GENOVA DIAGNOSTICS EUROPE

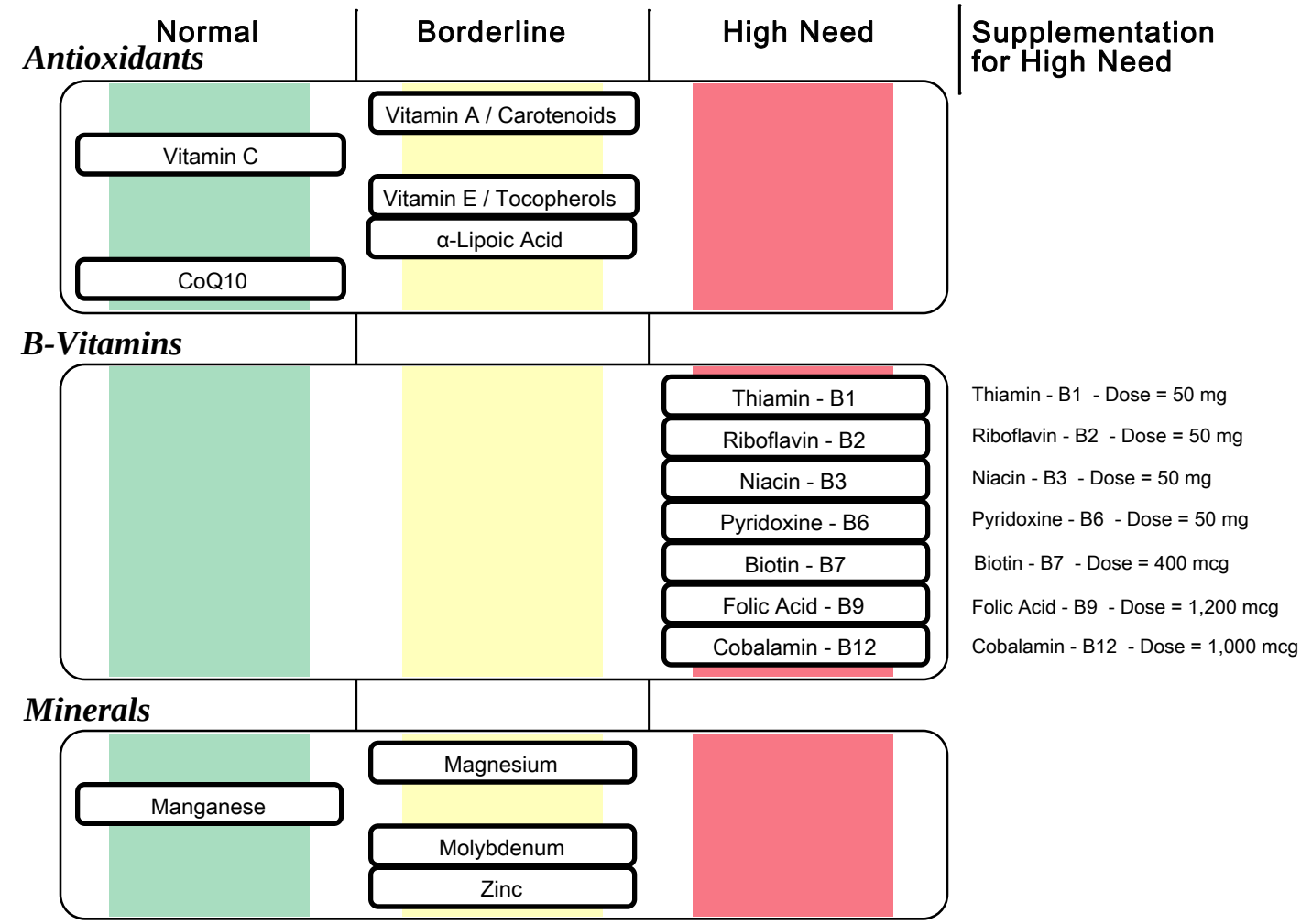
46-50 Coombe Road
New Malden
Surrey KT3 4QF

63 Zillicoa Street
Asheville, NC 28801 USA

Patient:
DOB:
Sex:
MRN:

Order Number:
Completed:
Received:
Collected:

ONE Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	5,000 IU	
Vitamin C	75 mg	250 mg	
Vitamin E / Tocopherols	22 IU	200 IU	
α-Lipoic Acid		100 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	50 mg	
Riboflavin - B2	1.1 mg	50 mg	
Niacin - B3	14 mg	50 mg	
Pyridoxine - B6	1.3 mg	50 mg	
Biotin - B7	30 mcg	400 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	1,000 mcg	
Minerals			
Magnesium	320 mg	600 mg	
Manganese	1.8 mg	3.0 mg	
Molybdenum	45 mcg	150 mcg	
Zinc	8 mg	20 mg	
Digestive Support			
Probiotics		50 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	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		

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

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

Key

Normal | Borderline | High Need

Interpretation At-A-Glance

Nutritional Needs

Antioxidants

Vitamin A / Carotenoids

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

Vitamin C

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

Vitamin E / Tocopherols

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

α-Lipoic Acid

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

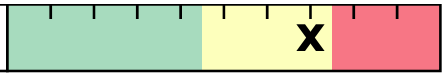
CoQ10

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

Glutathione

- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.

Plant-based Antioxidants



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

Key

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

Interpretation At-A-Glance

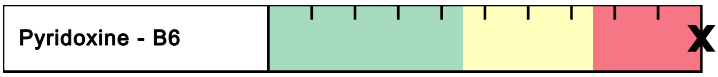
Nutritional Needs

B-Vitamins

Thiamin - B1

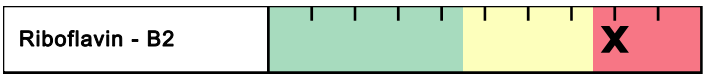
- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency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

Pyridoxine - B6



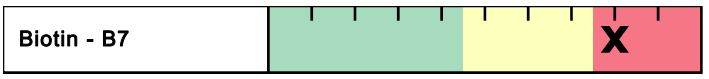
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or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

Riboflavin - B2



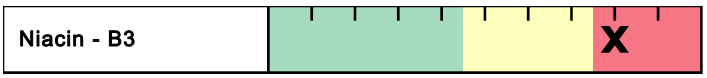
- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.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

Biotin - B7



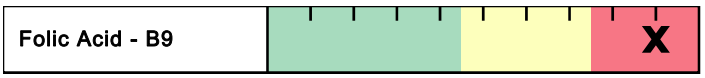
- Biotin is a cofactor for enzymes involved in functions such as fatty acid (FA) synthesis, mitochondrial FA oxidation, gluconeogenesis, and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN use, anticonvulsants, high-dose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

Niacin - B3



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

Folic Acid - B9



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

Cobalamin - B12

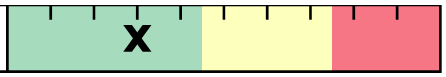
- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2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

Interpretation At-A-Glance

Nutritional Needs

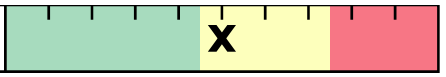
Minerals

Manganese



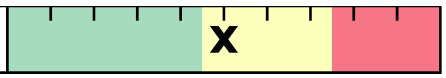
- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing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

Magnesium



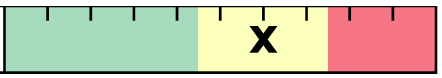
- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses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

Molybdenum



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

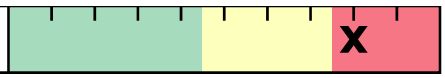
Zinc



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

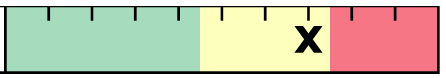
Digestive Support

Need for Probiotics



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

Need for Pancreatic Enzymes



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

Interpretation At-A-Glance

Functional Imbalances

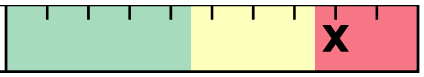
Mitochondrial Dysfunction

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

Toxic Exposure

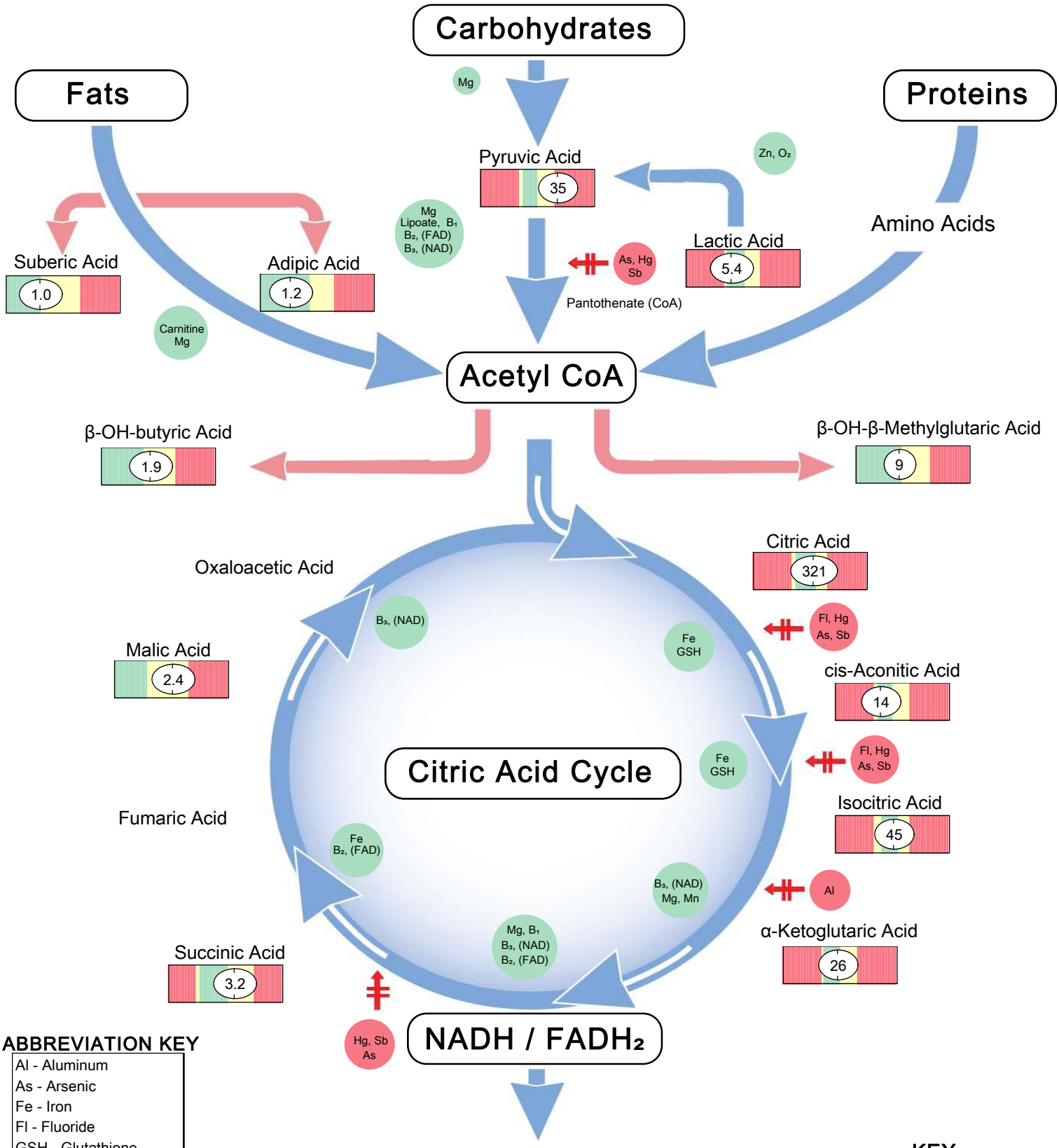
- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal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

Need for Methylation



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

At-A-Glance



ABBREVIATION KEY

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

KEY

Green = cofactor

Red = inhibitor

Metabolic Analysis Markers (Urine)

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

Malabsorption and Dysbiosis Markers

Malabsorption Markers

		Reference Range
Indoleacetic Acid (IAA)	2.6	<= 4.2
Phenylacetic Acid (PAA)	0.16	<= 0.12

Bacterial Dysbiosis Markers

		Reference Range
Dihydroxyphenylpropionic Acid (DHPPA)	3.1	<= 5.3
3-Hydroxyphenylacetic Acid	6.3	<= 8.1
4-Hydroxyphenylacetic Acid	30	<= 29
Benzoic Acid	0.09	<= 0.05
Hippuric Acid	237	<= 603

Yeast / Fungal Dysbiosis Markers

		Reference Range
Arabinose	88	<= 96
Citramalic Acid	4.3	<= 5.8
Tartaric Acid	7	<= 15

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism

		Reference Range
Lactic Acid	5.4	1.9-19.8
Pyruvic Acid	35	7-32
β-OH-Butyric Acid (BHBA)	1.9	<= 2.8

Energy Metabolism

		Reference Range
Citric Acid	321	40-520
Cis-Aconitic Acid	14	10-36
Isocitric Acid	45	22-65
α-Ketoglutaric Acid (AKG)	26	4-52
Succinic Acid	3.2	0.4-4.6
Malic Acid	2.4	<= 3.0
β-OH-β-Methylglutaric Acid (HMG)	9	<= 15

Fatty Acid Metabolism

		Reference Range
Adipic Acid	1.2	<= 2.8
Suberic Acid	1.0	<= 2.1

Creatinine Concentration

		Reference Range
Creatinine ◆	7.3	3.1-19.5 mmol/L

Neurotransmitter Metabolites

		Reference Range
Vanilmandelic Acid	2.0	0.4-3.6
Homovanillic Acid	3.5	1.2-5.3
5-OH-indoleacetic Acid	10.6	3.8-12.1
3-Methyl-4-OH-phenylglycol	0.09	0.02-0.22
Kynurenic Acid	9.6	<= 7.1
Quinolinic Acid	3.6	<= 9.1
Kynurenic / Quinolinic Ratio	2.67	>= 0.44

Vitamin Markers

		Reference Range
α-Ketoadipic Acid	0.7	<= 1.7
α-Ketoisovaleric Acid	0.56	<= 0.97
α-Ketoisocaproic Acid	0.87	<= 0.89
α-Keto-β-Methylvaleric Acid	1.8	<= 2.1
Formiminoglutamic Acid (FIGlu)	2.3	<= 1.5
Glutaric Acid	0.32	<= 0.51
Isovalerylglycine	4.7	<= 3.7
Methylmalonic Acid	1.7	<= 1.9
Xanthurenic Acid	1.31	<= 0.96
3-Hydroxypropionic Acid	14	5-22
3-Hydroxyisovaleric Acid	21	<= 29

Toxin & Detoxification Markers

		Reference Range
α-Ketophenylacetic Acid (from Styrene)	0.26	<= 0.46
α-Hydroxyisobutyric Acid (from MTBE)	8.6	<= 6.7
Orotic Acid	0.74	0.33-1.01
Pyroglutamic Acid	34	16-34

Tyrosine Metabolism

		Reference Range
Homogentisic Acid	14	<= 19
2-Hydroxyphenylacetic Acid	0.73	<= 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 (Urine FMV)

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

Nutritionally Essential Amino Acids

Amino Acid	Reference Range
Arginine	3-43
Histidine	124-894
Isoleucine	3-28
Leucine	4-46
Lysine	11-175
Methionine	2-18
Phenylalanine	8-71
Taurine	21-424
Threonine	17-135
Tryptophan	5-53
Valine	7-49

Nonessential Protein Amino Acids

Amino Acid	Reference Range
Alanine	63-356
Asparagine	25-166
Aspartic Acid	<= 14
Cysteine (FMV urine)	8-74
Cystine (FMV Urine)	10-104
γ-Aminobutyric Acid	<= 5
Glutamic Acid	4-27
Glutamine	110-632
Proline	1-13
Tyrosine	11-135

Creatinine Concentration

	Reference Range
Creatinine ◆	3.1-19.5 mmol/L

Amino Acid reference ranges are age specific.

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Methodology: LC/MS/MS, Enzymatic and Alkaline Picrate

Intermediary Metabolites

B Vitamin Markers	Reference Range
α-Aminoadipic	2-47
α-Amino-N-butyric Acid	2-25
β-Aminoisobutyric Acid	11-160
Cystathionine	2-68
3-Methylhistidine	44-281

Urea Cycle Markers

Citrulline	0.6-3.9
Ornithine	2-21
Urea ◆	168-465 mmol/g creatinine

Glycine/Serine Metabolites

Glycine	95-683
Serine	40-163
Ethanolamine	50-235
Phosphoethanolamine	1-13
Phosphoserine	3-13
Sarcosine	<= 1.1

Dietary Peptide Related Markers

	Reference Range
Anserine (dipeptide)	0.4-105.1
Carnosine (dipeptide)	1-28
1-Methylhistidine	38-988
β-Alanine	<= 22

Oxidative Stress Markers

Oxidative Stress Markers

		Reference Range
Lipid Peroxides (urine)	10.0	<=10.0 micromol/g Creat.
8-OHdG (urine)	8	<=16 mcg/g Creat.

Lab Comments

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

Metabolic Analysis Commentary

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

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.

Pyruvic Acid is measured to be elevated. Pyruvic acid, or pyruvate, is an important intermediate in the body's energy metabolism pathways. In glycolysis, glucose is oxidized to pyruvate and eventually to acetyl CoA, the major chemical fuel for the citric acid cycle in the mitochondria of our cells. Elevated pyruvate usually indicates weakness in the enzyme system that produces acetyl coenzyme A from pyruvate, the pyruvate dehydrogenase complex. This complex requires the cofactors lipoic acid, vitamin B1 as thiamin pyrophosphate, vitamin B2 as FAD, vitamin B3 as NAD, magnesium and ATP. A deficiency of any of these nutrient cofactors could cause elevated pyruvate levels. High pyruvate can also occur in (primary), type 1 insulin-dependent diabetes because the dehydrogenase enzyme's activity is stimulated by insulin. High pyruvate is not expected in type 2 diabetes (non-insulin dependent) or in insulin resistance. The toxic elements arsenic, antimony, mercury and cadmium can inhibit pyruvate dehydrogenase, causing elevated pyruvate. Genetic (autosomal recessive) deficiency in pyruvate dehydrogenase is rare with a frequency of occurrence of about one in 250,000.

A second enzyme that processes pyruvate is pyruvate carboxylase, responsible for the conversion of pyruvate into oxaloacetate, which can eventually lead to gluconeogenesis. This enzyme is biotin-dependent and is stimulated when there is a cellular abundance of acetyl CoA and ATP. Genetic deficiency of pyruvate carboxylase is also very rare, but nutrient deficiencies (biotin, manganese and magnesium) may cause mild/moderate elevations of pyruvate.

Symptoms consistent with elevated pyruvate include weakness and fatigue, ataxia and other neurological problems, which may occur in extreme cases and when lactic acid is also notably elevated. Severe pyruvic acidemia can cause psychomotor retardation in children that worsens with age.

Kynurenic Acid is high; it is a possible metabolite of tryptophan, and it comes directly from kynurenine, an intermediate in tryptophan metabolism. Metabolism of kynurenine is dependent upon reduced, phosphorylated vitamin

Commentary

B3 as NADPH and upon kynureninase which is very sensitive to vitamin B6 function as pyridoxal 5-phosphate. Usually, elevated kynurenic acid means that vitamin B6 is functionally deficient. This impacts the body's ability to form nicotinic acid (vitamin B3) and picolinic acid, both of which are eventual metabolites of kynurenine and tryptophan. Severe vitamin B3 deficiency results in pellagra. Vitamin B6 deficiency symptoms are consistent with elevated kynurenic acid: fatigue, irritability, GI distress, neuritis and neuropathy.

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.

Xanthurenic acid (XA) is a metabolite of tryptophan. When tryptophan intake is increased, the XA excretion increases. Xanthurenic acid secretion is higher among women in general, in women taking oral contraceptives, and in women with PMS, thus there appears a relationship to high XA excretion and high estrogen levels, likely to also manifest in pregnant women. An increased excretion of XA is also present in vitamin B6 deficiency, and is normalized by administration of vitamin B6.

Isovalerylglycine (IVG) is a product of leucine catabolism, and has been observed to be elevated in the urine with increased leucine intake, anorexia nervosa or an enzyme defect. There are numerous variants of the enzyme errors, some of which respond to combined treatment with carnitine and glycine by increasing the excretion (detoxification) of the IVG. There are additional cases where riboflavin appears to be an important way to correct the metabolic difficulties. High levels could be due to high leucine intake, dramatic dietary issues such as anorexia or potential enzyme defect, which are often accompanied by significant muscular symptoms such as weakness or hypotonia. High levels of IVG benefit therapeutically from carnitine, glycine, and riboflavin.

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

4-OH phenylacetic acid (p-hydroxyphenylacetic acid) is high. This compound is derived from gut microflora metabolism of L-tyrosine, as well as food flavonoids and phenols. Foods high in tyramine, (bananas, sharp cheeses,

Commentary

red wines) are also a likely source of increased urinary levels. 4OHPAA is also found in the urine via microbial metabolism of procyanadins as found in berries and grapeseed extracts. As such research would indicate, this biomarker tends to be higher in vegetarian-based diets compared to those with high meat intake. Liver cirrhosis may also result in elevated levels.[v] In the pediatric population, high levels may be related to bacterial overgrowth, short-gut or blind-loop syndromes.

Amino Acid Commentary

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Anserine, a dietary dipeptide, is higher than the reference range. This peptide comes from fish, fowl and some animal protein, principally from tuna, salmon, chicken, turkey, duck and rabbit. Anserine does not occur in human organs but dietary uptake is common for non-vegetarians. Elevated anserine may result from a dietary overload of protein, may be temporary or episodic, and may have no clinical consequence. However, zinc deficiency can be a cause of peptidase weakness; also, pancreatic dysfunction or digestive disorder can result in increased uptake and excretion of anserine. Elevated anserine together with subnormal levels of essential or semiessential amino acids is consistent with incomplete digestive proteolysis and malabsorption. Further diagnostic testing to assess maldigestion should be considered.

Beta-alanine is measured to be high in the urine. Often this amino acid is elevated when the dietary peptides anserine and carnosine are elevated because they contain beta-alanine. Beta-alanine also is a breakdown product of the pyrimidine bases cytosine and uracil. Catabolism of damaged or diseased body tissue, tumors and malignancy feature increased production and urinary disposal of beta-alanine. Besides elevated anserine or carnosine and accelerated catabolism of unwanted body tissue, the next most likely source of beta-alanine is imbalanced gut flora. Some beta-alanine is produced by normal gut flora which also make pantothenic acid from it. Elevated levels of staphylococcus or streptococcus, use of antibiotics, and breakdown of yeast or fungi in the body can result in increased levels of urinary beta-alanine. Continuously elevated beta-alanine can be detrimental by impairing renal conservation of taurine.

Taurine is measured to be elevated in the urine, which is consistent with excess dietary intake, or with urinary wasting due to poor renal conservation. 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. Urinary wasting can be secondary to generally increased renal clearance or nephrotic syndromes. Wasting can also occur when the similarly-structured amino acid beta-alanine is elevated or is present in kidney tubules. In molybdenum deficiency or sulfite oxidase impairment, elevated urine taurine results as a mode of sulfur excretion.

Renal wasting of taurine can be medically significant if it affects one or more of taurine's many important functions -

- Conjugation of cholesterol (as cholyl-coenzyme A) to form taurocholic acid, an important component of bile and a major utilization of cholesterol.
- Mediation of the flux of electrolyte elements at the plasma membrane of cells. Deficient taurine may result in increased cellular calcium and sodium and reduced magnesium.
- Increased resistance to aggregation of blood platelets and decreased thromboxane release if aggregation does occur.
- Sparing of magnesium - globally. Urinary magnesium wasting can result from taurine insufficiency. Magnesium deficiency may cause fatigue, depression, muscle tremor and hypertension.
- Antioxidant functions. Taurine scavenges excess hypochlorite ion, OCl-, in leukocytes and facilitates effective phagocytosis by enhancing survival of leukocytes. Deficient taurine may lead to increased inflammatory response to: toxins, foreign proteins, and xenobiotic chamicals including aldehydes, alcohols, amines, petroleum solvents, and chlorine or chlorite (bleach).
- Neurotransmitter functions. Taurine strongly influences neuronal concentrations and activities of GABA and glutamic acid. Taurine can have anti-convulsant and anti-epileptic effects.

Pathologies attributed to taurine insufficiency include: biliary insufficiency, fat malabsorption (steatorrhea), cardiac arrhythmia, congestive heart failure, poor vision, retinal degeneration, granulomatous disorder of neutrophils, immune dysfunction, enhanced inflammatory response to xenobiotics, convulsions and seizures.

The uncommon condition of overall taurine excess (hypertaurinuria with hypertaurinemia) usually is insufficiency of

Commentary

sulfite oxidase activity, possibly due to molybdenum deficiency. In this condition there is increased urinary sulfites and decreased sulfates. If molybdenum is deficient, uric acid levels are reduced, xanthine is increased and aldehyde detoxication is impaired (aldehyde intolerance).

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 moderate levels of urinary 1-methylhistidine are normal. However, high levels suggest increased uptake of short-chain peptides, possibly increased gut permeability, and increased hydrolysis of short-chain dietary peptides by peptidases in blood, liver and spleen. Elevated 1-methylhistidine suggests one or more of: dietary overload of anserine-source foods, 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.

Glycine and serine are elevated. Also, glycine and serine may be elevated in any condition of impaired nitrogen detoxication. There is interconversion between these two amino acids in body tissues, and each also has numerous, separate metabolic pathways. Many of these pathways are dependent upon coenzyme activity of vitamin B6 as pyridoxal 5-phosphate, while several are dependent upon folate, riboflavin as FAD, niacin as NAD, and magnesium as an enzyme activator. Adequacy of these nutrients, especially vitamin B6, should be investigated. Also, glycine and serine may be elevated in any condition of impaired nitrogen detoxication and they are elevated (with other amino acids) in generalized hyperaminoaciduria.

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

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

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

Lysine together with **arginine** and/or **ornithine** are elevated in the urine, consistent with **hyperdibasic aminoaciduria** . This condition may be a renal transport defect for lysine, ornithine and arginine (but not cystine). Impaired urea formation with hyperammonemia may occur due to insufficient levels of arginine and ornithine in the liver. The increased renal clearance of lysine, arginine and ornithine is considered to be genetic with autosomal recessive inheritance. A plasma amino acid analysis is suggested to evaluate blood levels of arginine, ornithine and lysine.

A second possibility is hyperlysinuria with hyperlysinemia due to impaired metabolism of lysine. The lysine excess competitively inhibits the arginase enzyme causing arginine also to be in excess. Hyperammonemia is possible if the arginase inhibition impairs formation of urea. "Lysinuric protein intolerance" is a descriptive term applied when hyperammonemia results from the metabolism disorder with lysine. Lysinemia with lysinuria can be acquired via metabolic cofactor insufficiency or can be of genetic origin. Metabolic cofactors that assist lysine metabolism are: alpha-ketoglutaric acid, niacin (as NADPH) and vitamin B1. Mitochondrial damage, toxicity, manganese deficiency, and aluminum excess can adversely affect these cofactors.

Oxidative Stress Commentary

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

Patient values for the Oxidative Stress Markers are within Genova Diagnostics reference ranges.

GENOVA DIAGNOSTICS EUROPE

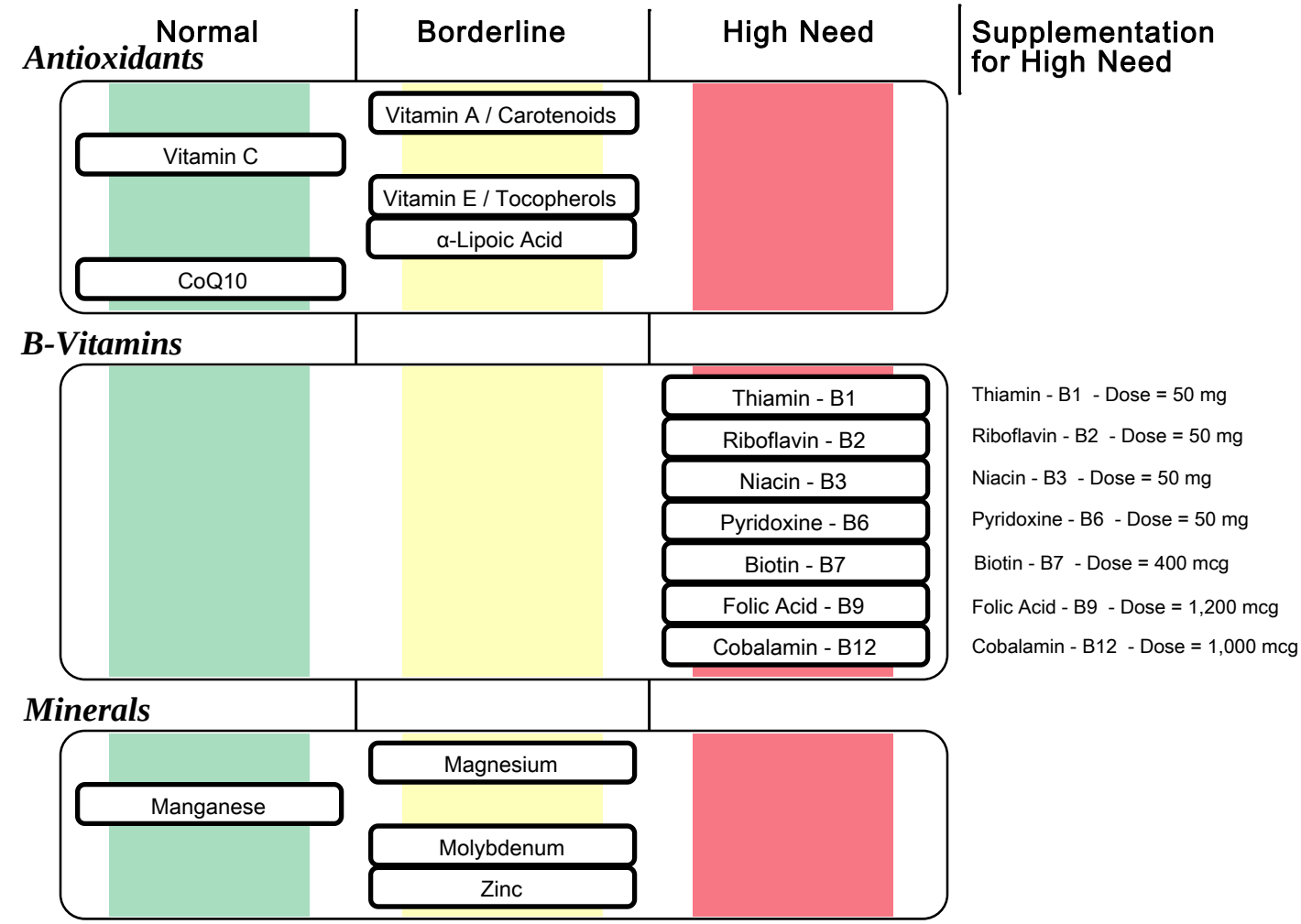
46-50 Coombe Road
New Malden
Surrey KT3 4QF

63 Zillicoa Street
Asheville, NC 28801 USA

Patient:
DOB:
Sex:
MRN:

Order Number:
Completed:
Received:
Collected:

ONE Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	5,000 IU	
Vitamin C	75 mg	250 mg	
Vitamin E / Tocopherols	22 IU	200 IU	
α-Lipoic Acid		100 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	50 mg	
Riboflavin - B2	1.1 mg	50 mg	
Niacin - B3	14 mg	50 mg	
Pyridoxine - B6	1.3 mg	50 mg	
Biotin - B7	30 mcg	400 mcg	
Folic Acid - B9	400 mcg	1,200 mcg	
Cobalamin - B12	2.4 mcg	1,000 mcg	
Minerals			
Magnesium	320 mg	600 mg	
Manganese	1.8 mg	3.0 mg	
Molybdenum	45 mcg	150 mcg	
Zinc	8 mg	20 mg	
Digestive Support			
Probiotics		50 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	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		

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

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

Key

Normal | Borderline | High Need

Interpretation At-A-Glance

Nutritional Needs

Antioxidants

Vitamin A / Carotenoids

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

Vitamin C

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

Vitamin E / Tocopherols

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

α-Lipoic Acid

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

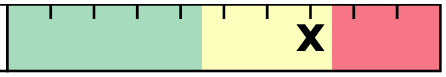
CoQ10

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

Glutathione

- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.

Plant-based Antioxidants



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

Key

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

Interpretation At-A-Glance

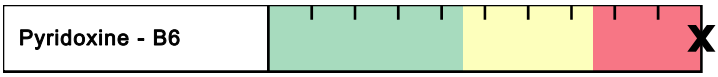
Nutritional Needs

B-Vitamins

Thiamin - B1

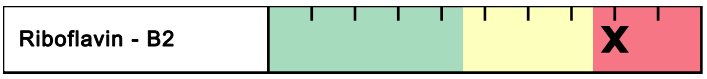
- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency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

Pyridoxine - B6



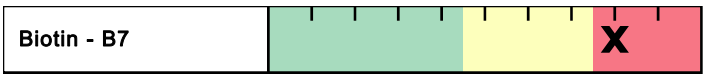
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or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

Riboflavin - B2



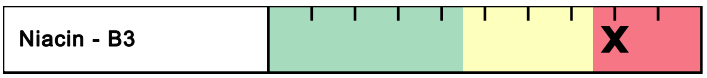
- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.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

Biotin - B7



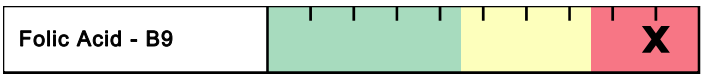
- Biotin is a cofactor for enzymes involved in functions such as fatty acid (FA) synthesis, mitochondrial FA oxidation, gluconeogenesis, and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN use, anticonvulsants, high-dose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

Niacin - B3



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

Folic Acid - B9



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

Cobalamin - B12

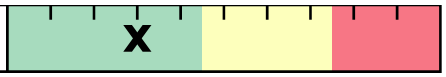
- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2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

Interpretation At-A-Glance

Nutritional Needs

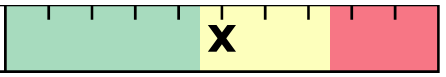
Minerals

Manganese



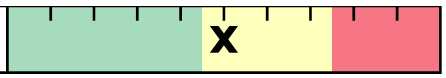
- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing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

Magnesium



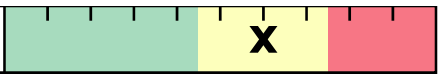
- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses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

Molybdenum



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

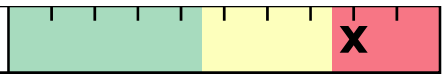
Zinc



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

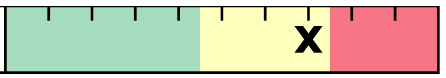
Digestive Support

Need for Probiotics



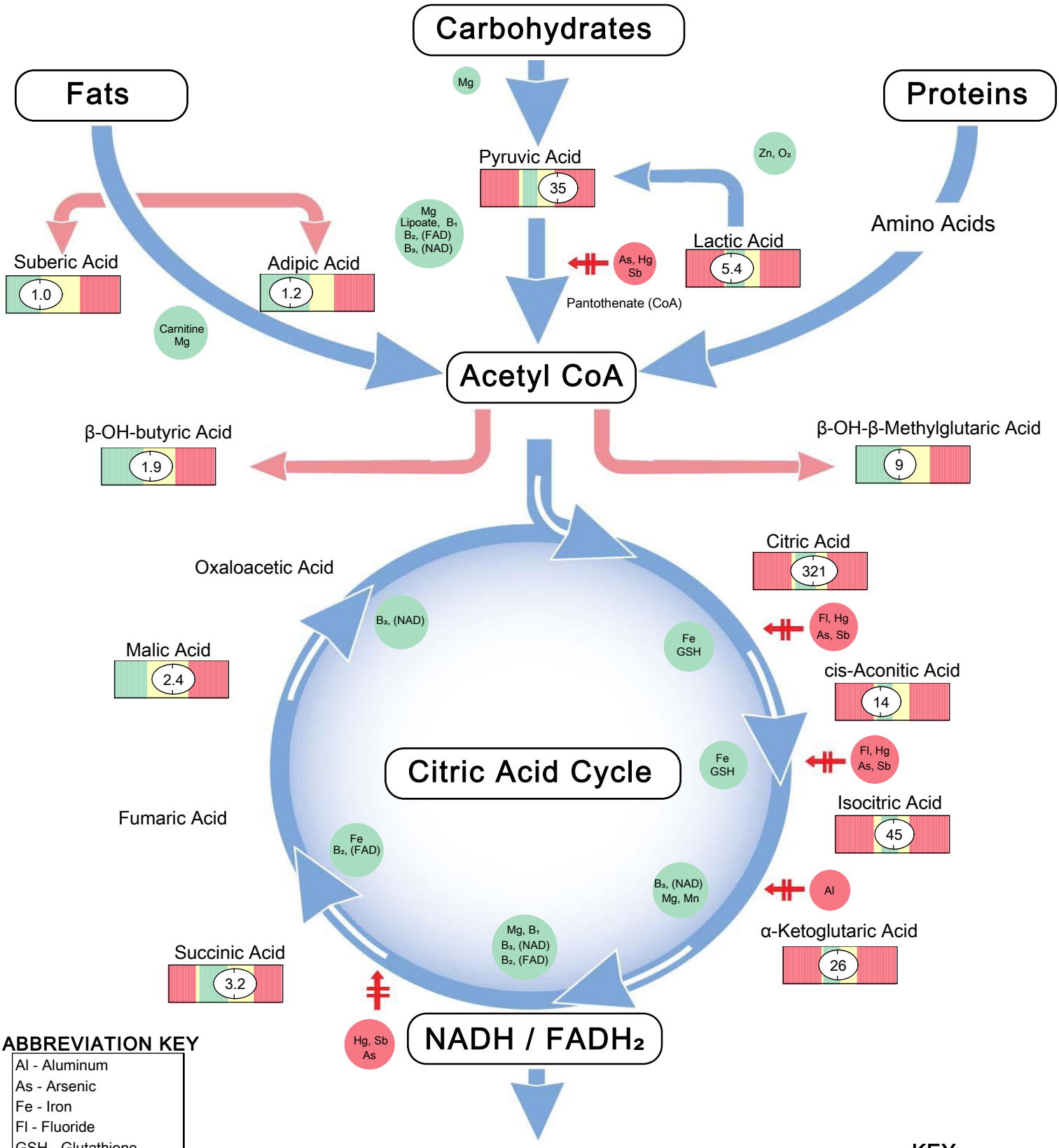
- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhancement of digestion & absorption; decreasing severity of diarrheal illness; modulation of immune function & intestinal permeability.
- Alterations of gastrointestinal microflora may result from C-section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

Need for Pancreatic Enzymes



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

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

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

Metabolic Analysis Markers (Urine)

Malabsorption and Dysbiosis Markers

Malabsorption Markers

		Reference Range
Indoleacetic Acid (IAA)	2.6	<= 4.2
Phenylacetic Acid (PAA)	0.16	<= 0.12

Bacterial Dysbiosis Markers

		Reference Range
Dihydroxyphenylpropionic Acid (DHPPA)	3.1	<= 5.3
3-Hydroxyphenylacetic Acid	6.3	<= 8.1
4-Hydroxyphenylacetic Acid	30	<= 29
Benzoic Acid	0.09	<= 0.05
Hippuric Acid	237	<= 603

Yeast / Fungal Dysbiosis Markers

		Reference Range
Arabinose	88	<= 96
Citramalic Acid	4.3	<= 5.8
Tartaric Acid	7	<= 15

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism

		Reference Range
Lactic Acid	5.4	1.9-19.8
Pyruvic Acid	35	7-32
β-OH-Butyric Acid (BHBA)	1.9	<= 2.8

Energy Metabolism

		Reference Range
Citric Acid	321	40-520
Cis-Aconitic Acid	14	10-36
Isocitric Acid	45	22-65
α-Ketoglutaric Acid (AKG)	26	4-52
Succinic Acid	3.2	0.4-4.6
Malic Acid	2.4	<= 3.0
β-OH-β-Methylglutaric Acid (HMG)	9	<= 15

Fatty Acid Metabolism

		Reference Range
Adipic Acid	1.2	<= 2.8
Suberic Acid	1.0	<= 2.1

Creatinine Concentration

		Reference Range
Creatinine ◆	7.3	3.1-19.5 mmol/L

Neurotransmitter Metabolites

		Reference Range
Vanilmandelic Acid	2.0	0.4-3.6
Homovanillic Acid	3.5	1.2-5.3
5-OH-indoleacetic Acid	10.6	3.8-12.1
3-Methyl-4-OH-phenylglycol	0.09	0.02-0.22
Kynurenic Acid	9.6	<= 7.1
Quinolinic Acid	3.6	<= 9.1
Kynurenic / Quinolinic Ratio	2.67	>= 0.44

Vitamin Markers

		Reference Range
α-Ketoadipic Acid	0.7	<= 1.7
α-Ketoisovaleric Acid	0.56	<= 0.97
α-Ketoisocaproic Acid	0.87	<= 0.89
α-Keto-β-Methylvaleric Acid	1.8	<= 2.1
Formiminoglutamic Acid (FIGlu)	2.3	<= 1.5
Glutaric Acid	0.32	<= 0.51
Isovalerylglycine	4.7	<= 3.7
Methylmalonic Acid	1.7	<= 1.9
Xanthurenic Acid	1.31	<= 0.96
3-Hydroxypropionic Acid	14	5-22
3-Hydroxyisovaleric Acid	21	<= 29

Toxin & Detoxification Markers

		Reference Range
α-Ketophenylacetic Acid (from Styrene)	0.26	<= 0.46
α-Hydroxyisobutyric Acid (from MTBE)	8.6	<= 6.7
Orotic Acid	0.74	0.33-1.01
Pyroglutamic Acid	34	16-34

Tyrosine Metabolism

		Reference Range
Homogentisic Acid	14	<= 19
2-Hydroxyphenylacetic Acid	0.73	<= 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 (Urine FMV)

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

Nutritionally Essential Amino Acids

Amino Acid		Reference Range
Arginine	36	3-43
Histidine	860	124-894
Isoleucine	20	3-28
Leucine	46	4-46
Lysine	233	11-175
Methionine	22	2-18
Phenylalanine	57	8-71
Taurine	489	21-424
Threonine	146	17-135
Tryptophan	42	5-53
Valine	46	7-49

Nonessential Protein Amino Acids

Amino Acid		Reference Range
Alanine	188	63-356
Asparagine	122	25-166
Aspartic Acid	16	<= 14
Cysteine (FMV urine)	37	8-74
Cystine (FMV Urine)	57	10-104
γ-Aminobutyric Acid	4	<= 5
Glutamic Acid	17	4-27
Glutamine	331	110-632
Proline	5	1-13
Tyrosine	87	11-135

Creatinine Concentration

		Reference Range
Creatinine ◆	7.6	3.1-19.5 mmol/L

Amino Acid reference ranges are age specific.

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

Methodology: LC/MS/MS, Enzymatic and Alkaline Picrate

Intermediary Metabolites

B Vitamin Markers		Reference Range
α-Aminoadipic	41	2-47
α-Amino-N-butyric Acid	9	2-25
β-Aminoisobutyric Acid	66	11-160
Cystathionine	29	2-68
3-Methylhistidine	254	44-281

Urea Cycle Markers

Citrulline	3.9	0.6-3.9
Ornithine	31	2-21
Urea ◆	315	168-465 mmol/g creatinine

Glycine/Serine Metabolites

Glycine	911	95-683
Serine	180	40-163
Ethanolamine	194	50-235
Phosphoethanolamine	9	1-13
Phosphoserine	7	3-13
Sarcosine	1.6	<= 1.1

Dietary Peptide Related Markers

		Reference Range
Anserine (dipeptide)	195.8	0.4-105.1
Carnosine (dipeptide)	7	1-28
1-Methylhistidine	2,459	38-988
β-Alanine	57	<= 22

Oxidative Stress Markers

Oxidative Stress Markers

		Reference Range
Lipid Peroxides (urine)	10.0	<=10.0 micromol/g Creat.
8-OHdG (urine)	8	<=16 mcg/g Creat.

Lab Comments

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.