsants, high-dose B5, sulfa 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.

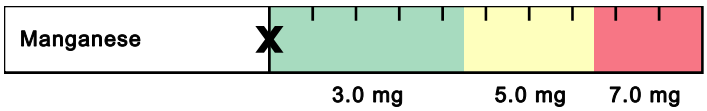
Cobalamin - B12

- 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.

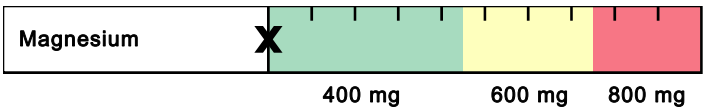
NutrEval Plasma amino acids — Interpretation At-A-Glance

Nutritional Needs

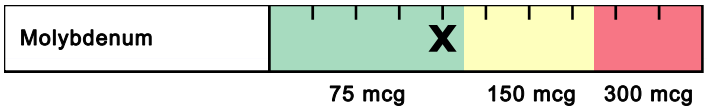
Minerals



- 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.



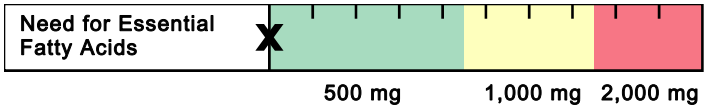
- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses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

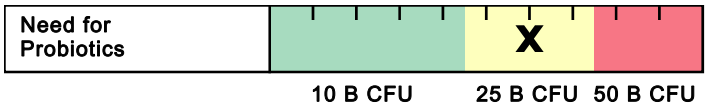
- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency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

Essential Fatty Acids

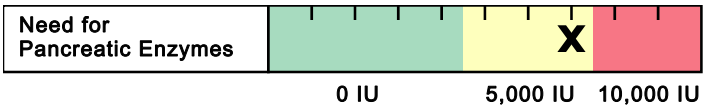


- Omega-3 (O3) and Omega-6 (O6) fatty acids are polyunsaturated fatty acids that cannot be synthesized by the human body. They are classified as essential nutrients and must be obtained from dietary sources.
- The standard American diet is much higher in O6 than O3 fatty acids. Deficiency of EFAs may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

Digestive Support



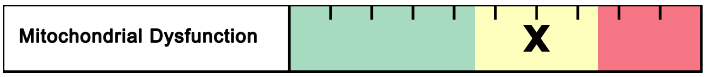
- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhance digestion & absorption; decrease severity of diarrheal illness; modulate of immune function & intestinal permeability.
- Alterations of gastrointestinal microflora may result from C-section delivery,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



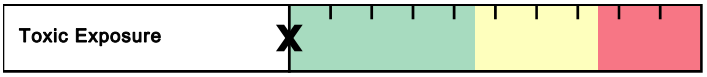
- Pancreatic enzymes are secreted by the exocrine glands of the pancreas and include protease/peptidase, lipase and amylase.
- Pancreatic exocrine insufficiency may be primary or secondary in nature. Any indication of insufficiency warrants further evaluation for underlying cause (i.e., celiac disease, 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

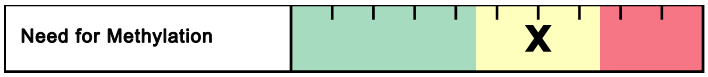
Functional Imbalances



- 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.

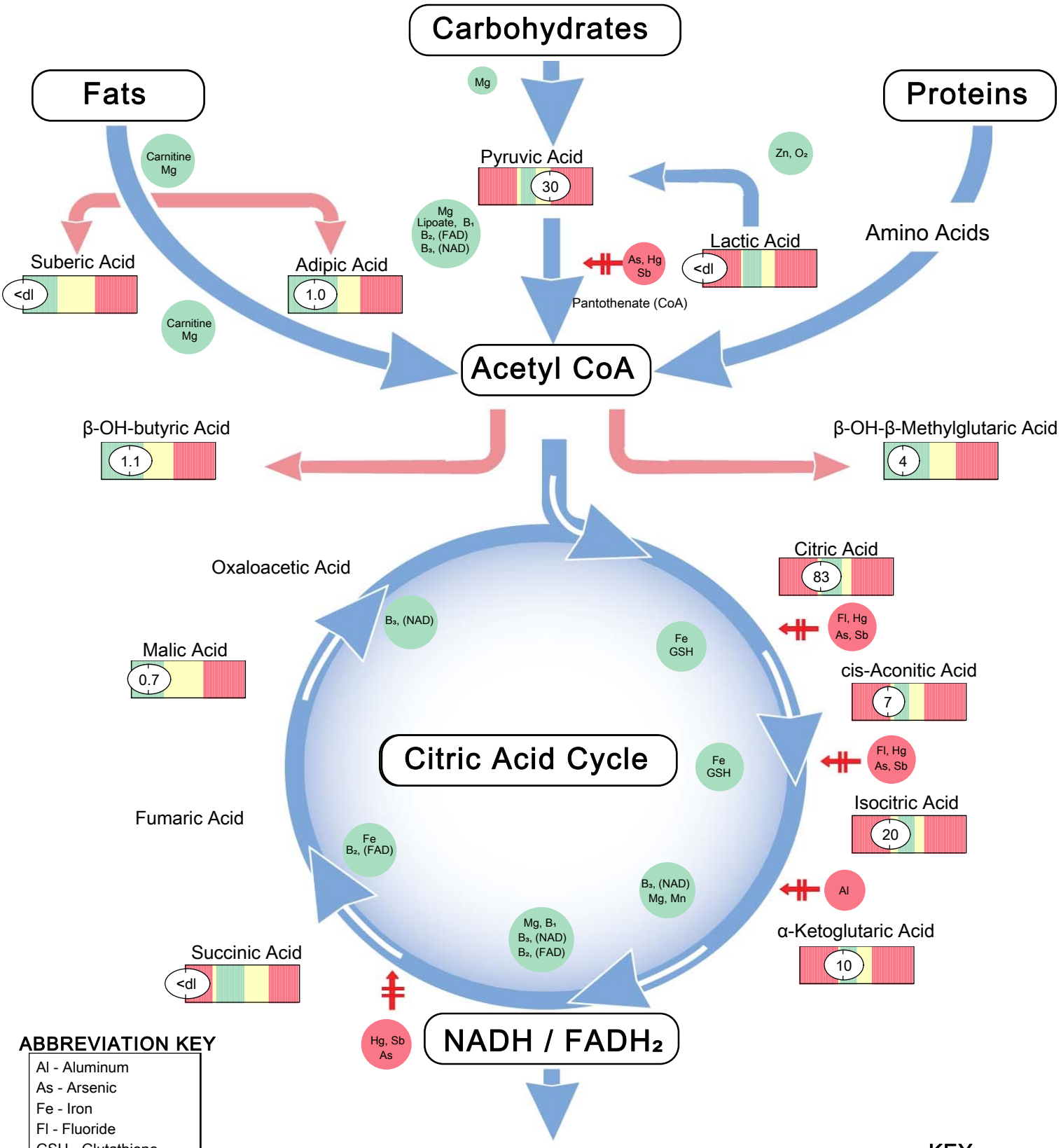


- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal 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.



- 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

Electron Transport and Oxidative Phosphorylation

$(2)\ H + 1/2\ O_2 \rightarrow H_2O$

KEY

Green = cofactor

Red = inhibitor

Metabolic Analysis Markers

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

Malabsorption and Dysbiosis Markers

Malabsorption Markers

	Reference Range
Indoleacetic Acid (IAA) 1.7	<= 4.2
Phenylacetic Acid (PAA) 0.20	<= 0.12

Bacterial Dysbiosis Markers

	Reference Range
Dihydroxyphenylpropionic Acid (DHPPA) 0.3	<= 5.3
3-Hydroxyphenylacetic Acid 2.4	<= 8.1
4-Hydroxyphenylacetic Acid 24	<= 29
Benzoic Acid 0.10	<= 0.05
Hippuric Acid <dl	<= 603

Yeast / Fungal Dysbiosis Markers

	Reference Range
Arabinose 15	<= 96
Citramalic Acid 1.8	<= 5.8
Tartaric Acid <dl	<= 15

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism

	Reference Range
Lactic Acid <dl	1.9-19.8
Pyruvic Acid 30	7-32
β-OH-Butyric Acid (BHBA) 1.1	<= 2.8

Energy Metabolism

	Reference Range
Citric Acid 83	40-520
Cis-Aconitic Acid 7	10-36
Isocitric Acid 20	22-65
α-Ketoglutaric Acid (AKG) 10	4-52
Succinic Acid <dl	0.4-4.6
Malic Acid 0.7	<= 3.0
β-OH-β-Methylglutaric Acid (HMG) 4	<= 15

Fatty Acid Metabolism

	Reference Range
Adipic Acid 1.0	<= 2.8
Suberic Acid <dl	<= 2.1

Creatinine Concentration

	Reference Range
Creatinine ◆ 10.6	3.1-19.5 mmol/L

Neurotransmitter Metabolites

	Reference Range
Vanilmandelic Acid 1.3	0.4-3.6
Homovanillic Acid 1.9	1.2-5.3
5-OH-indoleacetic Acid 7.0	3.8-12.1
3-Methyl-4-OH-phenylglycol 0.14	0.02-0.22
Kynurenic Acid 6.1	<= 7.1
Quinolinic Acid 4.4	<= 9.1
Kynurenic / Quinolinic Ratio 1.39	>= 0.44

Vitamin Markers

	Reference Range
α-Ketoadipic Acid 0.7	<= 1.7
α-Ketoisovaleric Acid 0.67	<= 0.97
α-Ketoisocaproic Acid 0.75	<= 0.89
α-Keto-β-Methylvaleric Acid 2.4	<= 2.1
Formiminoglutamic Acid (FIGlu) 1.7	<= 1.5
Glutaric Acid 0.19	<= 0.51
Isovalerylglycine 1.6	<= 3.7
Methylmalonic Acid 0.7	<= 1.9
Xanthurenic Acid 0.75	<= 0.96
3-Hydroxypropionic Acid 9	5-22
3-Hydroxyisovaleric Acid 16	<= 29

Toxin & Detoxification Markers

	Reference Range
α-Ketophenylacetic Acid (from Styrene) 0.27	<= 0.46
α-Hydroxyisobutyric Acid (from MTBE) 2.7	<= 6.7
Orotic Acid 0.74	0.33-1.01
Pyroglutamic Acid 15	16-34

Tyrosine Metabolism

	Reference Range
Homogentisic Acid 6	<= 19
2-Hydroxyphenylacetic Acid 0.57	<= 0.76

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 (Plasma)

All biomarkers reported in micromoles per deciliter unless stated otherwise.

Nutritionally Essential Amino Acids

Amino Acid		Reference Range
Arginine	11.1	7.5-13.0
Histidine	10.8	7.9-12.1
Isoleucine	8.03	5.40-10.50
Leucine	14.1	10.5-18.0
Lysine	27.6	15.5-27.5
Methionine	3.3	2.5-4.9
Phenylalanine	6.14	4.60-7.90
Taurine	10.40	5.25-9.00
Threonine	17.29	6.40-14.00
Tryptophan	3.67	3.30-6.50
Valine	26.4	19.0-36.0

Nonessential Protein Amino Acids

Amino Acid		Reference Range
Alanine	33	26-55
Asparagine	6.1	4.0-7.2
Aspartic Acid	0.45	0.20-0.60
Cyst(e)ine	7.3	4.9-8.0
γ-Aminobutyric Acid	<dl	<= 0.02
Glutamic Acid	3.2	0.5-7.0
Glutamine	61	50-70
Proline	16	10-32
Tyrosine	6.9	5.1-10.0

Markers for Plasma Representativeness

		Reference Range
Glutamine/Glutamate	18.90	>= 8.00
Ammonia	2.7	<= 6.5
Asparagine/Aspartate	13.49	>= 6.00

Plasma Representativeness Index	10	Ref Range 5 – 10

Intermediary Metabolites

B Vitamin Markers		Reference Range
α-Aminoadipic Acid	0.51	<= 0.80
α-Amino-N-butyric Acid	2.90	1.25-3.50
β-Aminoisobutyric Acid	<dl	<= 0.30
Cystathionine	<dl	<= 0.03
3-Methylhistidine	0.69	<= 0.75

Urea Cycle Markers		
Ammonia	2.7	<= 6.5
Citrulline	3.3	2.8-5.6
Ornithine	8.89	4.25-11.50
Urea	575	320-970

Glycine/Serine Metabolites		
Glycine	23	19-43
Serine	9.9	8.0-15.5
Ethanolamine	0.37	0.50-1.20
Phosphoethanolamine	0.28	0.15-0.45
Phosphoserine	0.32	0.31-0.74
Sarcosine	<dl	<= 0.15

Dietary Peptide Related Markers

		Reference Range
1-Methylhistidine	4.98	<= 1.65
β-Alanine	0.3	<= 0.4

Amino Acid Reference Ranges are Age Specific

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

Essential and Metabolic Fatty Acids Markers (RBCs)

Omega 3 Fatty Acids

Analyte	(cold water fish, flax, walnut)	Reference Range
α-Linolenic (ALA) 18:3 n3	0.12	>= 0.09 wt %
Eicosapentaenoic (EPA) 20:5 n3	3.17	>= 0.16 wt %
Docosapentaenoic (DPA) 22:5 n3	3.52	>= 1.14 wt %
Docosahexaenoic (DHA) 22:6 n3	7.1	>= 2.1 wt %
% Omega 3s	13.9	>= 3.8

Omega 9 Fatty Acids

Analyte	(olive oil)	Reference Range
Oleic 18:1 n9	12	10-13 wt %
Nervonic 24:1 n9	2.6	2.1-3.5 wt %
% Omega 9s	14.3	13.3-16.6

Saturated Fatty Acids

Analyte	(meat, dairy, coconuts, palm oils)	Reference Range
Palmitic C16:0	21	18-23 wt %
Stearic C18:0	17	14-17 wt %
Arachidic C20:0	0.22	0.22-0.35 wt %
Behenic C22:0	0.82	0.92-1.68 wt %
Tricosanoic C23:0	0.25	0.12-0.18 wt %
Lignoceric C24:0	2.6	2.1-3.8 wt %
Pentadecanoic C15:0	0.13	0.07-0.15 wt %
Margaric C17:0	0.28	0.22-0.37 wt %
% Saturated Fats	42.3	39.8-43.6

Omega 6 Fatty Acids

Analyte	(vegetable oil, grains, most meats, dairy)	Reference Range
Linoleic (LA) 18:2 n6	10.9	10.5-16.9 wt %
γ-Linolenic (GLA) 18:3 n6	0.06	0.03-0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3 n6	1.65	>= 1.19 wt %
Arachidonic (AA) 20:4 n6	14	15-21 wt %
Docosatetraenoic (DTA) 22:4 n6	1.19	1.50-4.20 wt %
Eicosadienoic 20:2 n6	0.32	<= 0.26 wt %
% Omega 6s	27.9	30.5-39.7

Monounsaturated Fats

Omega 7 Fats		Reference Range
Palmitoleic 16:1 n7	0.27	<= 0.64 wt %
Vaccenic 18:1 n7	0.92	<= 1.13 wt %
Trans Fat		
Elaidic 18:1 n9t	0.31	<= 0.59 wt %

Delta - 6 Desaturase Activity

	Upregulated Functional Impaired	
Linoleic / DGLA 18:2 n6 / 20:3 n6	6.6	6.0-12.3

Cardiovascular Risk

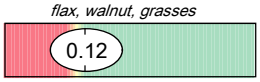
Analyte		Reference Range
Omega 6s / Omega 3s	2.0	3.4-10.7
AA / EPA 20:4 n6 / 20:5 n3	4	12-125
Omega 3 Index	10.3	>= 4.0

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

Essential Fatty Acid Metabolism

Omega 3 Family

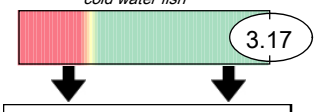
α-Linolenic Acid
flax, walnut, grasses



Stearidonic acid

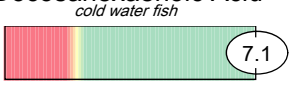
Eicosatetraenoic acid, ETA

Eicosapentaenoic Acid
cold water fish



Docosapentaenoic Acid

Docosahexaenoic Acid
cold water fish



Delta-6 Desaturase
Vitamin and Mineral Cofactors:
FAD (B2), Niacin (B3)
Pyridoxal-5-phosphate (B6)
Vitamin C, Insulin, Zn, Mg

Elongase
Vitamin and Mineral Cofactors:
Niacin (B3)
Pyridoxal-5-phosphate (B6)
Pantothenic Acid (B5)
Biotin, Vitamin C

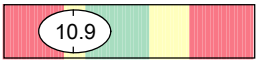
Delta-5 Desaturase
Vitamin and Mineral Cofactors:
FAD (B2), Niacin (B3)
Pyridoxal-5-phosphate (B6)
Vitamin C, Insulin, Zn, Mg

Elongase
Vitamin and Mineral Cofactors:
Niacin (B3)
Pyridoxal-5-phosphate (B6), Biotin
Pantothenic Acid (B5), Vitamin C

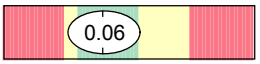
Elongase
Delta-6 Desaturase
Vitamin and Mineral Cofactors:
FAD (B2), Niacin (B3)
Pyridoxal-5-phosphate (B6), Biotin
Vitamin C, Zn, Mg, Carnitine
Pantothenic Acid (B5)

Omega 6 Family

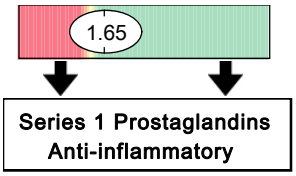
Linoleic Acid
grains, vegetable oils



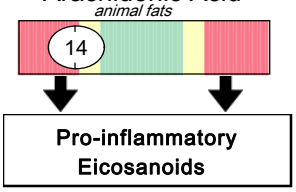
γ-Linolenic Acid
evening primrose, borage, black currant



Dihomo-γ-Linolenic Acid



Arachidonic Acid
animal fats



Docosatetraenoic Acid

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

Oxidative Stress Markers

Oxidative Stress Markers

		Reference Range
Glutathione (whole blood)	939	>=669 micromol/L
Lipid Peroxides (urine)	5.4	<=10.0 micromol/g Creat.
8-OHdG (urine)	4	<=16 mcg/g Creat.
Coenzyme Q10, Ubiquinone (plasma)	1.06	0.46-1.72 mcg/mL

The Oxidative Stress reference ranges are based on an adult population.

Elemental Markers (RBCs)

Nutrient Elements

Element	Reference Range	Reference Range
Copper	0.571	0.466-0.721 mcg/g
Magnesium	40.3	30.1-56.5 mcg/g
Manganese	0.012	0.007-0.038 mcg/g
Potassium	2,418	2,220-3,626 mcg/g
Selenium	0.41	0.25-0.76 mcg/g
Zinc	7.2	7.8-13.1 mcg/g

Toxic Elements

Element	Reference Range	Reference Range
Lead	0.047	<= 0.048 mcg/g
Mercury	<dl	<= 0.0039 mcg/g
Antimony	0.001	<= 0.002 mcg/g
Arsenic	0.012	<= 0.071 mcg/g
Cadmium	0.000	<= 0.001 mcg/g
Tin	<dl	<= 0.0009 mcg/g

The Elemental reference ranges are based on an adult population.

Lab Comments

Lab Comments

***Requisition/Sample labeling discrepancy noted. Ordering physician has been contacted and authorizes testing to be performed. 12/01/2014 EA2*

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.

Commentary

Phenylacetic Acid (PAA) is elevated. If the essential amino acid phenylalanine is not sufficiently digested and absorbed in the small intestine, it is carried to the large bowel where anaerobic bacteria convert it to phenylethylamine. This is then absorbed, and in body tissues such as the liver, it is converted by deamination to PAA, which is excreted in the urine. Some species of Clostridia can produce PAA directly from aromatic amino acids. Its presence at elevated levels indicates one or more of the following: gastric hypochlorhydria or pepsin inactivity, impaired digestive peptidase function in the small intestine, rate-limited or insufficient absorption or mucosal transport in the small intestine, abnormal intestinal motility (partly regulated by cholecystokinin and secretin), or presence of colonic or other bacteria in the small intestine (dysbiosis).

Additionally, some elevation of PAA may occur in the uncommon instances of phenylketonuria and with Type I tyrosinemia (tyrosinosis). With phenylketonuria, 2-hydroxyphenylacetate (2-HPAA) would be significantly elevated. An amino acid analysis also is helpful in diagnosing such conditions.

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.

Lactic Acid , or lactate, is measured to be low. Lactate is formed from pyruvate in anaerobic or oxygen starved (hypoxic) circumstances to allow for ongoing production of ATP in these anaerobic conditions. There are no known clinical problems associated with low lactic acid. Low levels are usually a result of reduced amounts of its precursor, pyruvic acid.

Cis-aconitic Acid (CAA) is measured to be subnormal, while its precursor, citric acid is not deficient. This may occur with low carbohydrate diets, fasting or anorexic conditions; citric acid may then be only marginal. On the other hand, normal or elevated citric acid with low cis-aconitic acid may be the result of urinary citrate wasting (leading to deficiency) or of weakness in the enzyme that transforms citrate into cis-aconitate. This enzyme (aconitase) requires cysteine or glutathione in the reduced state and ferrous iron (Fe+2). Oxidant stress can inhibit aconitase as can toxic elements that bind to sulfhydryl groups (mercury, arsenic, antimony). Fluorine or fluoride that forms fluorocitrate is also a very potent inhibitor of aconitase.

Isocitric Acid is measured to be subnormal. This may be due to deficient or low-normal levels of its precursors, cis-aconitate or citrate. It may also be due to depleted alpha-ketoglutarate, which it forms in the citric acid cycle; check for low alpha-ketoglutarate in this report. The same enzyme, aconitase, forms cis-aconitic acid and isocitric acid, and requires reduced cysteine or glutathione and ferrous iron (Fe+2). Oxidant stress can inhibit it, as can arsenic, mercury or antimony. Fluoride that becomes fluorocitrate can strongly inhibit aconitase and impair formation of isocitrate.

Succinic acid participates in the citric acid cycle, acting to donate electrons to the mitochondrial electron transport and leading to formation of fumaric acid. Common in foods such as cantaloupe, it is also a food additive, providing flow-altering effects and a tart flavor. It appears that lacto-ovo vegetarians may show decreased levels in the urine and chronic fatigue patients may also show low levels, although studies on this topic are mixed. Low levels may also be an indicator of B12 or folate deficiency.

Alpha-keto-beta-methylvaleric Acid (AKBM) is measured to be elevated. AKBM comes from the essential amino acid isoleucine via transamination. Moderate elevations of AKBM usually mean that AKBM's further

Commentary

metabolism to the compound, alpha-methylbutyryl-CoA, is impaired either by coenzyme/cofactor insufficiency or by (genetic) weakness in the enzyme complex. The dehydrogenase enzyme complex that accomplishes this requires lipoic acid, vitamin B1 as thiamin pyrophosphate and vitamin B2 as FAD. Vitamin B3 as NAD is a necessary cofactor, which removes hydrogen to become NADH. The other necessary cofactor is coenzyme A, requiring pantothenic acid, cysteine, and magnesium. Elevated levels of AKBM may indicate low levels of any of these nutrients.

The toxic elements arsenic, antimony, mercury and cadmium may also weaken lipoic acid and dehydrogenase activity. Very high elevation of AKBM and its sister keto acids (alpha-ketoisovaleric, alpha-ketoisocaproic) constitute a rare disorder called "maple syrup urine disease". When AKBM is elevated, isoleucine may also be elevated per urine or plasma amino acid analysis.

Formiminoglutamic Acid "FIGlu" is elevated in the urine. FIGlu stands for formiminoglutamic acid, a substance produced in body tissue from the dietary amino acid histidine. FIGlu needs tetrahydrofolate (THF), a reduced form of folic acid, to be changed into forms that are metabolically useful.

Elevated urine FIGlu can occur with several circumstances. Dietary deficiency of folic acid or severe oxidant stress that limits biologic reduction of folic acid to the THF form can cause this elevation. Histidine as a supplemented nutrient can contribute to urine FIGlu levels, especially if taken in amounts that exceed 50 mg/Kg body weight. Metabolism of folic acid can be impaired if vitamin B12 is insufficient or if its metabolism is disordered. So, elevated FIGlu also can mean that some form of B12 or cobalamin is needed. The enzyme that promotes processing of FIGlu and THF requires pyridoxal 5-phosphate as a coenzyme, and vitamin B6 deficiency also may contribute to elevated FIGlu. Finally, there are rare disorders in purine synthesis that impair normal utilization of folate forms that come from FIGlu and THF. Abnormal levels of uric acid, succinylpurines, inosine or adenosine may be investigated if FIGlu levels remain elevated despite folate, cobalamin, pyridoxine and antioxidant therapy.

Elevated FIGlu can be coincident with homocystinuria and predisposition to cardiovascular disease. In children, elevated FIGlu and folate and/or vitamin B12 dysfunctions may be associated with mental retardation, autism, growth failure and seizures. Folate and/or vitamin B12 insufficiencies can be secondary to gastrointestinal disorders or poor quality diet, and deficiencies of both have been noted in elderly populations.

Pyroglutamic Acid (5-oxoproline) is measured to be subnormal. Pyroglutamic acid primarily arises during the "gamma-glutamyl cycle" which splits glutathione (GSH) into cysteinylglycine and a gamma-glutamyl moiety. The gamma-glutamyl part attaches to another amino acid or short-chain peptide, or joins with an element (essential mineral) for transport across a membrane or into a cell. Uptake of such nutrients from the small intestine depends primarily upon this process. The enzyme gamma-glutamylcyclotransferase finishes the transport function by splitting off what was carried and changing the gamma-glutamyl part into pyroglutamic acid. Insufficiency of pyroglutamic acid may result from: insufficiency of reduced glutathione ("GSH"), toxicity (causing depletion of GSH), oxidant stress limiting the reduced form of glutathione, magnesium deficiency which can limit the rate of endogenous GSH formation, and deficiency of cysteine (the rate-limiting amino acid for GSH formation). Symptoms of nutrient malabsorption, oxidant stress and/or toxicity are consistent with subnormal pyroglutamate.

Amino Acid Markers (Plasma)

Commentary

<dl = Unable to calculate results due to less than detectable levels of analyte.

REPRESENTATIVENESS INDEX

Genova Diagnostics uses a new, much improved procedure for preserving plasma amino acids. Nevertheless, spoilage and decay could occur. To check this, two key ratios are monitored by computer and portrayed at the beginning of the report.

The **glutamine/glutamate ratio** can indicate specimen decay. When aged, heated, or improperly preserved, plasma glutamine decays to glutamic acid and ammonia. Hence, low glutamine/glutamate ratio may reflect decay. A high glutamine/glutamate ratio is metabolic and does not reflect on specimen representativeness.

The **asparagine/aspartic acid ratio** may also indicate improperly preserved plasma. Decay causes asparagine to become aspartic acid and ammonia.

The **ammonia concentration,** if elevated, could indicate decay of amino acids, as well as hyperammonemia of metabolic or bacterial origin. Thus, ammonia cannot be used alone to determine specimen quality.

The representativeness of the plasma is rated in the Representativeness Index Section of the Report.

Ethanolamine, an intermediate of the serine-to-choline metabolism sequence, is measured to be low. Ethanolamine is formed metabolically from serine and phosphatidylethanolamine; this endogenous formation is pyridoxal phosphate dependent and requires adequate serine. Consequences of ethanolamine insufficiency may be limited or insufficient levels of phosphoethanolamine, phosphatidylcholine and choline. Acetylcholine, the neurotransmitter, is formed from choline. Dietary lecithin provides an independent source of the neurotransmitter precursors. Ethanolamine insufficiency is significant if cholinergic functions are limited.

1-Methylhistidine is found to be elevated; it is a component of the dietary peptide anserine. Anserine is beta-alanyl-1-methyl-L-histidine, and it is known to come from chicken, turkey, duck, rabbit, tuna and salmon. Other food sources (especially trout and fowl) also are likely but are not documented. The peptidase enzyme that hydrolyzes anserine is present in the small intestine and also present in liver, spleen, and kidney tissues and in blood serum. Some direct uptake of dietary anserine is normal, and slight levels of 1-methylhistidine in the blood are not abnormal. However, high levels suggest increased uptake of short-chain peptides, possibly increased gut permeability, and decreased activity of digestive peptidases in the small intestine. There may or may not be associated symptomatology. 1-Methylhistidine itself is not known to be detrimental. Diagnostic testing of digestive capacity and gut permeability is suggested.

The nutritionally essential amino acid **lysine** is elevated. Hyperlysinemia can result from three abnormal conditions. Before considering these conditions, rule out use of lysine which is a common nutritional supplement, and violations of the 9-12 hour fasting period before blood drawing.

1. Hyperlysinemia can be an acquired condition caused by insufficiency of the cofactors required for its catabolism. Lysine becomes saccharopine by joining with alpha-ketoglutaric acid (a-kg); reduced, phosphorylated NAD is required. Alpha-ketoglutaric acid insufficiency occurs in: hyperammonemia, azotemia, possibly in manganese deficiency or aluminum excess (impairing activity of isocitrate dehydrogenase in the citric acid cycle), and in mitochondrial damage or toxicity conditions affecting oxidative phosphorylation. Limited NADPH might result from: niacin insufficiency, from thiamin insufficiency (affecting NADPH formation via the hexose monophosphate shunt), or from mitochondrial damage or dysfunction.

2. Hyperlysinemia can result from weakness of the lysine-to-saccharopine dehydrogenase enzyme, also called lysine oxoglutarate reductase. Episodic hyperargininemia can be secondary and due to competitive inhibition of arginase by excess lysine. Episodic hyperammonemia may be concurrent. The mode of inheritance is autosomal recessive; the condition is rare and is sometimes called familial hyperlysinemia.

3. Hyperlysinemia also can be secondary to saccharopinemia. This occurs with weakness of saccharopine

Commentary

dehydrogenase (glutaryl-lysine:NAD oxidoreductase). The mode of inheritance is unknown, and the occurrence is rare.

Taurine is elevated in the blood plasma. This amino acid conjugates cholesterol to form taurocholic acid which becomes a component of bile. Also, taurine is at very high concentrations in leukocytes where it controls excess levels of the hypochlorite ion that is generated during phagocytosis and oxidant response to toxins and microbial infections. In addition to biliary secretion in taurocholic form, unneeded taurine is a major urinary excretion. Excessive dietary intake of taurine-rich sources like seafood (especially shellfish), and from liver and organ meats may elevate plasma blood levels, as may consumption of taurine-supplemented sports and stimulant drinks. Elevated blood plasma taurine may also be secondary to several conditions.

1. Acute infectious or inflammatory response with destruction of some leukocytes

2. Renal failure or renal insufficiency, in which case, multiple elevations of analytes in plasma would be expected.

3. Biliary obstruction or liver disease with impaired formation or secretion of taurocholic acid

4. Thromboembolism (thrombocytes also contain high levels of taurine)

5. Cell fragility with hemolysis (erythrocytes also contain high levels of taurine)

6. Faulty whole blood-plasma specimen preparation containing residual and lysed cells.

7. Sulfite oxidase weakness or molybdenum deficiency with sulfite intolerance and elevated urinary sulfite.

The essential amino acid **threonine** is elevated. Rule out violation of the 9-12 hour fasting period prior to blood drawing. Specific metabolic disorders involving threonine are not documented. However, catabolism of threonine is very dependent upon pyridoxal 5-phosphate as a coenzyme. Elevated threonine may indicate insufficiency of vitamin B6. Elevated threonine also occurs in some liver disease including cirrhosis.

Essential & Metabolic Fatty Acids Markers (RBCs)

Commentary

Fatty Acids and Your Health

Doctors and nutritionists used to think that all fat was merely a way for the body to store calories for later use as energy, since, as we all know too well, if we eat excess food, our body converts those calories to fat. Only in the last century have we discovered that some fats are absolutely essential to health. Our bodies cannot make these fats, and so we must get them from our food, or our health will suffer. These Essential Fatty Acids (EFAs) have many functions in the body: they are the precursors for local "hormones"; they regulate all inflammation as well as all smooth muscle contraction and relaxation. These local hormones are given names like prostaglandins, leukotrienes and thromboxanes. EFAs are also essential components for all cell membranes. Their importance for health cannot be overemphasized since the brain, nerves, eyes, connective tissue, skin, blood vessels, and every cell in the body depend on a proper balance of essential fatty acids for optimal function. It is the fats found in red blood cell membranes, known as phospholipids, that this test measures.

Essential fatty acids are classified into fat "families": omega 3 fats and omega 6 fats. Non-essential fat "families" include omega-9 fats, saturated fats, omega-7 fats, and trans-fats. Optimal health depends on the proper balance of all fats - both essential and non-essential fats - in the diet. Proper balance means adequate amounts of each individual fat, without having too much, and maintaining proper balance between the various "families" of fats. Fat health also means avoiding potentially harmful fats such as trans fats found in shortening, margarine, fried foods and dairy. A proper balance of fatty acids will lead to mental health and proper nerve function, a healthy heart and circulatory system, reduced inflammation in general, proper gastrointestinal and lung function, a more balanced immune system, and even healthy skin, hair and nails. Fatty acid balance is also critical for the health of all pregnant women and their babies since the developing brain and nervous system of the baby requires large amounts of EFAs that must come from the mother. Fatty acid imbalances have been seen in many disease processes including heart disease, hypertension, insulin resistance and diabetes, asthma, painful menstruation, pre-menstrual syndrome (PMS), depression, attention deficit hyperactivity disorder (ADHD), senility, obsessive-compulsive disorder, and post-partum depression.

This Essential and Metabolic Fatty Acid Analysis allows your health care practitioner to examine the fats found in your red blood cell membranes. These fats represent the types of fats your body has available to make cell membranes and the local "hormones" that control inflammation and smooth muscle contraction throughout the body. Following your health care practitioner's advice on diet and fatty acid supplementation is likely to restore your fatty acids to a state of healthy balance.

Results of Your Individual Essential and Metabolic Fatty Acid Analysis

Linoleic acid (LA) is within the reference range, but below the functional physiologic range. LA is found in large quantities in virtually all vegetable oils (corn, peanut, soy, sunflower, safflower, canola, etc.). Given the large quantities of vegetable oil in the typical western diet, LA is usually seen only in people on a fat-free or severely fat-restricted diet. LA is the precursor essential fat for GLA, DGLA and arachidonic acid. Other dietary sources of LA include avocados, nuts, and seeds.

Linoleic acid stimulates normal cellular division and cellular repair. Inadequate LA may result in eczema-like skin eruptions, behavioral disturbances, increased thirst, growth retardation, and impaired wound healing.

Arachidonic acid (AA) is below the reference range. AA is essential for cell membrane structure, especially in nerve and brain cells. AA is also the main precursor for pro-inflammatory eicosanoid synthesis.

Commentary

Low levels of AA would lead to impaired cell membrane function that may manifest as neurological deficits. Low AA has been observed in children with attention deficit hyperactivity disorder and in patients with severe psychiatric illness. Low AA might also predispose a person to inadequate immune and inflammatory response, leading possibly to frequent infections or delayed wound healing.

Arachidonic acid is found pre-formed in egg yolks, bone marrow, and fatty (grain-fed) meats. Ordinarily, AA can be made from linoleic acid found in vegetable oils. However, high or even normal levels of linoleic acid along with low AA would suggest reduced delta-6 desaturase activity.

Pentadecanoic acid and/or Tricosanoic acid are above the reference range. Odd chain fatty acids are produced when endogenous fatty acid synthesis begins with propionic acid (3-carbon fatty acid) as substrate rather than acetic acid (2-carbon). Propionate is found in high quantities in butter and other dairy products. Propionate is also one of the short chain fatty acids produced by our gut bacteria in the fermentation (digestion) of water-soluble fiber. With adequate B12 and biotin, propionate can be converted into succinate for use in the citric acid cycle and energy production. High levels of odd chain fatty acids in cell membranes may indicate an increased need for B12 and biotin, or may result from an exceptionally high water-soluble fiber diet.

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.

Elemental Markers (RBCs)

Commentary

Zinc is below the reference range. Erythrocytes contain 75 to 85% of total whole blood zinc, bound to enzymes and to cell membranes. Important erythrocyte enzymes containing zinc are carbonic anhydrase and Cu,Zn-SOD. Zinc deficiency features lowered levels of zinc in erythrocytes with reduced activity of carbonic anhydrase occurring probably before reduced SOD activity occurs. However, erythrocyte zinc binding is relatively strong, and packed RBCs may not be the most sensitive or early indicator of zinc insufficiency. More sensitive are digestive peptidases (leucine aminopeptidase, carboxypeptidase, carnosinase). Urine amino acid analysis with measurement of anserine and carnosine peptides can be a very sensitive indicator of zinc function as an enzyme activator.

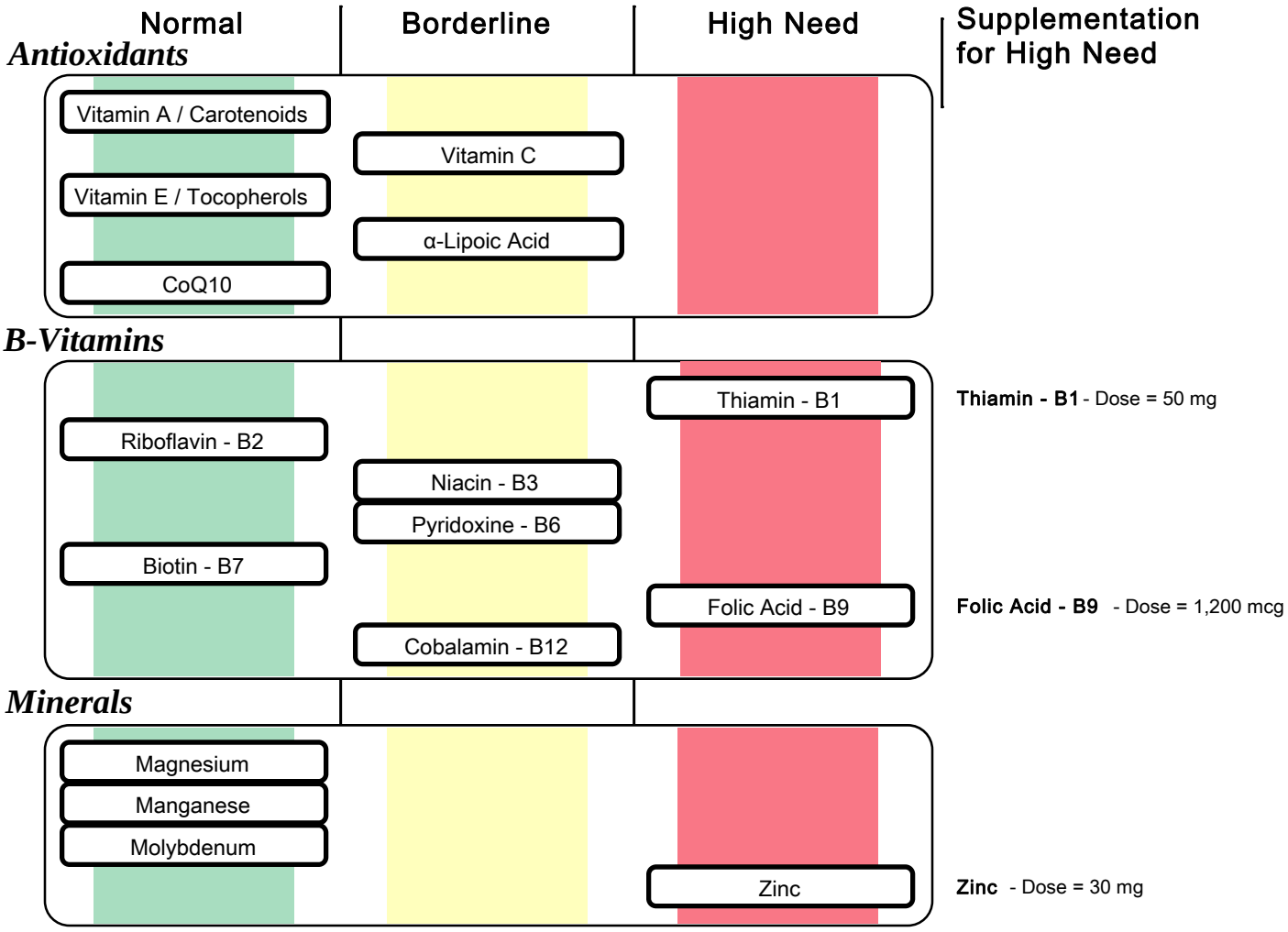
Zinc can be deficient in intestinal malabsorption, alcoholism, chronic ingestion of highly-processed or "junk" foods, chronic diarrhea, overuse of diuretics, and nephrotic syndrome. Excess copper interferes with zinc binding in blood plasma and reduces zinc retention. Excess iron intake may impair zinc absorption in the small intestine. Diabetes mellitus and hyperaminoaciduria may feature urinary wasting of zinc. Signs, symptoms, and conditions consistent with zinc insufficiency include: incomplete digestive proteolysis, food reactivities, reduced taste, reduced night vision, muscle aches, slowed wound healing, hair loss, dermatitis and sexual impotency. Mild lactic acidosis can be secondary to deficient zinc; lactic acid dehydrogenase requires zinc. Disordered insulin secretion from the pancreas can occur because insulin is stored in beta cells as a crystalline hexameric zinc complex. Immune dysfunction with impaired T-lymphocyte activity can be secondary to zinc insufficiency. In children, delayed growth or stunted growth may occur.

GENOVA DIAGNOSTICS

63 Zillicoa Street
Asheville, NC 28801

NutrEval™ Plasma amino acids

NutrEval Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	3,000 IU	3,000 IU	
Vitamin C	90 mg	500 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		100 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.2 mg	50 mg	
Riboflavin - B2	1.3 mg	10 mg	
Niacin - B3	16 mg	30 mg	
Pyridoxine - B6	1.3 mg	25 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	420 mg	400 mg	
Manganese	2.3 mg	3.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	11 mg	30 mg	
Essential Fatty Acids			
Omega-3 Oils	500 mg	500 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	0	Threonine	0
Histidine	0	Tryptophan	23
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

NutrEval® Plasma amino acids

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.

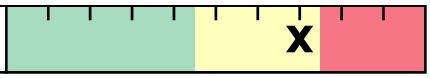
Vitamin C

- 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

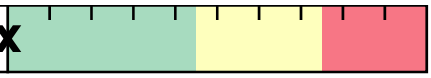
- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital,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



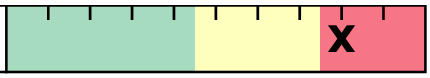
- α-Lipoic acid plays an important role in energy production, antioxidant activity (including the regeneration of vitamin C and glutathione), insulin signaling, cell signaling and the catabolism of α-keto acids and amino acids.
- High biotin intake can compete with lipoic acid for cell membrane entry.
- Optimal levels of α-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



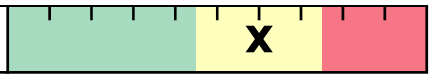
- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) 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

NutrEval Plasma amino acids

Interpretation At-A-Glance

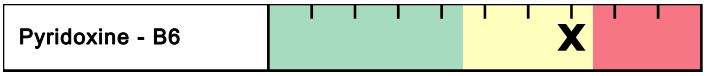
Nutritional Needs

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 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, 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.

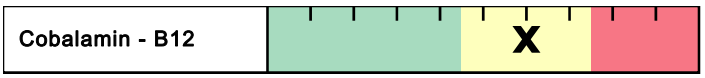
Niacin - B3

- 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

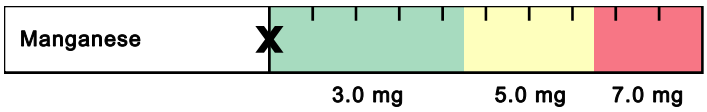


- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 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.

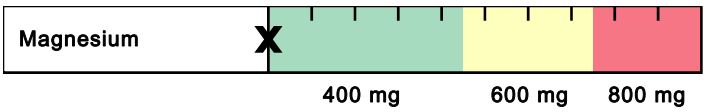
NutrEval Plasma amino acids — Interpretation At-A-Glance

Nutritional Needs

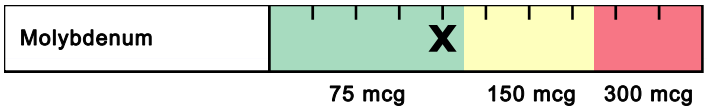
Minerals



- 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.



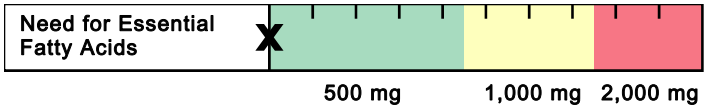
- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses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

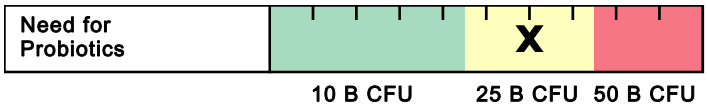
- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency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

Essential Fatty Acids

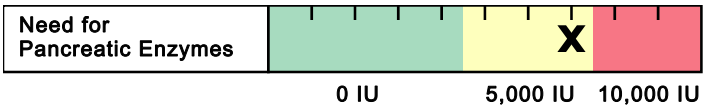


- Omega-3 (O3) and Omega-6 (O6) fatty acids are polyunsaturated fatty acids that cannot be synthesized by the human body. They are classified as essential nutrients and must be obtained from dietary sources.
- The standard American diet is much higher in O6 than O3 fatty acids. Deficiency of EFAs may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

Digestive Support



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



- 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.

NutrEval Plasma amino acids

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.

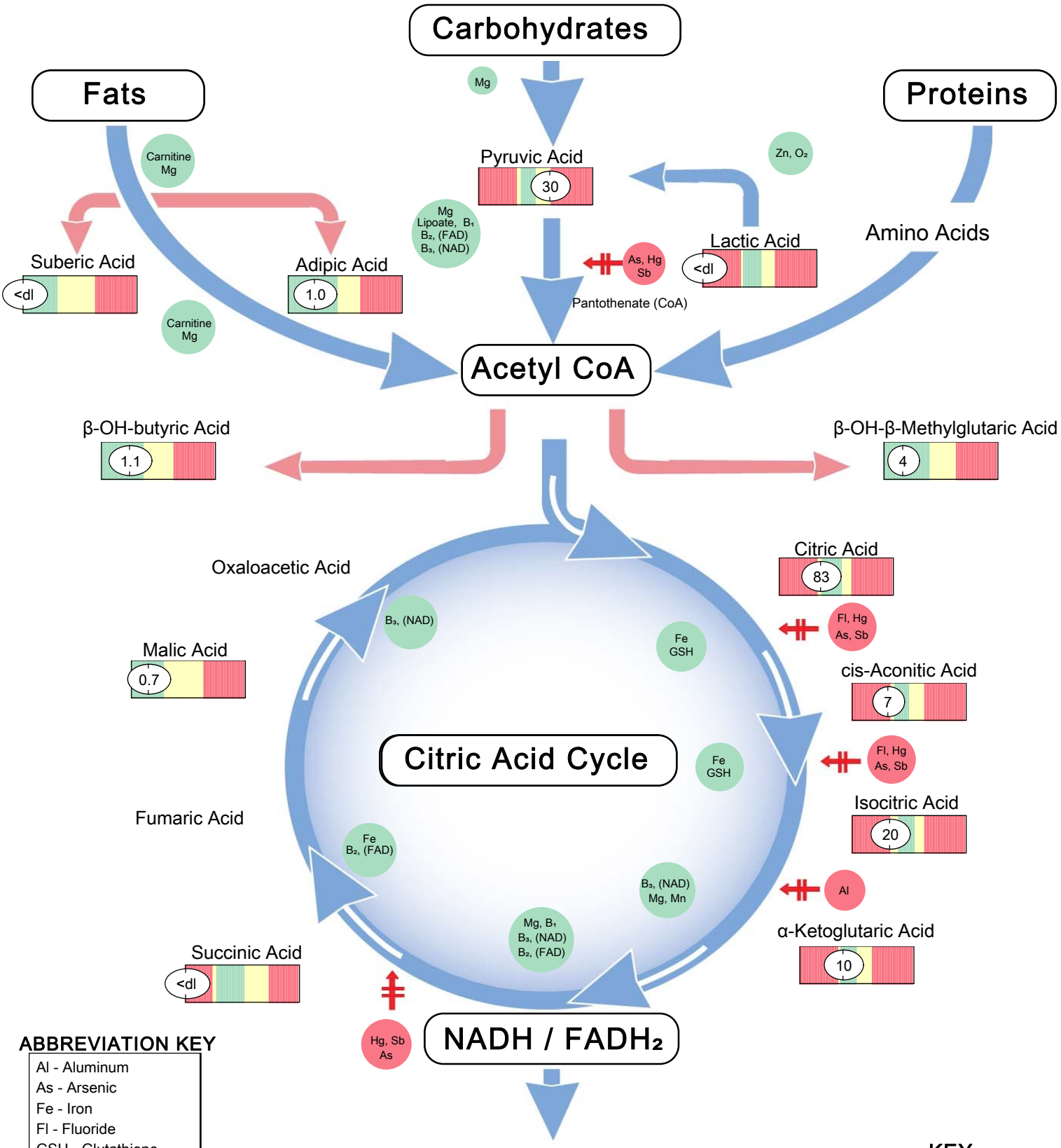
Toxic Exposure

- 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

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

Malabsorption and Dysbiosis Markers

Malabsorption Markers		Reference Range
Indoleacetic Acid (IAA)	1.7	<= 4.2
Phenylacetic Acid (PAA)	0.20	<= 0.12
Bacterial Dysbiosis Markers		
Dihydroxyphenylpropionic Acid (DHPPA)	0.3	<= 5.3
3-Hydroxyphenylacetic Acid	2.4	<= 8.1
4-Hydroxyphenylacetic Acid	24	<= 29
Benzoic Acid	0.10	<= 0.05
Hippuric Acid	<dl	<= 603
Yeast / Fungal Dysbiosis Markers		
Arabinose	15	<= 96
Citramalic Acid	1.8	<= 5.8
Tartaric Acid	<dl	<= 15

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism		Reference Range
Lactic Acid	<dl	1.9-19.8
Pyruvic Acid	30	7-32
β-OH-Butyric Acid (BHBA)	1.1	<= 2.8
Energy Metabolism		
Citric Acid	83	40-520
Cis-Aconitic Acid	7	10-36
Isocitric Acid	20	22-65
α-Ketoglutaric Acid (AKG)	10	4-52
Succinic Acid	<dl	0.4-4.6
Malic Acid	0.7	<= 3.0
β-OH-β-Methylglutaric Acid (HMG)	4	<= 15
Fatty Acid Metabolism		
Adipic Acid	1.0	<= 2.8
Suberic Acid	<dl	<= 2.1

Creatinine Concentration

		Reference Range
Creatinine ◆	10.6	3.1-19.5 mmol/L

Neurotransmitter Metabolites

		Reference Range
Vanilmandelic Acid	1.3	0.4-3.6
Homovanilic Acid	1.9	1.2-5.3
5-OH-indoleacetic Acid	7.0	3.8-12.1
3-Methyl-4-OH-phenylglycol	0.14	0.02-0.22
Kynurenic Acid	6.1	<= 7.1
Quinolinic Acid	4.4	<= 9.1
Kynurenic / Quinolinic Ratio	1.39	>= 0.44

Vitamin Markers

		Reference Range
α-Ketoadipic Acid	0.7	<= 1.7
α-Ketoisovaleric Acid	0.67	<= 0.97
α-Ketoisocaproic Acid	0.75	<= 0.89
α-Keto-β-Methylvaleric Acid	2.4	<= 2.1
Formiminoglutamic Acid (FIGlu)	1.7	<= 1.5
Glutaric Acid	0.19	<= 0.51
Isovalerylglycine	1.6	<= 3.7
Methylmalonic Acid	0.7	<= 1.9
Xanthurenic Acid	0.75	<= 0.96
3-Hydroxypropionic Acid	9	5-22
3-Hydroxyisovaleric Acid	16	<= 29

Toxin & Detoxification Markers

		Reference Range
α-Ketophenylacetic Acid (from Styrene)	0.27	<= 0.46
α-Hydroxyisobutyric Acid (from MTBE)	2.7	<= 6.7
Orotic Acid	0.74	0.33-1.01
Pyroglutamic Acid	15	16-34

Tyrosine Metabolism

		Reference Range
Homogentisic Acid	6	<= 19
2-Hydroxyphenylacetic Acid	0.57	<= 0.76

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 assays have not been cleared by the U.S. Food and Drug Administration.

Amino Acids (Plasma)

All biomarkers reported in micromoles per deciliter unless stated otherwise.

Nutritionally Essential Amino Acids

Amino Acid		Reference Range
Arginine	11.1	7.5-13.0
Histidine	10.8	7.9-12.1
Isoleucine	8.03	5.40-10.50
Leucine	14.1	10.5-18.0
Lysine	27.6	15.5-27.5
Methionine	3.3	2.5-4.9
Phenylalanine	6.14	4.60-7.90
Taurine	10.40	5.25-9.00
Threonine	17.29	6.40-14.00
Tryptophan	3.67	3.30-6.50
Valine	26.4	19.0-36.0

Nonessential Protein Amino Acids

Amino Acid		Reference Range
Alanine	33	26-55
Asparagine	6.1	4.0-7.2
Aspartic Acid	0.45	0.20-0.60
Cyst(e)ine	7.3	4.9-8.0
γ-Aminobutyric Acid	<dl	<= 0.02
Glutamic Acid	3.2	0.5-7.0
Glutamine	61	50-70
Proline	16	10-32
Tyrosine	6.9	5.1-10.0

Markers for Plasma Representativeness

		Reference Range
Glutamine/Glutamate	18.90	>= 8.00
Ammonia	2.7	<= 6.5
Asparagine/Aspartate	13.49	>= 6.00

Plasma Representativeness Index	10	Ref Range 5 – 10

Intermediary Metabolites

B Vitamin Markers		Reference Range
α-Aminoadipic Acid	0.51	<= 0.80
α-Amino-N-butyric Acid	2.90	1.25-3.50
β-Aminoisobutyric Acid	<dl	<= 0.30
Cystathionine	<dl	<= 0.03
3-Methylhistidine	0.69	<= 0.75

Urea Cycle Markers		
Ammonia	2.7	<= 6.5
Citrulline	3.3	2.8-5.6
Ornithine	8.89	4.25-11.50
Urea	575	320-970

Glycine/Serine Metabolites		
Glycine	23	19-43
Serine	9.9	8.0-15.5
Ethanolamine	0.37	0.50-1.20
Phosphoethanolamine	0.28	0.15-0.45
Phosphoserine	0.32	0.31-0.74
Sarcosine	<dl	<= 0.15

Dietary Peptide Related Markers

		Reference Range
1-Methylhistidine	4.98	<= 1.65
β-Alanine	0.3	<= 0.4

Amino Acid Reference Ranges are Age Specific

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

Essential and Metabolic Fatty Acids Markers (RBCs)

Omega 3 Fatty Acids

Analyte (cold water fish, flax, walnut)		Reference Range
α-Linolenic (ALA) 18:3 n3	0.12	>= 0.09 wt %
Eicosapentaenoic (EPA) 20:5 n3	3.17	>= 0.16 wt %
Docosapentaenoic (DPA) 22:5 n3	3.52	>= 1.14 wt %
Docosahexaenoic (DHA) 22:6 n3	7.1	>= 2.1 wt %
% Omega 3s	13.9	>= 3.8

Omega 9 Fatty Acids

Analyte (olive oil)		Reference Range
Oleic 18:1 n9	12	10-13 wt %
Nervonic 24:1 n9	2.6	2.1-3.5 wt %
% Omega 9s	14.3	13.3-16.6

Saturated Fatty Acids

Analyte (meat, dairy, coconuts, palm oils)		Reference Range
Palmitic C16:0	21	18-23 wt %
Stearic C18:0	17	14-17 wt %
Arachidic C20:0	0.22	0.22-0.35 wt %
Behenic C22:0	0.82	0.92-1.68 wt %
Tricosanoic C23:0	0.25	0.12-0.18 wt %
Lignoceric C24:0	2.6	2.1-3.8 wt %
Pentadecanoic C15:0	0.13	0.07-0.15 wt %
Margaric C17:0	0.28	0.22-0.37 wt %
% Saturated Fats	42.3	39.8-43.6

Omega 6 Fatty Acids

Analyte (vegetable oil, grains, most meats, dairy)		Reference Range
Linoleic (LA) 18:2 n6	10.9	10.5-16.9 wt %
γ-Linolenic (GLA) 18:3 n6	0.06	0.03-0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3 n6	1.65	>= 1.19 wt %
Arachidonic (AA) 20:4 n6	14	15-21 wt %
Docosatetraenoic (DTA) 22:4 n6	1.19	1.50-4.20 wt %
Eicosadienoic 20:2 n6	0.32	<= 0.26 wt %
% Omega 6s	27.9	30.5-39.7

Monounsaturated Fats

Omega 7 Fats		Reference Range
Palmitoleic 16:1 n7	0.27	<= 0.64 wt %
Vaccenic 18:1 n7	0.92	<= 1.13 wt %
Trans Fat		
Elaidic 18:1 n9t	0.31	<= 0.59 wt %

Delta - 6 Desaturase Activity

	Upregulated Functional Impaired	
Linoleic / DGLA 18:2 n6 / 20:3 n6	6.6	6.0-12.3

Cardiovascular Risk

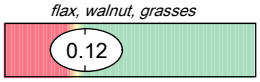
Analyte		Reference Range
Omega 6s / Omega 3s	2.0	3.4-10.7
AA / EPA 20:4 n6 / 20:5 n3	4	12-125
Omega 3 Index	10.3	>= 4.0

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

Essential Fatty Acid Metabolism

Omega 3 Family

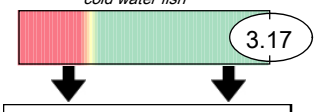
α-Linolenic Acid
flax, walnut, grasses



Stearidonic acid

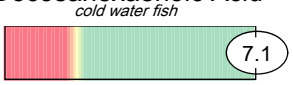
Eicosatetraenoic acid, ETA

Eicosapentaenoic Acid
cold water fish



Docosapentaenoic Acid

Docosahexaenoic Acid
cold water fish



Delta-6 Desaturase
Vitamin and Mineral Cofactors:
FAD (B2), Niacin (B3)
Pyridoxal-5-phosphate (B6)
Vitamin C, Insulin, Zn, Mg

Elongase
Vitamin and Mineral Cofactors:
Niacin (B3)
Pyridoxal-5-phosphate (B6)
Pantothenic Acid (B5)
Biotin, Vitamin C

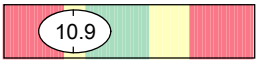
Delta-5 Desaturase
Vitamin and Mineral Cofactors:
FAD (B2), Niacin (B3)
Pyridoxal-5-phosphate (B6)
Vitamin C, Insulin, Zn, Mg

Elongase
Vitamin and Mineral Cofactors:
Niacin (B3)
Pyridoxal-5-phosphate (B6), Biotin
Pantothenic Acid (B5), Vitamin C

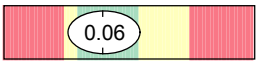
Elongase
Delta-6 Desaturase
Vitamin and Mineral Cofactors:
FAD (B2), Niacin (B3)
Pyridoxal-5-phosphate (B6), Biotin
Vitamin C, Zn, Mg, Carnitine
Pantothenic Acid (B5)

Omega 6 Family

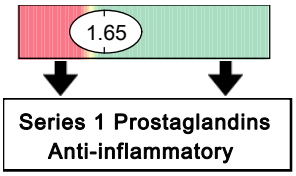
Linoleic Acid
grains, vegetable oils



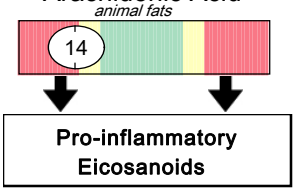
γ-Linolenic Acid
evening primrose, borage, black currant



Dihomo-γ-Linolenic Acid



Arachidonic Acid
animal fats



Docosatetraenoic Acid

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

Oxidative Stress Markers

Oxidative Stress Markers

		Reference Range
Glutathione (whole blood)	939	>=669 micromol/L
Lipid Peroxides (urine)	5.4	<=10.0 micromol/g Creat.
8-OHdG (urine)	4	<=16 mcg/g Creat.
Coenzyme Q10, Ubiquinone (plasma)	1.06	0.46-1.72 mcg/mL

The Oxidative Stress reference ranges are based on an adult population.

Elemental Markers (RBCs)

Nutrient Elements

Element	Reference Range	Reference Range
Copper	0.571	0.466-0.721 mcg/g
Magnesium	40.3	30.1-56.5 mcg/g
Manganese	0.012	0.007-0.038 mcg/g
Potassium	2,418	2,220-3,626 mcg/g
Selenium	0.41	0.25-0.76 mcg/g
Zinc	7.2	7.8-13.1 mcg/g

Toxic Elements

Element	Reference Range	Reference Range
Lead	0.047	<= 0.048 mcg/g
Mercury	<dl	<= 0.0039 mcg/g
Antimony	0.001	<= 0.002 mcg/g
Arsenic	0.012	<= 0.071 mcg/g
Cadmium	0.000	<= 0.001 mcg/g
Tin	<dl	<= 0.0009 mcg/g

The Elemental reference ranges are based on an adult population.

Lab Comments

Lab Comments

***Requisition/Sample labeling discrepancy noted. Ordering physician has been contacted and authorizes testing to be performed. 12/01/2014 EA2*

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.

Commentary

Phenylacetic Acid (PAA) is elevated. If the essential amino acid phenylalanine is not sufficiently digested and absorbed in the small intestine, it is carried to the large bowel where anaerobic bacteria convert it to phenylethylamine. This is then absorbed, and in body tissues such as the liver, it is converted by deamination to PAA, which is excreted in the urine. Some species of Clostridia can produce PAA directly from aromatic amino acids. Its presence at elevated levels indicates one or more of the following: gastric hypochlorhydria or pepsin inactivity, impaired digestive peptidase function in the small intestine, rate-limited or insufficient absorption or mucosal transport in the small intestine, abnormal intestinal motility (partly regulated by cholecystokinin and secretin), or presence of colonic or other bacteria in the small intestine (dysbiosis).

Additionally, some elevation of PAA may occur in the uncommon instances of phenylketonuria and with Type I tyrosinemia (tyrosinosis). With phenylketonuria, 2-hydroxyphenylacetate (2-HPAA) would be significantly elevated. An amino acid analysis also is helpful in diagnosing such conditions.

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.

Lactic Acid , or lactate, is measured to be low. Lactate is formed from pyruvate in anaerobic or oxygen starved (hypoxic) circumstances to allow for ongoing production of ATP in these anaerobic conditions. There are no known clinical problems associated with low lactic acid. Low levels are usually a result of reduced amounts of its precursor, pyruvic acid.

Cis-aconitic Acid (CAA) is measured to be subnormal, while its precursor, citric acid is not deficient. This may occur with low carbohydrate diets, fasting or anorexic conditions; citric acid may then be only marginal. On the other hand, normal or elevated citric acid with low cis-aconitic acid may be the result of urinary citrate wasting (leading to deficiency) or of weakness in the enzyme that transforms citrate into cis-aconitate. This enzyme (aconitase) requires cysteine or glutathione in the reduced state and ferrous iron (Fe+2). Oxidant stress can inhibit aconitase as can toxic elements that bind to sulfhydryl groups (mercury, arsenic, antimony). Fluorine or fluoride that forms fluorocitrate is also a very potent inhibitor of aconitase.

Isocitric Acid is measured to be subnormal. This may be due to deficient or low-normal levels of its precursors, cis-aconitate or citrate. It may also be due to depleted alpha-ketoglutarate, which it forms in the citric acid cycle; check for low alpha-ketoglutarate in this report. The same enzyme, aconitase, forms cis-aconitic acid and isocitric acid, and requires reduced cysteine or glutathione and ferrous iron (Fe+2). Oxidant stress can inhibit it, as can arsenic, mercury or antimony. Fluoride that becomes fluorocitrate can strongly inhibit aconitase and impair formation of isocitrate.

Succinic acid participates in the citric acid cycle, acting to donate electrons to the mitochondrial electron transport and leading to formation of fumaric acid. Common in foods such as cantaloupe, it is also a food additive, providing flow-altering effects and a tart flavor. It appears that lacto-ovo vegetarians may show decreased levels in the urine and chronic fatigue patients may also show low levels, although studies on this topic are mixed. Low levels may also be an indicator of B12 or folate deficiency.

Alpha-keto-beta-methylvaleric Acid (AKBM) is measured to be elevated. AKBM comes from the essential amino acid isoleucine via transamination. Moderate elevations of AKBM usually mean that AKBM's further

Commentary

metabolism to the compound, alpha-methylbutyryl-CoA, is impaired either by coenzyme/cofactor insufficiency or by (genetic) weakness in the enzyme complex. The dehydrogenase enzyme complex that accomplishes this requires lipoic acid, vitamin B1 as thiamin pyrophosphate and vitamin B2 as FAD. Vitamin B3 as NAD is a necessary cofactor, which removes hydrogen to become NADH. The other necessary cofactor is coenzyme A, requiring pantothenic acid, cysteine, and magnesium. Elevated levels of AKBM may indicate low levels of any of these nutrients.

The toxic elements arsenic, antimony, mercury and cadmium may also weaken lipoic acid and dehydrogenase activity. Very high elevation of AKBM and its sister keto acids (alpha-ketoisovaleric, alpha-ketoisocaproic) constitute a rare disorder called "maple syrup urine disease". When AKBM is elevated, isoleucine may also be elevated per urine or plasma amino acid analysis.

Formiminoglutamic Acid "FIGlu" is elevated in the urine. FIGlu stands for formiminoglutamic acid, a substance produced in body tissue from the dietary amino acid histidine. FIGlu needs tetrahydrofolate (THF), a reduced form of folic acid, to be changed into forms that are metabolically useful.

Elevated urine FIGlu can occur with several circumstances. Dietary deficiency of folic acid or severe oxidant stress that limits biologic reduction of folic acid to the THF form can cause this elevation. Histidine as a supplemented nutrient can contribute to urine FIGlu levels, especially if taken in amounts that exceed 50 mg/Kg body weight. Metabolism of folic acid can be impaired if vitamin B12 is insufficient or if its metabolism is disordered. So, elevated FIGlu also can mean that some form of B12 or cobalamin is needed. The enzyme that promotes processing of FIGlu and THF requires pyridoxal 5-phosphate as a coenzyme, and vitamin B6 deficiency also may contribute to elevated FIGlu. Finally, there are rare disorders in purine synthesis that impair normal utilization of folate forms that come from FIGlu and THF. Abnormal levels of uric acid, succinylpurines, inosine or adenosine may be investigated if FIGlu levels remain elevated despite folate, cobalamin, pyridoxine and antioxidant therapy.

Elevated FIGlu can be coincident with homocystinuria and predisposition to cardiovascular disease. In children, elevated FIGlu and folate and/or vitamin B12 dysfunctions may be associated with mental retardation, autism, growth failure and seizures. Folate and/or vitamin B12 insufficiencies can be secondary to gastrointestinal disorders or poor quality diet, and deficiencies of both have been noted in elderly populations.

Pyroglutamic Acid (5-oxoproline) is measured to be subnormal. Pyroglutamic acid primarily arises during the "gamma-glutamyl cycle" which splits glutathione (GSH) into cysteinylglycine and a gamma-glutamyl moiety. The gamma-glutamyl part attaches to another amino acid or short-chain peptide, or joins with an element (essential mineral) for transport across a membrane or into a cell. Uptake of such nutrients from the small intestine depends primarily upon this process. The enzyme gamma-glutamylcyclotransferase finishes the transport function by splitting off what was carried and changing the gamma-glutamyl part into pyroglutamic acid. Insufficiency of pyroglutamic acid may result from: insufficiency of reduced glutathione ("GSH"), toxicity (causing depletion of GSH), oxidant stress limiting the reduced form of glutathione, magnesium deficiency which can limit the rate of endogenous GSH formation, and deficiency of cysteine (the rate-limiting amino acid for GSH formation). Symptoms of nutrient malabsorption, oxidant stress and/or toxicity are consistent with subnormal pyroglutamate.

Amino Acid Markers (Plasma)

Commentary

<dl = Unable to calculate results due to less than detectable levels of analyte.

REPRESENTATIVENESS INDEX

Genova Diagnostics uses a new, much improved procedure for preserving plasma amino acids. Nevertheless, spoilage and decay could occur. To check this, two key ratios are monitored by computer and portrayed at the beginning of the report.

The **glutamine/glutamate ratio** can indicate specimen decay. When aged, heated, or improperly preserved, plasma glutamine decays to glutamic acid and ammonia. Hence, low glutamine/glutamate ratio may reflect decay. A high glutamine/glutamate ratio is metabolic and does not reflect on specimen representativeness.

The **asparagine/aspartic acid ratio** may also indicate improperly preserved plasma. Decay causes asparagine to become aspartic acid and ammonia.

The **ammonia concentration,** if elevated, could indicate decay of amino acids, as well as hyperammonemia of metabolic or bacterial origin. Thus, ammonia cannot be used alone to determine specimen quality.

The representativeness of the plasma is rated in the Representativeness Index Section of the Report.

Ethanolamine, an intermediate of the serine-to-choline metabolism sequence, is measured to be low. Ethanolamine is formed metabolically from serine and phosphatidylethanolamine; this endogenous formation is pyridoxal phosphate dependent and requires adequate serine. Consequences of ethanolamine insufficiency may be limited or insufficient levels of phosphoethanolamine, phosphatidylcholine and choline. Acetylcholine, the neurotransmitter, is formed from choline. Dietary lecithin provides an independent source of the neurotransmitter precursors. Ethanolamine insufficiency is significant if cholinergic functions are limited.

1-Methylhistidine is found to be elevated; it is a component of the dietary peptide anserine. Anserine is beta-alanyl-1-methyl-L-histidine, and it is known to come from chicken, turkey, duck, rabbit, tuna and salmon. Other food sources (especially trout and fowl) also are likely but are not documented. The peptidase enzyme that hydrolyzes anserine is present in the small intestine and also present in liver, spleen, and kidney tissues and in blood serum. Some direct uptake of dietary anserine is normal, and slight levels of 1-methylhistidine in the blood are not abnormal. However, high levels suggest increased uptake of short-chain peptides, possibly increased gut permeability, and decreased activity of digestive peptidases in the small intestine. There may or may not be associated symptomatology. 1-Methylhistidine itself is not known to be detrimental. Diagnostic testing of digestive capacity and gut permeability is suggested.

The nutritionally essential amino acid **lysine** is elevated. Hyperlysinemia can result from three abnormal conditions. Before considering these conditions, rule out use of lysine which is a common nutritional supplement, and violations of the 9-12 hour fasting period before blood drawing.

1. Hyperlysinemia can be an acquired condition caused by insufficiency of the cofactors required for its catabolism. Lysine becomes saccharopine by joining with alpha-ketoglutaric acid (a-kg); reduced, phosphorylated NAD is required. Alpha-ketoglutaric acid insufficiency occurs in: hyperammonemia, azotemia, possibly in manganese deficiency or aluminum excess (impairing activity of isocitrate dehydrogenase in the citric acid cycle), and in mitochondrial damage or toxicity conditions affecting oxidative phosphorylation. Limited NADPH might result from: niacin insufficiency, from thiamin insufficiency (affecting NADPH formation via the hexose monophosphate shunt), or from mitochondrial damage or dysfunction.

2. Hyperlysinemia can result from weakness of the lysine-to-saccharopine dehydrogenase enzyme, also called lysine oxoglutarate reductase. Episodic hyperargininemia can be secondary and due to competitive inhibition of arginase by excess lysine. Episodic hyperammonemia may be concurrent. The mode of inheritance is autosomal recessive; the condition is rare and is sometimes called familial hyperlysinemia.

3. Hyperlysinemia also can be secondary to saccharopinemia. This occurs with weakness of saccharopine

Commentary

dehydrogenase (glutaryl-lysine:NAD oxidoreductase). The mode of inheritance is unknown, and the occurrence is rare.

Taurine is elevated in the blood plasma. This amino acid conjugates cholesterol to form taurocholic acid which becomes a component of bile. Also, taurine is at very high concentrations in leukocytes where it controls excess levels of the hypochlorite ion that is generated during phagocytosis and oxidant response to toxins and microbial infections. In addition to biliary secretion in taurocholic form, unneeded taurine is a major urinary excretion. Excessive dietary intake of taurine-rich sources like seafood (especially shellfish), and from liver and organ meats may elevate plasma blood levels, as may consumption of taurine-supplemented sports and stimulant drinks. Elevated blood plasma taurine may also be secondary to several conditions.

1. Acute infectious or inflammatory response with destruction of some leukocytes

2. Renal failure or renal insufficiency, in which case, multiple elevations of analytes in plasma would be expected.

3. Biliary obstruction or liver disease with impaired formation or secretion of taurocholic acid

4. Thromboembolism (thrombocytes also contain high levels of taurine)

5. Cell fragility with hemolysis (erythrocytes also contain high levels of taurine)

6. Faulty whole blood-plasma specimen preparation containing residual and lysed cells.

7. Sulfite oxidase weakness or molybdenum deficiency with sulfite intolerance and elevated urinary sulfite.

The essential amino acid **threonine** is elevated. Rule out violation of the 9-12 hour fasting period prior to blood drawing. Specific metabolic disorders involving threonine are not documented. However, catabolism of threonine is very dependent upon pyridoxal 5-phosphate as a coenzyme. Elevated threonine may indicate insufficiency of vitamin B6. Elevated threonine also occurs in some liver disease including cirrhosis.

Essential & Metabolic Fatty Acids Markers (RBCs)

Commentary

Fatty Acids and Your Health

Doctors and nutritionists used to think that all fat was merely a way for the body to store calories for later use as energy, since, as we all know too well, if we eat excess food, our body converts those calories to fat. Only in the last century have we discovered that some fats are absolutely essential to health. Our bodies cannot make these fats, and so we must get them from our food, or our health will suffer. These Essential Fatty Acids (EFAs) have many functions in the body: they are the precursors for local "hormones"; they regulate all inflammation as well as all smooth muscle contraction and relaxation. These local hormones are given names like prostaglandins, leukotrienes and thromboxanes. EFAs are also essential components for all cell membranes. Their importance for health cannot be overemphasized since the brain, nerves, eyes, connective tissue, skin, blood vessels, and every cell in the body depend on a proper balance of essential fatty acids for optimal function. It is the fats found in red blood cell membranes, known as phospholipids, that this test measures.

Essential fatty acids are classified into fat "families": omega 3 fats and omega 6 fats. Non-essential fat "families" include omega-9 fats, saturated fats, omega-7 fats, and trans-fats. Optimal health depends on the proper balance of all fats - both essential and non-essential fats - in the diet. Proper balance means adequate amounts of each individual fat, without having too much, and maintaining proper balance between the various "families" of fats. Fat health also means avoiding potentially harmful fats such as trans fats found in shortening, margarine, fried foods and dairy. A proper balance of fatty acids will lead to mental health and proper nerve function, a healthy heart and circulatory system, reduced inflammation in general, proper gastrointestinal and lung function, a more balanced immune system, and even healthy skin, hair and nails. Fatty acid balance is also critical for the health of all pregnant women and their babies since the developing brain and nervous system of the baby requires large amounts of EFAs that must come from the mother. Fatty acid imbalances have been seen in many disease processes including heart disease, hypertension, insulin resistance and diabetes, asthma, painful menstruation, pre-menstrual syndrome (PMS), depression, attention deficit hyperactivity disorder (ADHD), senility, obsessive-compulsive disorder, and post-partum depression.

This Essential and Metabolic Fatty Acid Analysis allows your health care practitioner to examine the fats found in your red blood cell membranes. These fats represent the types of fats your body has available to make cell membranes and the local "hormones" that control inflammation and smooth muscle contraction throughout the body. Following your health care practitioner's advice on diet and fatty acid supplementation is likely to restore your fatty acids to a state of healthy balance.

Results of Your Individual Essential and Metabolic Fatty Acid Analysis

Linoleic acid (LA) is within the reference range, but below the functional physiologic range. LA is found in large quantities in virtually all vegetable oils (corn, peanut, soy, sunflower, safflower, canola, etc.). Given the large quantities of vegetable oil in the typical western diet, LA is usually seen only in people on a fat-free or severely fat-restricted diet. LA is the precursor essential fat for GLA, DGLA and arachidonic acid. Other dietary sources of LA include avocados, nuts, and seeds.

Linoleic acid stimulates normal cellular division and cellular repair. Inadequate LA may result in eczema-like skin eruptions, behavioral disturbances, increased thirst, growth retardation, and impaired wound healing.

Arachidonic acid (AA) is below the reference range. AA is essential for cell membrane structure, especially in nerve and brain cells. AA is also the main precursor for pro-inflammatory eicosanoid synthesis.

Commentary

Low levels of AA would lead to impaired cell membrane function that may manifest as neurological deficits. Low AA has been observed in children with attention deficit hyperactivity disorder and in patients with severe psychiatric illness. Low AA might also predispose a person to inadequate immune and inflammatory response, leading possibly to frequent infections or delayed wound healing.

Arachidonic acid is found pre-formed in egg yolks, bone marrow, and fatty (grain-fed) meats. Ordinarily, AA can be made from linoleic acid found in vegetable oils. However, high or even normal levels of linoleic acid along with low AA would suggest reduced delta-6 desaturase activity.

Pentadecanoic acid and/or Tricosanoic acid are above the reference range. Odd chain fatty acids are produced when endogenous fatty acid synthesis begins with propionic acid (3-carbon fatty acid) as substrate rather than acetic acid (2-carbon). Propionate is found in high quantities in butter and other dairy products. Propionate is also one of the short chain fatty acids produced by our gut bacteria in the fermentation (digestion) of water-soluble fiber. With adequate B12 and biotin, propionate can be converted into succinate for use in the citric acid cycle and energy production. High levels of odd chain fatty acids in cell membranes may indicate an increased need for B12 and biotin, or may result from an exceptionally high water-soluble fiber diet.

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.

Elemental Markers (RBCs)

Commentary

Zinc is below the reference range. Erythrocytes contain 75 to 85% of total whole blood zinc, bound to enzymes and to cell membranes. Important erythrocyte enzymes containing zinc are carbonic anhydrase and Cu,Zn-SOD. Zinc deficiency features lowered levels of zinc in erythrocytes with reduced activity of carbonic anhydrase occurring probably before reduced SOD activity occurs. However, erythrocyte zinc binding is relatively strong, and packed RBCs may not be the most sensitive or early indicator of zinc insufficiency. More sensitive are digestive peptidases (leucine aminopeptidase, carboxypeptidase, carnosinase). Urine amino acid analysis with measurement of anserine and carnosine peptides can be a very sensitive indicator of zinc function as an enzyme activator.

Zinc can be deficient in intestinal malabsorption, alcoholism, chronic ingestion of highly-processed or "junk" foods, chronic diarrhea, overuse of diuretics, and nephrotic syndrome. Excess copper interferes with zinc binding in blood plasma and reduces zinc retention. Excess iron intake may impair zinc absorption in the small intestine. Diabetes mellitus and hyperaminoaciduria may feature urinary wasting of zinc. Signs, symptoms, and conditions consistent with zinc insufficiency include: incomplete digestive proteolysis, food reactivities, reduced taste, reduced night vision, muscle aches, slowed wound healing, hair loss, dermatitis and sexual impotency. Mild lactic acidosis can be secondary to deficient zinc; lactic acid dehydrogenase requires zinc. Disordered insulin secretion from the pancreas can occur because insulin is stored in beta cells as a crystalline hexameric zinc complex. Immune dysfunction with impaired T-lymphocyte activity can be secondary to zinc insufficiency. In children, delayed growth or stunted growth may occur.