The Great Plains Laboratory, Inc.

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Requisition #:	454276	*Physician:*	AMY HERLIHY
Patient Name:	Sean Gubbins	*Date of Collection:*	8/9/2016
Patient Age:	8	*Time of Collection:*	00:00 AM
Patient Sex:	M	*Print Date:*	08/18/2016

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	≤ 5.0		1.8	1.8
2 5-Hydroxymethyl-2-furoic	≤ 28		5.0	5.0
3 3-Oxoglutaric	≤ 0.46		0	0.00
4 Furan-2,5-dicarboxylic	≤ 18		4.7	4.7
5 Furancarbonylglycine	≤ 3.1		1.5	1.5
6 Tartaric	≤ 6.5		0.72	0.72
7 Arabinose	≤ 50	H	100	100
8 Carboxycitric	≤ 25		0.23	0.23
9 Tricarballylic	≤ 1.3		0.32	0.32
Bacterial Markers				
10 Hippuric	≤ 680		261	261
11 2-Hydroxyphenylacetic	≤ 0.86		0.27	0.27
12 4-Hydroxybenzoic	≤ 3.0		0.72	0.72
13 4-Hydroxyhippuric	≤ 30		5.4	5.4
14 DHPPA (Beneficial Bacteria)	≤ 0.59		0.13	0.13
Clostridia Bacterial Markers				
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	2.0 - 32		12	12
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 220		52	52
17 4-Cresol *(C. difficile)*	≤ 84		24	24
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	0.60 - 14	L	0.52	0.52

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	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
Oxalate Metabolites					
19	Glyceric	0.74 - 13		3.4	3.4
20	Glycolic	27 - 221		81	81
21	Oxalic	35 - 185		114	114
Glycolytic Cycle Metabolites					
22	Lactic	2.6 - 48		14	14
23	Pyruvic	0.32 - 8.8		3.5	3.5
Mitochondrial Markers - Krebs Cycle Metabolites					
24	Succinic	≤ 23		6.4	6.4
25	Fumaric	≤ 1.8		0.45	0.45
26	Malic	≤ 2.3		1.6	1.6
27	2-Oxoglutaric	≤ 96		45	45
28	Aconitic	9.8 - 39		12	12
29	Citric	≤ 597		351	351
Mitochondrial Markers - Amino Acid Metabolites					
30	3-Methylglutaric	0.01 - 0.97		0.27	0.27
31	3-Hydroxyglutaric	≤ 16		7.1	7.1
32	3-Methylglutaconic	≤ 6.9		1.9	1.9
Neurotransmitter Metabolites					
Phenylalanine and Tyrosine Metabolites					
33	Homovanillic (HVA) *(dopamine)*	0.49 - 13		2.0	2.0
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.72 - 6.4		2.4	2.4
35	HVA / VMA Ratio	0.23 - 2.8		0.82	0.82
Tryptophan Metabolites					
36	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 11		0.42	0.42
37	Quinolinic	0.48 - 8.8		3.8	3.8
38	Kynurenic	≤ 4.2		1.6	1.6
39	Quinolinic / 5-HIAA Ratio	≤ 2.5	H	9.1	9.1

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	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
Pyrimidine Metabolites - Folate Metabolism					
40	Uracil	≤ 16		3.2	3.2
41	Thymine	≤ 0.91		0.14	0.14
Ketone and Fatty Acid Oxidation					
42	3-Hydroxybutyric	≤ 4.8	H	6.7	6.7
43	Acetoacetic	≤ 10	H	13	13
44	4-Hydroxybutyric	≤ 4.7		2.5	2.5
45	Ethylmalonic	0.06 - 4.8		3.5	3.5
46	Methylsuccinic	≤ 4.0		1.6	1.6
47	Adipic	0.19 - 6.5	H	12	12
48	Suberic	≤ 7.0		3.5	3.5
49	Sebacic	≤ 0.61		0.07	0.07
Nutritional Markers					
Vitamin B12					
50	Methylmalonic ✱	≤ 5.2		4.2	4.2
Vitamin B6					
51	Pyridoxic (B6)	≤ 53		9.9	9.9
Vitamin B5					
52	Pantothenic (B5)	≤ 14		1.9	1.9
Vitamin B2 (Riboflavin)					
53	Glutaric ✱	≤ 1.4	H	1.7	1.7
Vitamin C					
54	Ascorbic	10 - 200	L	0	0.00
Vitamin Q10 (CoQ10)					
55	3-Hydroxy-3-methylglutaric ✱	≤ 88		34	34
Glutathione Precursor and Chelating Agent					
56	N-Acetylcysteine (NAC)	≤ 0.34		0	0.00
Biotin (Vitamin H)					
57	Methylcitric ✱	≤ 5.7		3.2	3.2

✱ ***A high value for this marker may indicate a deficiency of this vitamin.***

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	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
	Indicators of Detoxification				
	Glutathione				
58	Pyroglutamic ✸	13 - 62		26	26
59	2-Hydroxybutyric ✸	0.19 - 2.0	H	3.2	3.2
	Ammonia Excess				
60	Orotic	0.04 - 0.80		0.69	0.69
	Aspartame, salicylates, or GI bacteria				
61	2-Hydroxyhippuric	≤ 1.2		0.36	0.36

✸ ***A high value for this marker may indicate a Glutathione deficiency.***

Amino Acid Metabolites

	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
62	2-Hydroxyisovaleric	≤ 0.55		0	0.00
63	2-Oxoisovaleric	≤ 2.5		0	0.00
64	3-Methyl-2-oxovaleric	≤ 1.1		0.24	0.24
65	2-Hydroxyisocaproic	≤ 0.68		0	0.00
66	2-Oxoisocaproic	≤ 0.46		0.28	0.28
67	2-Oxo-4-methiolbutyric	≤ 0.33		0.13	0.13
68	Mandelic	≤ 0.30		0	0.00
69	Phenyllactic	≤ 0.19		0.03	0.03
70	Phenylpyruvic	≤ 4.0		3.3	3.3
71	Homogentisic	≤ 0.61		0	0.00
72	4-Hydroxyphenyllactic	0.05 - 1.1		0.23	0.23
73	N-Acetylaspartic	≤ 5.9		1.2	1.2
74	Malonic	≤ 18		2.9	2.9

Mineral Metabolism

	Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Under Age 13
75	Phosphoric	1 000 - 7 300		2 329	2329

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Indicator of Fluid Intake

76	*Creatinine	178	mg/dL

*The creatinine test is performed to adjust metabolic marker results for differences in fluid intake. Urinary creatinine has limited diagnostic value due to variability as a result of recent fluid intake. Samples are rejected if creatinine is below 20 mg/dL unless the client requests results knowing of our rejection criteria.

Explanation of Report Format

The reference ranges for organic acids were established using samples collected from typical individuals of all ages with no known physiological or psychological disorders. The ranges were determined by calculating the mean and standard deviation (SD) and are defined as ± 2SD of the mean. Reference ranges are age and gender specific, consisting of Male Adult (≥13 years), Female Adult (≥13 years), Male Child (<13 years), and Female Child (<13 years).

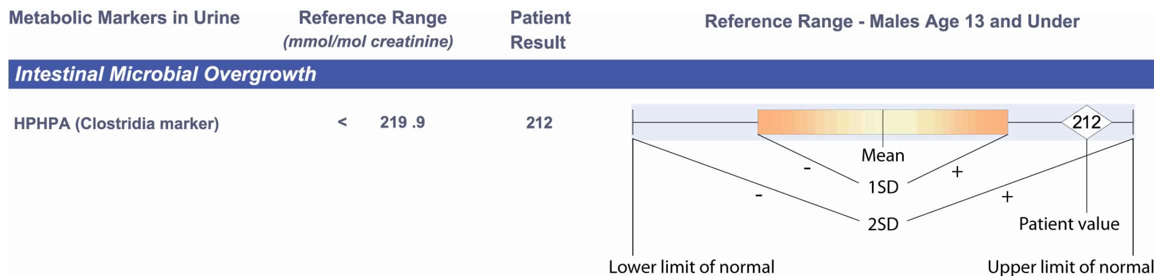
There are two types of graphical representations of patient values found in the new report format of both the standard Organic Acids Test and the Microbial Organic Acids Test.

The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

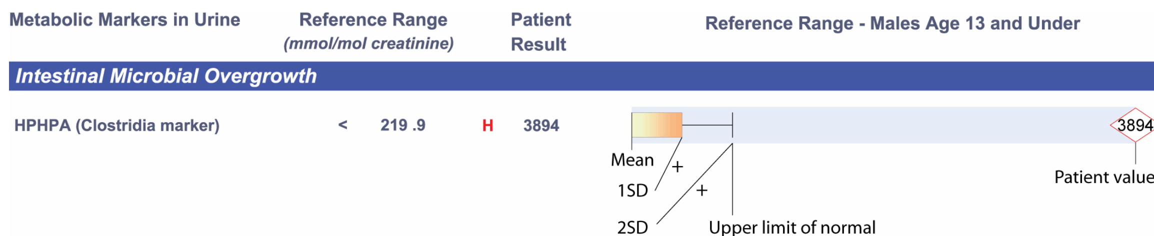
The second graph will occur when the value of the patient exceeds the upper limit of normal. In such cases, the graphical reference range is “shrunk” so that the degree of abnormality can be appreciated at a glance. In this case, the lower limits of normal are not shown, only the upper limit of normal is shown.

In both cases, the value of the patient is given to the left of the graph and is repeated on the graph inside a diamond. If the value is within the normal range, the diamond will be outlined in black. If the value is high or low, the diamond will be outlined in red.

Example of Value Within Reference Range



Example of Elevated Value



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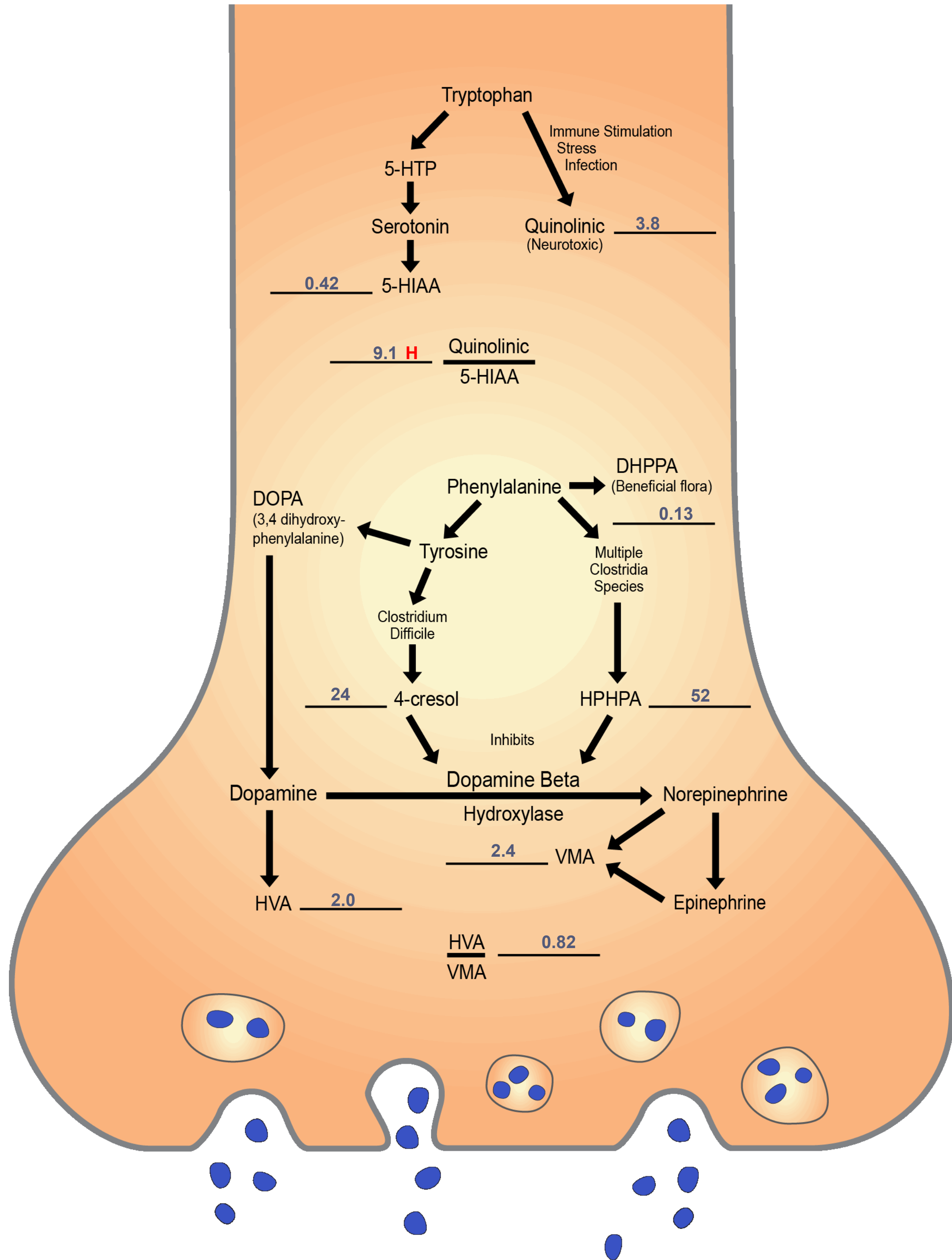
Neurotransmitter Metabolism Markers



The diagram contains the patient's test results for neurotransmitter metabolites and shows their relationship with key biochemical pathways within the axon terminal of nerve cells. The effect of microbial byproducts on the blockage of the conversion of dopamine to norepinephrine is also indicated.

Interpretation

High yeast/fungal metabolites (Markers 1,2,3,4,5,6,7,8) indicate a yeast/fungal overgrowth of the gastrointestinal tract. Prescription or natural (botanical) anti-fungals, along with supplementation of high potency multi-strain probiotics (20-50 billion cfu's), may reduce yeast/fungal levels.

HVA levels below the mean (Marker 33) may indicate lower production of the neurotransmitter dopamine, perhaps due to low dietary intake of the amino acid precursors phenylalanine or tyrosine. Homovanillic acid is a metabolite of the neurotransmitter dopamine. Supplementation with phenylalanine or tyrosine may be beneficial. Enzyme cofactors magnesium, B6 (pyridoxine) or biopterin may also be deficient; neurotransmitter levels may increase with supplementation with these cofactors if these are deficient.

VMA levels below the mean (Marker 34) may indicate lower production of the neurotransmitter norepinephrine or the hormone adrenaline, perhaps due to low dietary intake of the amino acid precursors phenylalanine or tyrosine. Vanylmandelic acid (VMA) is a metabolite of norepinephrine or adrenaline. Low VMA may also result from blocked conversion of dopamine to norepinephrine by *Clostridia* metabolites. Supplementation with phenylalanine or tyrosine may be beneficial. Enzyme cofactors magnesium, B6 (pyridoxine) or biopterin may also be deficient and respond to supplementation.

5-hydroxyindoleacetic acid (5-HIAA) levels below the mean (Marker 36) may indicate lower production of the neurotransmitter serotonin. 5-hydroxy-indoleacetic acid is a metabolite of serotonin. Low values have been correlated with symptoms of depression. Supplementation with the precursor 5-HTP (5-hydroxytryptophan) at 50-300 mg/day may be beneficial. Supplementation with tryptophan itself may form the neurotoxic metabolite quinolinic acid, however, 5-HTP is not metabolized to quinolinic acid. Excessive tryptophan supplementation has been associated with eosinophilia myalgia syndrome.

High quinolinic acid / 5-HIAA ratio (Marker 39) indicates an imbalance of these organic acids and may be a sign of neural excitotoxicity. Quinolinic acid is an excitotoxic stimulant of certain brain cells that have NMDA-type receptors. Overstimulated nerve cells may die. Brain toxicity due to quinolinic acid has been implicated in Alzheimer's disease, autism, Huntington's disease, stroke, dementia of old age, depression, HIV-associated dementia, and schizophrenia. However, quinolinic acid is derived from the amino acid tryptophan and is an important intermediate that the body uses to make the essential nutritional cofactor nicotinamide adenine dinucleotide (NAD), which can also be derived from niacin (B3).

An elevated ratio is not specific for a particular medical condition and is commonly associated with excessive inflammation due to recurrent infections. If quinolinic acid is not elevated, low 5-HIAA from serotonin may be the source of the imbalance. Supplementation with 5-HTP may increase serotonin levels, but 5-HTP is not metabolized to quinolinic acid. Immune overstimulation, excess adrenal production of cortisol due to stress, or high exposure to phthalates may also increase the quinolinic acid/5-HIAA acid ratio.

The drug deprenyl or the dietary supplements carnitine, melatonin, capsaicin, turmeric (curcumin) and garlic may reduce brain damage caused by quinolinic acid. Niacin (nicotinic acid) and niacinamide may also reduce quinolinic acid production by decreasing tryptophan shunting to the quinolinic acid pathway. Inositol hexaniacinate as an adult dose of 500-1000 mg does not cause niacin flush.

High 3-hydroxybutyric and/or acetoacetic acids (Markers 42, 43) indicate increased metabolic utilization of fatty acids. These ketones are associated with diabetes mellitus, fasting, dieting (ketogenic or SCD diet), or illness such as nausea or flu, among many other causes. Regardless of cause, supplementation with L-carnitine or acetyl-L-carnitine (500-1000mg per day) may be beneficial.

High adipic acid (Marker 47) may indicate an abnormality in fatty acid metabolism. Elevated adipic acid may also be due to ingestion of large amounts of gelatin (extremely high in adipic acid) or "junk foods" that contain adipic acid as an additive. Other causes of elevated adipic acid include ingestion of medium-chain triglycerides (MCT or coconut oil), carnitine deficiency, or fasting. [The acyl carnitine profile (Duke University Biochemical Genetics Laboratory, http://medgenetics.pediatrics.duke.edu) can rule out fatty acid oxidation defects.] Some children are biochemically sensitive to adipic acid. Consider elimination of gelatin and certain processed foods if a diet journal indicates sensitivity to foods containing adipic acid. Supplementation with L-carnitine or acetyl-L-carnitine (500-1000 mg per day) may be beneficial.

Pyridoxic acid (B6) levels below the mean (Marker 51) may be associated with less than optimum health conditions (low intake, malabsorption, or dysbiosis). Supplementation with B6 (20 - 50 mg/day) or a multivitamin may be beneficial.

Pantothenic acid (B5) levels below the mean (Marker 52) may be associated with less than optimum health conditions. Supplementation with B5 (250 mg/day) or a multivitamin may be beneficial.

High glutaric acid (Marker 53) can result from glutaric acidemias, fatty acid oxidation defects, riboflavin deficiency, ingestion of medium-chain triglycerides, metabolic effects of valproic acid (Depakene), and celiac disease. The genetic disorders are usually diagnosed in children but have occasionally been detected in adults. The probability of a genetic disease is higher when values exceed 10 mmol/mol creatinine but such diseases may also be present with lower urine values. DNA tests have been developed for the confirmation of both types of genetic disorders but may not be commercially available. This compound may be elevated in about 10% of children with autism. Regardless of the cause, supplementation with riboflavin (20-100 mg/day) and coenzyme Q-10 (50-100 mg/day) may be beneficial.

Glutaric acidemia type I is associated with elevations of 3-hydroxyglutaric and glutaconic acid. Normal values of 3-hydroxyglutaric acid greatly reduce but do not completely eliminate the possibility of glutaric acidemia type I. This disease has been associated with clinical symptoms ranging from near normal to encephalopathy, cerebral palsy, and other neurological abnormalities. Some individuals with glutaric acidemia type I have developed bleeding in the brain or eyes that may be mistaken for the effects of child abuse. Treatment of this disorder includes special diets low in lysine and carnitine supplementation.

Glutaric academia type II, also called acyl-CoA dehydrogenase deficiency, caused by a genetic defect in one of the mitochondrial electron transport proteins, is associated with dysmorphic features, seizures, hypoglycemia, and developmental delay. Glutaric acidemia II is commonly associated with elevations of 2-hydroxyglutaric acid as well as isovalerylglycine, hexanoylglycine, isobutyrylglycine, ethylmalonic acid, methylsuccinic acid, and adipic, suberic, and sebacic acids.

Ascorbic acid (vitamin C) levels below the mean (Marker 54) may indicate a less than optimum level of the antioxidant vitamin C. Suggested supplementation is 1000 mg/day of buffered vitamin C, divided into 2-3 doses.

High 2-hydroxybutyric acid (Marker 59) This organic acid is elevated when there is increased production of sulfur amino acids derived from homocysteine. The reasons for an increase can be due to the following reasons (which are not mutually exclusive):

1. There is increased need for glutathione to detoxify a host of toxic chemicals, resulting in increased shunting of homocysteine into the production of cysteine for glutathione. This is the most common reason.
2. There are genetic variants of the DNA such that methylation of homocysteine by betaine homocysteine methyl transferase or methionine synthase is impaired.
3. There are nutritional deficiencies of betaine, methylcobalamin, or methyltetrahydrofolate that reduce the enzyme activities of the enzymes in #2 above.
4. There is a genetic variant in cystathionine beta synthase (CBS) enzyme such that there is excessive shunting of homocysteine into cysteine production that results in excessive 2-hydroxybutyric acid formation.

Low citramalic, 2-hydroxyphenylacetic, 4-hydroxyphenylacetic, 4-hydroxybenzoic, 4-hydroxyhippuric, 3-indoleacetic, glyceric, glycolic, oxalic, lactic, pyruvic, 2-hydroxybutyric, fumaric, malic, aconitic, quinolinic, kynurenic, quinolinic/5-HIAA ratio, thymine, ethylmalonic, methylsuccinic, adipic, suberic, glutaric, 3-hydroxy-3-methylglutaric, methylcitric, or orotic values have no known clinical significance.

Low values for amino acid metabolites (Markers 62-74) indicate the absence of genetic disorders of amino acid metabolism. These markers are deamination (ammonia removed) byproducts that are very elevated only when a key enzyme has low activity; slight elevations may indicate a genetic variation or heterozygous condition which may be mitigated with diet or supplementation. Low values are not associated with inadequate protein intake and have not been proven to indicate specific amino acid deficiencies.

High quality nutritional supplements can be purchased through your practitioner or at New Beginnings Nutritionals, www.NBNUS.com <http://www.NBNUS.com> , or call 877-575-2467.