Elemental Markers (RBCs)

Toxic Elements

Element	Reference Range	Reference Range
Lead	0.027	<= 0.048 mcg/g
Mercury	<dl	<= 0.0039 mcg/g
Antimony	0.000	<= 0.002 mcg/g
Arsenic	0.007	<= 0.071 mcg/g
Cadmium	<dl	<= 0.001 mcg/g
Tin	<dl	<= 0.0009 mcg/g

Nutrient Elements

Element	Reference Range	Reference Range
Copper	0.623	0.466-0.721 mcg/g
Magnesium	43.3	30.1-56.5 mcg/g
Manganese	0.011	0.007-0.038 mcg/g
Potassium	2,764	2,220-3,626 mcg/g
Selenium	0.29	0.25-0.76 mcg/g
Zinc	10.7	7.8-13.1 mcg/g

The Reference Range is a statistical interval based upon those values between the 2.5th percentile and the 97.5th percentile of the reference population. The dotted box within the reference range depicts an optimal target interval. Values within the reference range but outside the dotted box are not necessarily abnormal. This representation has been established, based upon current medical literature, scientific analysis of reference range study data points and clinical experience. These Elemental reference ranges are based on an adult population.

Oxidative Stress Markers

Oxidative Stress Markers

Analyte	Reference Range
Glutathione	1,699 >= 669 micromol/L
Lipid Peroxides	7.4 <= 10.0 micromol/L
8-OHdG	12 <= 16 mcg/g Creat.
Coenzyme Q10, Ubiquinone (plasma)	0.81 0.43-1.49 mcg/mL

Commentary

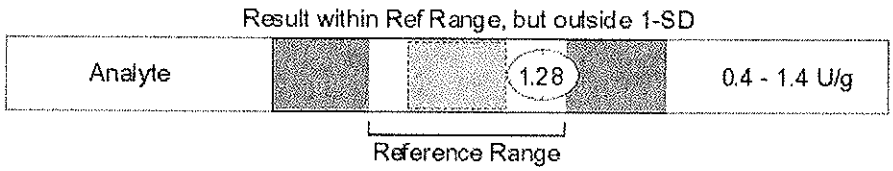
Lab Comments
Urine amino acid results confirmed by repeat analysis. 02/21/2011 FS
Organic Acids assay repeated to confirm results. ck 03/01/2011

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆ as cleared by the U.S. Food and Drug Administration, assays are For Research Use Only.

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.

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

One Standard Deviation (1 S.D.) is a statistical interval representing 68% of the reference population. Values between 1 and 2 S.D. are not necessarily abnormal. Clinical correlation is suggested. (See example below)



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

Commentary

MARKERS CHARACTERISTIC OF INTESTINAL MALABSORPTION AND/OR DYSBIOSIS

Three of these chemical markers are formed by yeast/fungal organisms, usually but not necessarily in the gut: arabinose, beta-ketoglutaric acid and citramalic acid. Citramalate can also be formed by anaerobic bacteria. The remaining chemical markers of this section are the result of malabsorption, gut bacterial action, and in some cases, hepatic detoxication of chemicals produced by dysbiotic flora.

NEUROTRANSMITTER METABOLITES

These metabolites are end products of neurotransmitter metabolism, either the adrenal catecholamines or serotonin (5-HIAA). Abnormal levels correlate with mood swings, mental dysperceptions, anxiety, or depressive disorders.

All of these metabolites are within their reference ranges; there are no abnormals.

ANALYTES CHARACTERISTIC OF CELLULAR ENERGY AND MITOCHONDRIAL FUNCTION

These markers are metabolites from four important biochemical pathways in the body, all of which significantly impact the production and availability of energy at the cellular level: glycolysis, the citric acid cycle (Krebs cycle) and both beta-oxidation and omega-oxidation of fatty acids. These analytes provide unique insight into macronutrient catabolism and mitochondrial function in cells. Abnormal levels may be associated with fatigue, malaise, myalgia, headache, muscle weakness, myopathy, hypotonia, or acid-base imbalance. This test is intended to be a diagnostic aid for acquired disorders in these pathways. It is not intended for diagnosis of inborn errors of organic acid metabolism, as this would require extensive molecular genetics testing. However, significantly abnormal findings could be consistent with such inborn errors.

If significant abnormalities persist after removal of toxics, supplementation of appropriate nutrients, dietary and hormonal adjustments, and correction of intestinal dysbiosis or infection, it is suggested that the patient be referred to a medical center with capabilities for diagnosis and treatment of congenital metabolic defects.

Beta-hydroxybutyric Acid (BHBA) is elevated. BHBA is a "ketone body". Excess BHBA is consistent with ketosis or ketoacidosis (a type of metabolic acidosis). Under normal conditions, carbohydrates or fatty acids are metabolized to acetyl CoA; the acetyl CoA then enters the mitochondria and combines with oxaloacetic acid to form citric acid, in the first "step" of the citric acid cycle. In the case of a high-fat diet or inadequate carbohydrates (leading to low oxaloacetic acid and increased breakdown of fat for energy), more acetyl CoA is formed, which then forms acetoacetyl CoA and eventually leads to the formation of BHBA and other ketones.

The ketone BHBA cannot be metabolized in liver cells, and it is transported via the blood stream to muscle, brain, heart and kidney tissues for oxidation, to meet their energy needs. Ketoacidosis may occur with: fasting, anorexia or starvation, diabetes, or during and following an extended period of severe exercise. Ketogenic diets may also result in elevated urine BHBA. Less common conditions causing ketoacidosis are those originating from metabolic or (severe) nutritional deficiencies such as methylmalonic aciduria, due to B12 deficiency.

The severity of ketosis is not accurately reflected by the degree of ketonuria. Only a small amount of the body burden

Commentary

of ketones is excreted in urine; most must be oxidized in extrahepatic tissue using (and depleting) available oxygen.

COFACTOR-DEPENDENT AND METABOLITES FROM AMINO ACID CATABOLISM

These analytes are formed from essential and protein amino acids via amino group transfer or by other enzymatic transformations. Many are sensitive to vitamin functions as coenzymes and to minerals as enzyme activators. Excesses or deficiencies may lead to various conditions depending upon the particular metabolic imbalance, including fatigue, headaches, myalgias, metabolic acidoses, dietary intolerances, neurological problems, and cognitive disorders.

Commentary

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REPRESENTATIVENESS INDEX

Urine amino acid levels usually are representative of blood levels and reflect dietary uptake and metabolism as well as excretion. However, abnormal renal clearance, loss of urine during the collection period, decay or spoilage, and presence of blood in the urine could cause the urine specimen to be unrepresentative. The possibility of such problems can be judged from analytical measurements which are portrayed in the first section of the report: Markers for Urine Representativeness.

The **glutamine/glutamate ratio** can indicate specimen decay. When aged or improperly preserved, urine glutamine decays to glutamic acid and ammonia. However, in metabolic acidosis some glutamine is transformed into glutamic acid and ammonium ion as a pH-balancing mechanism. Also, high glutamic acid occurs in gout. Hence, low glutamine/glutamate ratio may reflect decay or it may be of metabolic origin. High glutamine/glutamate ratio is metabolic and does not reflect on specimen representativeness.

The **ammonia concentration**, if elevated, usually indicates overall decay of amino acids. An exception would be elevated ammonia concentration with hyperammonemia of metabolic or bacterial origin. Very low ammonia concentration suggests low urine nitrogen levels and may occur in protein-deficient diets. Blood amino acid levels may then be normal or low-normal.

The **arginine/ornithine ratio** generally reflects whether the sample is purely urine or whether hematuria is present. A low ratio is consistent with blood in the urine. This is not foolproof, because high ornithine relative to arginine also may occur with a specific urea cycle weakness (OCT enzyme dysfunction, rare), and with pyridoxal phosphate or transamination weakness affecting ornithine. Urine should not be collected for acid analysis by women during menses. Blood in urine can notably distort the results.

The computer scores the above four Markers for Representativeness and computes a Representativeness Index. An index of 10 means all markers are within expected limits. **An index below 5 suggests a repeat amino acid analysis with a new urine specimen.**

Lysine is low in the urine. This nutritionally essential amino acid is needed for formation of body proteins and enzymes. Transaminase enzymes, those that catalyze transfer of amino groups from amino acids to organic or ketoacids, include lysine (as a lysyl residue) which is the anchor point for coenzyme pyridoxal phosphate. Much of the coenzyme activity of vitamin B6 is linked to lysine by this structure. Lysine is abundant in protein foods - meat, fish, fowl, and legumes - but may be insufficient in some vegetarian diets, particularly those based on corn, rice or cereal grains. Symptoms consistent with lysine insufficiency include weight loss, poor appetite, muscle weakness, poor muscle tone, growth failure (infants, children), and anemia.

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.

Beta-aminoisobutyric acid (B-AIB) is a product of catabolism of pyrimidine nucleotides and it is an intermediate of valine-to-succinic acid metabolism. In valine-to-succinic acid metabolism, B-AIB is directly formed from methylmalonic acid semialdehyde. B-AIB is elevated for this individual which implies one of four possible conditions.

1. Vitamin B12 coenzyme function (as adenosylcobalamin) is weak. Elevated methylmalonic acid in urine

Commentary

(methylmalonic aciduria) would confirm this. Vitamin B12 deficiency or adenosylcobalamin coenzyme defect would be causative.

2. Vitamin B6 coenzyme function (as pyridoxal phosphate) is weak. B-AIB also transaminates to its keto analog.

3. The specific B-AIB-to-pyruvic acid transaminase is weak or absent. This is considered a benign variant of metabolism and is present in about 25% of Chinese and Japanese individuals and in about 8% of Scandinavian and Northwestern Europeans.

4. Accelerated catabolism of DNA and RNA is occurring. Catabolism of damaged or diseased tissue, tumors and malignancy feature increased formation and excretion of B-AIB.

In addition to the above conditions, Downs syndrome individuals usually are B-AIB excretors. It is not known whether one of the above four mechanisms is responsible.

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.

Commentary

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

Tryptophan is elevated in the urine. Other elevations that would be expected in Hartnup syndrome are not present, so the tryptophan elevation probably is not due to a general (hereditary) transport defect for monoamine-monocarboxylic acids. This elevation of tryptophan suggests lowered blood tryptophan and perhaps low serotonin. Blood plasma tryptophan may be measured by plasma amino acid analysis; serotonin should be measured in blood platelets. Symptoms consistent with tryptophan deficiency are mainly those of serotonin insufficiency and may include: insomnia, anxiety, enhanced response to external stimuli (light, sound), and abnormal food cravings.

The amino acid **methionine** is measured to be elevated in this individual's urine. This implies rate-limited or impaired metabolism of this essential amino acid. Methionine leads to: S-adenosylmethionine ("SAM", a primary methylating agent in metabolism), cysteine (the limiting factor for glutathione formation and a functional part of many peptides and proteins), and to taurine (an antioxidant, mediator of electrolyte flux at the cellular level, and a conjugating agent for cholesterol).

A rate limitation in metabolism of methionine could have far-reaching consequences and multiple symptomatology. For example, impaired methylation with disordered metabolism of adrenal catecholamines is postulated to be one possible cause of chronic mental depression. The rate limitation might be with methionine itself. Methionine becomes SAM in a magnesium-dependent process that combines methionine with adenosine triphosphate ("ATP"). The SAM-forming enzyme is methionine-adenosyl transferase which has several isozymes in humans. These isozymes are present in liver, erythrocytes, lymphocytes and fibroblasts. Cell mitochondrial diseases or toxic damage may limit ATP resulting in rate-limited formation of SAM. Administration of magnesium is anecdotally credited with lowering excess methionine and normalizing SAM levels.

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

Commentary

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.

Citrulline , a urea cycle intermediate, is elevated. Also, elevations are noted for some of the amino acids that are characteristically high when nitrogen detoxication is rate-limited. This may indicate weakness in the citrulline-to-argininosuccinic acid enzyme which is cytosolic and functions in the liver as part of the urea cycle and also functions in kidney fibroblasts. It is assisted by ATP (magnesium dependent), and aspartic acid is a necessary cosubstrate. If the urea cycle function is impaired, consistent findings would be: elevated venous ammonia (hyperammonemia), reduced plasma alpha-ketoglutaric acid (by organic acid analysis), and reduced blood and urine urea levels. A venous blood ammonia determination, 2-4 hours postprandial, can be used to assess the ammonia status.

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.

Dihomo Gamma Linolenic Acid (DGLA) is below the reference range. DGLA is the main precursor fat for the

Commentary

production of highly anti-inflammatory eicosanoids, especially the series 1 prostaglandins. Low DGLA is often associated with inflammatory conditions such as heart disease, arthritis, inflammatory bowel disorders, eczema, and psoriasis. Since DGLA-derived eicosanoids also promote smooth muscle relaxation, low DGLA levels may contribute to increased smooth muscle contraction, and subsequently to conditions like hypertension, asthma, painful menstruation, and irritable bowel syndrome.

Low DGLA can result from impaired conversion of linoleic acid into gamma-linolenic acid (and subsequently into DGLA) or from an increased conversion of DGLA into arachidonic acid or both. Delta-6 desaturase is the enzyme responsible for converting LA into GLA and may be impaired with age, alcohol use, genetic defect, or nutrient deficiency. An elevated linoleic/DGLA ratio or an elevated eicosadienoic/DGLA ratio (see p.3 of this report) would strongly suggest impaired delta-6 desaturase activity. Supplementation with GLA-containing oils like evening primrose, borage or black currant seed oils bypasses delta-6 desaturase.

A low DGLA/arachidonic acid ratio (see p.3 of this report) would indicate a likely increased activity of delta-5 desaturase. Insulin activates delta-5 desaturase. A high carbohydrate (sugars and starch) diet increases insulin secretion and action in the body. Consumption of a higher protein and higher fiber and complex carbohydrate diet reduces insulin action in the body. Eicosapentaenoic acid (EPA) supplementation, found in fish and fish oils, has also been shown to reduce delta-5 desaturase activity, reducing the conversion of DGLA into AA.

Oleic acid is within the reference range, but below the functional physiologic range. Oleic acid is important in maintaining cell membrane fluidity. Low oleic acid may indicate decreased delta-9 desaturase activity. Vitamin and mineral cofactor supplementation should be considered. These include B vitamins (especially B2, B3, and B6), vitamin C, zinc, and magnesium.

Olive oil is ~80% oleic acid; using olive oil as the primary dietary oil can increase oleic acid in cell membrane phospholipids. High-oleic safflower oil and high-oleic sunflower oil are available in health food stores and also constitute excellent sources of oleic acid.

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.

CLINICAL APPLICATIONS

The grouping of various analytes and ratios into clinical condition categories is based on speculative biochemical knowledge and is intended for research purposes only. Such groupings are not intended to diagnose any specific disease or condition. As always, laboratory findings are but a small part of the overall diagnostic process and should be correlated with patient history, signs and symptoms and other laboratory findings.

Inflammation Markers

Commentary

Eicosanoids made from 20-carbon essential fatty acids are responsible for initiating, perpetuating and terminating inflammation. Inflammation is not a bad thing in itself; inflammation is the first step of tissue repair and helps to turn on our immune system. However, if the inflammation response gets out of hand, it can be devastating to our health. Fatty acid balance is necessary to control the inflammation process. The inflammation index reflects the patient's current tendency towards inflammation and inflammatory conditions.

Membrane Fluidity

Membrane fluidity is critical for the health of the cell and hence of the body. On the one hand, the membrane needs to be rigid enough to provide sound cellular structural architecture. On the other, the membrane needs to be fluid enough to allow nutrients in and waste products out, as well as to permit the free floating of cellular receptors in its phospholipid bi-layer. The more saturated the fats in a membrane are, the more rigid the membrane, and this is especially true of very long chain fatty acids like lignoceric and nervonic acids. Conversely, the more polyunsaturated the fats in a membrane are, the more fluid the membrane. DHA, being the most polyunsaturated fatty acid in the body with six double bonds, does more than any other fat to promote fluidity. Indeed, cells with low DHA in their phospholipid membrane have been shown to have altered hormone-receptor binding capacity. For example, some hormones like estrogen, progesterone, and angiotensin bind tighter to their receptors, causing increased cellular stimulation. Other hormones like insulin and serotonin will hardly bind at all to their receptors. Researchers speculate that this may help explain the association between low DHA levels and diseases like breast cancer, PMS, hypertension, diabetes, and depression.

Desaturase Activity

The relative amount of fatty acid substrates and products of desaturase reactions allows us to speculate on the functional capacity of those enzyme systems. They may be impaired, up-regulated, or functioning within normal limits. All desaturase enzymes are thought to be somewhat impaired if excess trans fatty acids are in the cell. Elaidic acid is the most commonly found trans fatty acid found in cell membranes.

The linoleic/DGLA ratio is high which may indicate impaired delta-6 desaturase enzyme activity. Impaired delta-6 activity would be confirmed if the eicosadienoic/DGLA ratio were also high since eicosadienoic acid represents the elongation of linoleic acid before it has undergone desaturation. However, a high linoleic/DGLA ratio, alone, is sufficient to suggest impaired delta-6 activity. Typical remedies include supplementing with vitamins B2, B3, B6, C, and the minerals zinc and magnesium. The enzyme may be bypassed by supplementing oils containing pre-formed GLA oils such as evening primrose, borage, or black currant seed oil.

The DGLA/AA ratio is low, suggesting up-regulated delta-5 desaturase activity. Excess insulin secretion and action is a likely contributor to increased delta-5 activity, and the most likely cause of excess insulin is a high carbohydrate (sugar and starch) diet. Eating a higher protein, higher fiber diet may be beneficial. Also EPA (fish oil) supplementation has been shown to slow the activity of delta-5 desaturase, since EPA is a normal product of this enzyme.

Insulin Dynamics

Cells with decreased membrane fluidity (higher % saturated fats and lower DHA and other PUFAs) have been shown to be insulin resistant (insulin cannot bind to its receptors on the cell surface). Insulin resistance is believed to play a

Commentary

significant role in the development of heart disease, hypertension, diabetes and central obesity.

A high-carbohydrate (sugar and starch), low-fiber diet is believed to play a role in the development of insulin resistance. Ironically, while cells are still sensitive to increased insulin production, delta-6 and delta-5 desaturase activity is dramatically increased, generally leading to increased arachidonic acid synthesis and a greater tendency to inflammatory conditions. As insulin resistance develops, delta-6, delta-5, and delta-9 desaturase activity declines, resulting in increasing amounts of saturated fats being incorporated into cell membranes. This further exacerbates the insulin resistance. Polyunsaturated fatty acid supplementation, especially DHA supplementation, may be clinically helpful as part of a comprehensive treatment regimen in correcting insulin resistance. Insulin dynamics may be more fully explored using additional laboratory testing that measures fasting and 2 hour post-prandial insulin and glucose levels.

Elemental Markers (RBCs)

Commentary

All of the measured erythrocyte elements are within the laboratory reference range.