The Great Plains Laboratory, Inc.

William Shaw, Ph.D., Director | 11813 West 77th Street, Lenexa, KS 66214 | (913) 341-8949 | Fax (913) 341-6207

Requisition #:	[illegible]	**Physician:**	[illegible]
Patient Name:	[illegible]	**Date of Collection:**	3/3/2014
Patient Age:	22	**Time of Collection:**	07:00 AM
Patient Sex:	M	**Print Date:**	03/10/2014

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient	Reference Population - Males Age 13 and Over

Intestinal Microbial Overgrowth

Yeast and Fungal Markers

1	Citramalic	0.11 - 2.0		0.63		0.63
2	5-Hydroxymethyl-2-furoic	≤ 18		1.0		1.0
3	3-Oxoglutaric	≤ 0.11	H	0.13		0.13
4	Furan-2,5-dicarboxylic	≤ 13		4.7		4.7
5	Furancarbonylglycine	≤ 2.3		0		0.00
6	Tartaric	≤ 5.3		0.29		0.29
7	Arabinose	≤ 20	H	24		24
8	Carboxycitric	≤ 20		1.2		1.2
9	Tricarballylic	≤ 0.58		0.07		0.07

Malabsorption and Bacterial Markers

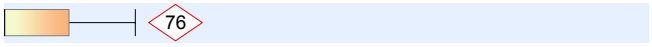
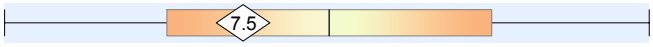
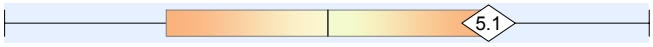
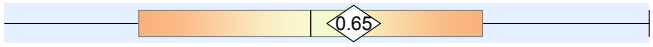
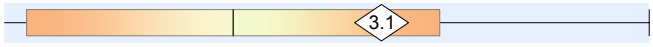
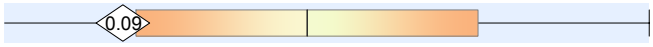
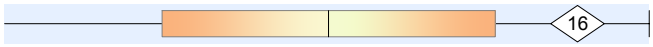
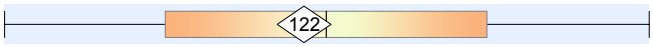
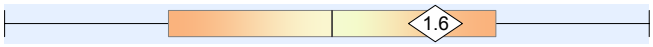
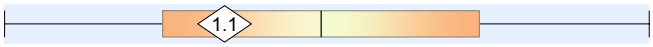
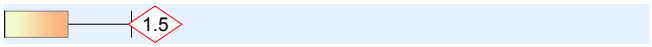
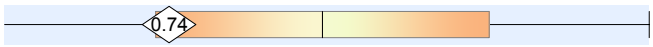
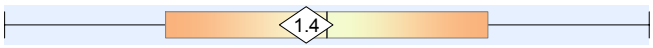
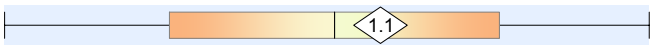
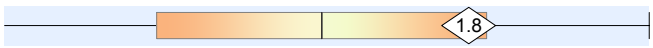
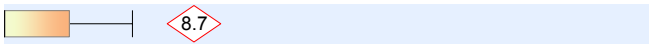
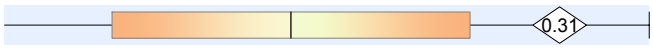
10	2-Hydroxyphenylacetic	0.03 - 0.47		0.36		0.36
11	4-Hydroxyphenylacetic	≤ 18		9.4		9.4
12	4-Hydroxybenzoic	0.01 - 0.73		0.43		0.43
13	4-Hydroxyhippuric	≤ 14		6.3		6.3
14	Hippuric	≤ 241	H	457		457
15	3-Indoleacetic	≤ 6.8		2.0		2.0
16	Succinic	≤ 5.3		3.1		3.1
17	HPHPA *(other pathogenic clostridia species)*	≤ 102		55		55
18	4-Cresol (C. difficile)	≤ 39		18		18
19	DHPPA (Beneficial Bacteria)	≤ 0.23		0.16		0.16

Testing performed by The Great Plains Laboratory, Inc., Lenexa, Kansas. The Great Plains Laboratory has developed and determined the performance characteristics of this test. This test has not been evaluated by the U.S. FDA; the FDA does not currently regulate such testing.

The Great Plains Laboratory, Inc.

Requisition #: 332440 **Physician:** [illegible]

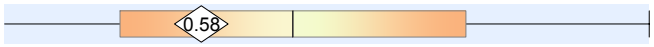
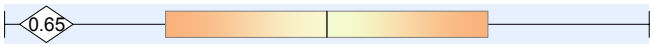
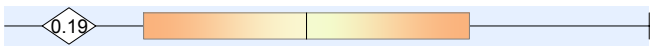
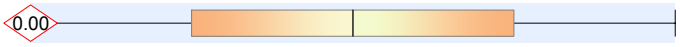
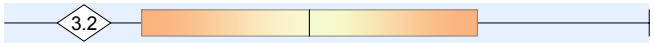
Patient Name: [illegible] **Date of Collection:** [illegible]

Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)			Patient	Reference Population - Males Age 13 and Over
Oxalate Metabolites						
20	Glyceric	0.21	- 4.9	H	8.0	
21	Glycolic	18	- 81		53	
22	Oxalic	8.9	- 67	H	76	
Glycolytic Cycle Metabolites						
23	Lactic	0.74	- 19		7.5	
24	Pyruvic	0.28	- 6.7		5.1	
25	2-Hydroxybutyric		≤ 1.2		0.65	
Krebs Cycle Metabolites						
26	Succinic		≤ 5.3		3.1	
27	Fumaric		≤ 0.49		0.09	
28	Malic		≤ 1.1		0.41	
29	2-Oxoglutaric		≤ 18		16	
30	Aconitic	4.1	- 23		6.4	
31	Citric	2.2	- 260		122	
Neurotransmitter Metabolites						
32	Homovanillic (HVA) *(dopamine)*	0.39	- 2.2		1.6	
33	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53	- 2.2		1.1	
34	HVA / VMA Ratio	0.32	- 1.4	H	1.5	
35	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤ 2.9		0.74	
36	Quinolinic	0.52	- 2.4		1.4	
37	Kynurenic	0.12	- 1.8		1.1	
38	Quinolinic / 5-HIAA Ratio		≤ 2.5		1.8	
Pyrimidine Metabolites - Folate Metabolism						
39	Uracil		≤ 6.9	H	8.7	
40	Thymine		≤ 0.36		0.31	

The Great Plains Laboratory, Inc.

Requisition #: [illegible] **Physician:** [illegible]

Patient Name: [illegible] **Date of Collection:** 3/3/2014

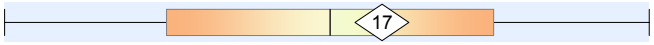
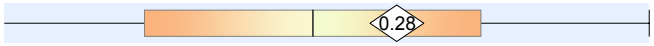
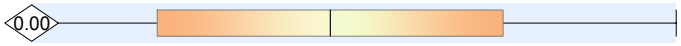
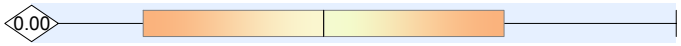
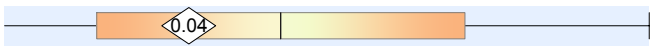
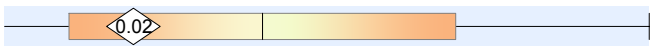
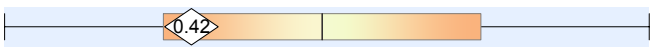
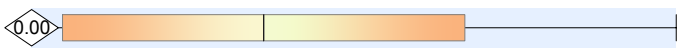
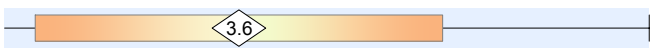
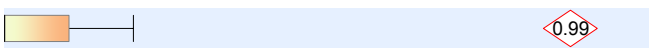
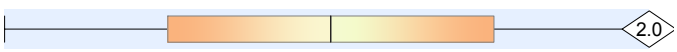
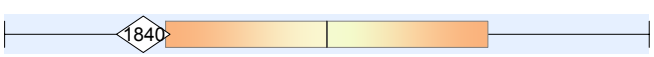
Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)	Patient	Reference Population - Males Age 13 and Over
Ketone and Fatty Acid Oxidation				
41	3-Hydroxybutyric	≤ 1.9	0.58	
42	Acetoacetic	≤ 10	0.65	
43	4-Hydroxybutyric	≤ 4.3	1.1	
44	Ethylmalonic	0.13 - 2.7	1.2	
45	Methylsuccinic	≤ 2.3	1.5	
46	Adipic	≤ 2.9	0.85	
47	Suberic	≤ 1.9	0.19	
48	Sebacic	≤ 0.14	0.08	
Nutritional Markers				
Vitamin B12				
49	Methylmalonic ✱	≤ 2.3	1.1	
Vitamin B6				
50	Pyridoxic (B6)	≤ 26	1.4	
Vitamin B5				
51	Pantothenic (B5)	≤ 5.4	3.0	
Vitamin B2 (Riboflavin)				
52	Glutaric ✱	≤ 0.43	0.17	
Vitamin C				
53	Ascorbic	10 - 200	L 0	
Vitamin Q10 (CoQ10)				
54	3-Hydroxy-3-methylglutaric ✱	≤ 26	3.2	
Glutathione Precursor and Chelating Agent				
55	N-Acetylcysteine (NAC)	≤ 0.13	0.06	
Biotin (Vitamin H)				
56	Methylcitric ✱	0.15 - 1.7	0.89	

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

The Great Plains Laboratory, Inc.

Requisition #: 332440 SSSSSS **Physician:** JAMES GREENBLATT MD SSSSSSSSSSSSSS

Patient Name: Mark Sample SSSSSSSS **Date of Collection:** 3/3/2014

Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)			Patient	Reference Population - Males Age 13 and Over
Indicators of Detoxification						
Glutathione						
57	Pyroglutamic ✱	5.7	-	25	17	
Ammonia Excess						
58	Orotic		≤	0.46	0.28	
59	2-Hydroxyhippuric		≤	0.86	0.84	
Amino Acid Metabolites						
60	2-Hydroxyisovaleric		≤	0.41	0	
61	2-Oxoisovaleric		≤	1.5	0	
62	3-Methyl-2-oxovaleric		≤	0.56	0.50	
63	2-Hydroxyisocaproic		≤	0.39	0.06	
64	2-Oxoisocaproic		≤	0.34	0.08	
65	2-Oxo-4-methiolbutyric		≤	0.14	0.04	
66	Mandelic		≤	0.09	0	
67	Phenyllactic		≤	0.10	0.02	
68	Phenylpyruvic	0.02	-	1.4	0.42	
69	Homogentisic		≤	0.23	0.01	
70	4-Hydroxyphenyllactic		≤	0.62	0.11	
71	N-Acetylaspartic		≤	2.5	0	
72	Malonic		≤	9.9	3.6	
73	3-Methylglutaric	0.02	-	0.38	H 0.99	
74	3-Hydroxyglutaric		≤	4.6	1.4	
75	3-Methylglutaconic	0.38	-	2.0	2.0	
Bone Metabolites						
76	Phosphoric	1 000	-	4 900	1 840	

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

The Great Plains Laboratory, Inc.

Requisition #: [illegible] **Physician:** [illegible]

Patient Name: [illegible] **Date of Collection:** 3/3/2014

Indicator of Fluid Intake

77	*Creatinine	85	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.

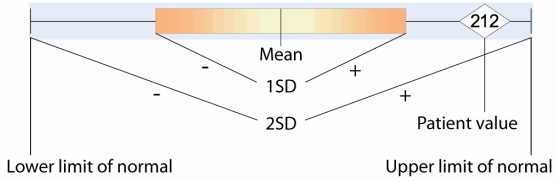
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

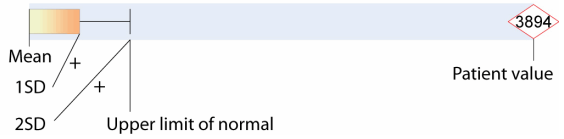
Example of Value Within Reference Range

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth				
HPHPA (Clostridia marker)	<	219 .9	212	

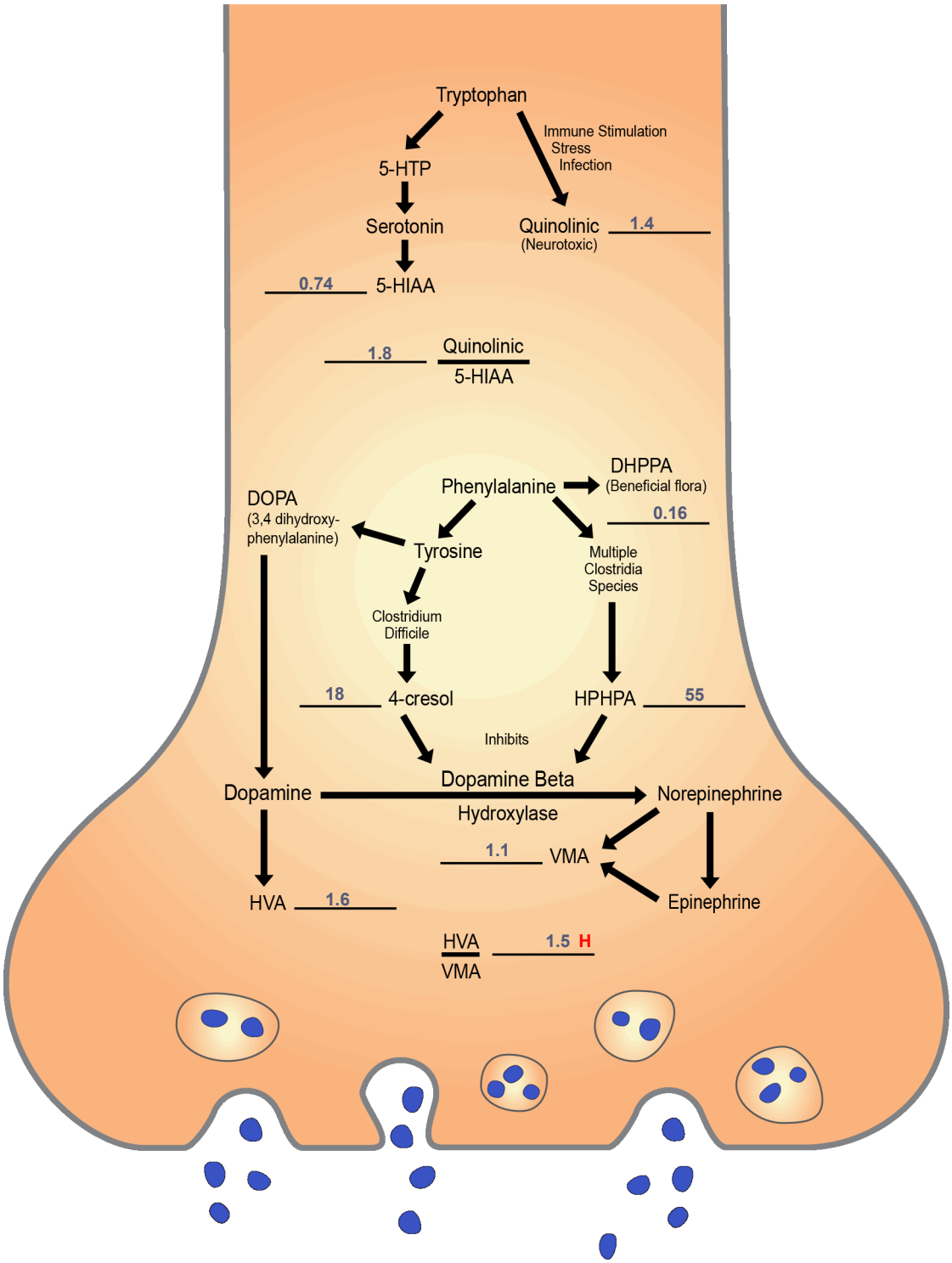


Example of Elevated Value

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth				
HPHPA (Clostridia marker)	<	219 .9	H 3894	



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.

The Great Plains Laboratory, Inc.

Requisition #:	[illegible]	***Physician:***	[illegible]
Patient Name:	[illegible]	***Date of Collection:***	3/3/2014

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.

High hippuric acid (Marker 14) may derive from food, GI bacterial activity, or exposure to the solvent toluene. Hippuric acid is a conjugate of glycine and benzoic acid formed in the liver. Most hippuric acid in urine is derived from microbial breakdown of chlorogenic acid to benzoic acid. Chlorogenic acid is a common substance in beverages and in many fruits and vegetables, including apples, pears, tea, coffee, sunflower seeds, carrots, blueberries, cherries, potatoes, tomatoes, eggplant, sweet potatoes, and peaches. Benzoic acid is present in high amounts in cranberry juice and is a food preservative. The workplace is the most common source of toluene exposure, but toluene may be absorbed from outgassing of new carpets and other building materials, or absorbed during recreational abuse of solvents such as glue-sniffing. Because most hippuric acid in urine is from GI sources, this marker is a poor indicator of toluene exposure and is being replaced by other markers in occupational safety testing. Bacterial overgrowth can be treated with natural anti-bacterial agents and/or probiotics (30-50 billion cfu's) that include *Lactobacillus rhamnosus*.

High oxalic with or without elevated glyceric or glycolic acids (Markers 20,21,22) may be associated with the genetic hyperoxalurias, autism, women with vulvar pain, fibromyalgia, and may also be due to high vitamin C intake. However, kidney stone formation from oxalic acid was not correlated with vitamin C intake in a very large study. Besides being present in varying concentrations in most vegetables and fruits, oxalates, the mineral conjugate base forms of oxalic acid, are also byproducts of molds such as *Aspergillus* and *Penicillium* and probably *Candida*. If yeast or fungal markers are elevated, antifungal therapy may reduce excess oxalates. High oxalates may cause anemia that is difficult to treat, skin ulcers, muscles pains, and heart abnormalities. Elevated oxalic acid is also the result of anti-freeze (ethylene glycol) poisoning. Oxalic acid is a toxic metabolite of trichloroacetic acid and other environmental pollutants. In addition, decomposing vitamin C may form oxalates during transport or storage.

Elevated oxalate values with a concomitant increase in glycolic acid may indicate genetic hyperoxaluria (type I), whereas increased glyceric acid may indicate a genetic hyperoxaluria (type II). Elevated oxalic acid with normal levels of glyceric or glycolic metabolites rules out a genetic cause for high oxalate. However, elevated oxalates may be due to a new genetic disorder, hyperoxaluria type III.

Regardless of its source, high oxalic acid may contribute to kidney stones and may also reduce ionized calcium. Oxalic acid absorption from the GI tract may be reduced by calcium citrate supplementation before meals. Vitamin B6, arginine, vitamin E, chondroitin sulfate, taurine, selenium, omega-3 fatty acids and/or N-acetyl glucosamine supplements may also reduce oxalates and/or their toxicity. Excessive fats in the diet may cause elevated oxalate if fatty acids are poorly absorbed because of bile salt deficiency. Unabsorbed free fatty acids bind calcium to form insoluble soaps, reducing calcium's ability to bind oxalate and increase its absorption. If taurine is low in a plasma amino acid profile, supplementation with taurine (1000 mg/day) may help stimulate bile salt production (taurocholic acid), leading to better fatty acid absorption and diminished oxalate absorption.

High levels of oxalates are common in autism. Malabsorption of fat and intestinal *Candida* overgrowth are probably the major causes for elevated oxalates in this disorder. Even individuals with elevated glyceric or glycolic acids may not have a genetic disease. To rule out genetic diseases in those people with abnormally high markers characteristic of the genetic diseases, do the following steps: (1) Follow the nutritional steps indicated in this interpretation for one month; (2) If *Candida* is present, treat *Candida* for at least one month; (3) Repeat the organic acid test after abstaining from vitamin C supplements for 48 hours; (4) If the biochemical markers characteristic of genetic oxalate disorders are still elevated in the repeat test, consider DNA tests for the most common mutations of oxalate metabolism. DNA testing for type I hyperoxaluria is available from the Mayo Clinic, Rochester, MN as test #89915 "*AGXT* Gene, Full Gene Analysis" and, for the p.Gly170Arg mutation only, as # 83643 "Alanine:Glyoxylate Aminotransferase [*AGXT*] Mutation Analysis [G170R], Blood"). Another option to confirm the genetic disease is a plasma oxalate test, also available from the Mayo Clinic (Phone 507.266.5700). Plasma oxalate values greater than 50 micromol/L are consistent with genetic oxalate diseases and may serve as an alternate confirmation test.

Bone tends to be the major repository of excess oxalate in patients with primary hyperoxaluria. Bone oxalate levels are negligible in healthy subjects. Oxalate deposition in the skeleton tends to increase bone resorption and decrease osteoblast activity.

Oxalates may also be deposited in the kidneys, joints, eyes, muscles, blood vessels, brain, and heart and may contribute to muscle pain in fibromyalgia. Oxalate crystal formation in the eyes may be a source of severe eye pain in individuals with autism who may exhibit eye-poking behaviors. High oxalates in the GI tract also may significantly reduce absorption of essential minerals such as calcium, magnesium, zinc, and others.

A low oxalate diet may also be particularly useful in the reduction of body oxalates even if dysbiosis of GI flora is the major source of oxalates. Foods especially high in oxalates include spinach, beets, chocolate, soy, peanuts, wheat bran, tea, cashews, pecans, almonds, berries, and many others. A complete list of high oxalate foods is available online at <http://www.greatplainslaboratory.com/home/eng/oxalates.asp> .

High HVA/VMA ratio (Marker 34) The most common reason for an elevation of the HVA/VMA ratio is the decreased conversion of dopamine to norepinephrine and epinephrine. The enzyme responsible for this conversion, dopamine betahydroxylase, is copper and vitamin C dependent, so an elevated ratio could be due to deficiencies of these cofactors. Another common factor is inhibition of this enzyme by *Clostridia* byproducts. A high HPHPA, 4-Cresol, or other elevations of metabolites would be consistent with the latter explanation.

VMA levels below the mean (Marker 33) 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 35) 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 uracil with normal/elevated thymine (Markers 39,40) is an abnormality that is found in about 10% of children with autism. Because folic acid is involved as a methyl donor in the conversion of uracil to thymine, this elevation may indicate a deficiency of folic acid or a defect in folic acid metabolism. Regardless of cause, supplementation with folic acid, folinic acid or methyl folate may be beneficial.

Pyridoxic acid (B6) levels below the mean (Marker 50) 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.

Ascorbic acid (vitamin C) levels below the mean (Marker 53) 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 3-methylglutaric and/or high 3-methylglutaconic acids (Markers 73,75) may be due to reduced capacity to metabolize the amino acid leucine. This abnormality is found in the genetic disease methylglutaconic aciduria and in mitochondrial disorders in which there are severe deficiencies of the respiratory complexes (Complex I, NADH ubiquinone oxidoreductase and complex IV, cytochrome c oxidase.). Small elevations may be due to impairment of mitochondrial function and may respond to the recommended supplements below. Typical results found in genetic defects are above 10 mmol/mol creatinine. A few non-genetic conditions including pregnancy and kidney failure may also produce elevation of these organic acids in urine. Confirmation of the genetic disease requires enzymes and/or DNA testing. Multiple genetic defects can cause the biochemical abnormality. Confirmation of mitochondrial disorder usually requires tissue biopsy for mitochondria testing. Symptoms differ within different types of genetic disorders, but in severe cases may include speech delay, delayed development of both mental and motor skills (psychomotor delay), metabolic acidosis, abnormal muscle tone (dystonia), and spasms and weakness affecting the arms and legs (spastic quadriparesis). Recommendations include supplementation with coenzyme Q-10 (300-600 mg), NAD 25-50mg, L-carnitine and acetyl-L-carnitine (1000-2000 mg), riboflavin (40-80 mg), nicotinamide (40-80 mg), biotin (4-8 mg), and vitamin E (200-400 IU's) per day.

Low values for amino acid metabolites (Markers 60-75) 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 qualitty nuttrittonal supplementts can be purchased tthrough your practtttoner or att New Beginnings Nuttritton. Visit www.nbnus.com <http://www.nbnus.com> or call 877-575-2467.

The nutritional recommendations in this test are not approved by the US FDA. Supplement recommendations are not intended to treat, cure, or prevent any disease and do not take the place of medical advice or treatment from a healthcare professional.

Certain uses of the compounds arabinose, citramalic, tartaric, 3-oxoglutaric, carboxycitric, 3,4-dihydroxyphenylpropionic acid, and 3-(3-hydroxyphenyl)-3-hydroxypropionic acid in their application to autism in the Organic Acid Test and Microbial Organic Acid Test are protected by USA patent 5,686,311 granted to The Great Plains Laboratory, Inc., November 11, 1997.