The Great Plains Laboratory, Inc.

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Requisition #:	326554	*Physician:*	RONALD HUNNINGHAKE MD
Patient Name:	Jonathan Barnett	*Date of Collection:*	1/8/2014
Patient Age:	57	*Time of Collection:*	06:30 AM
Patient Sex:	M	*Print Date:*	01/15/2014

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		0.59	0.59
2	5-Hydroxymethyl-2-furoic	≤ 18		7.4	7.4
3	3-Oxoglutaric	≤ 0.11		0.08	0.08
4	Furan-2,5-dicarboxylic	≤ 13		8.8	8.8
5	Furancarbonylglycine	≤ 2.3		1.7	1.7
6	Tartaric	≤ 5.3		1.6	1.6
7	Arabinose	≤ 20	H	62	62
8	Carboxycitric	≤ 20		1.0	1.0
9	Tricarballylic	≤ 0.58		0.15	0.15
Malabsorption and Bacterial Markers					
10	2-Hydroxyphenylacetic	0.03 - 0.47		0.25	0.25
11	4-Hydroxyphenylacetic	≤ 18		5.9	5.9
12	4-Hydroxybenzoic	0.01 - 0.73		0.21	0.21
13	4-Hydroxyhippuric	≤ 14		3.1	3.1
14	Hippuric	≤ 241		184	184
15	3-Indoleacetic	≤ 6.8		1.3	1.3
16	Succinic	≤ 5.3		5.1	5.1
17	HPHPA (other pathogenic clostridia species)	≤ 102		46	46
18	4-Cresol (C. difficile)	≤ 39		4.4	4.4
19	DHPPA (Beneficial Bacteria)	≤ 0.23		0.06	0.06

Wow Big Improvement

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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.

GT# 8/8283

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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		1.9	1.9
21	Glycolic	18 - 81		65	65
22	Oxalic	8.9 - 67	H	75	75
Glycolytic Cycle Metabolites					
23	Lactic	0.74 - 19		7.1	7.1
24	Pyruvic	0.28 - 6.7		1.5	1.5
25	2-Hydroxybutyric	≤ 1.2		0.64	0.64
Krebs Cycle Metabolites					
26	Succinic	≤ 5.3		5.1	5.1
27	Fumaric	≤ 0.49		0.15	0.15
28	Malic	≤ 1.1		0.48	0.48
29	2-Oxoglutaric	≤ 18		4.7	4.7
30	Aconitic	4.1 - 23		7.6	7.6
31	Citric	2.2 - 260		144	144
Neurotransmitter Metabolites					
32	Homovanillic (HVA) (dopamine)	0.39 - 2.2		0.83	0.83
33	Vanillylmandelic (VMA) (norepinephrine, epinephrine)	0.53 - 2.2		0.71	0.71
34	HVA / VMA Ratio	0.32 - 1.4		1.2	1.2
35	5-Hydroxyindoleacetic (5-HIAA) (serotonin)	≤ 2.9		0.79	0.79
36	Quinolinic	0.52 - 2.4		2.1	2.1
37	Kynurenic	0.12 - 1.8		1.4	1.4
38	Quinolinic / 5-HIAA Ratio	≤ 2.5	H	2.7	2.7
Pyrimidine Metabolites - Folate Metabolism					
39	Uracil	≤ 6.9		1.3	1.3
40	Thymine	≤ 0.36		0.09	0.09

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Ketone and Fatty Acid Oxidation					
41	3-Hydroxybutyric	≤ 1.9		0.48	0.48
42	Acetoacetic	≤ 10		2.7	2.7
43	4-Hydroxybutyric	≤ 4.3		1.9	1.9
44	Ethylmalonic	0.13 - 2.7		0.90	0.90
45	Methylsuccinic	≤ 2.3		1.9	1.9
46	Adipic	≤ 2.9		0.80	0.80
47	Suberic	≤ 1.9		1.4	1.4
48	Sebacic	≤ 0.14		0.05	0.05
Nutritional Markers					
Vitamin B12					
49	Methylmalonic ✱	≤ 2.3		1.2	1.2
Vitamin B6					
50	Pyridoxic (B6)	≤ 26		2.8	2.8
Vitamin B5					
51	Pantothenic (B5) good	≤ 5.4	H	39	39
Vitamin B2 (Riboflavin)					
52	Glutaric ✱	≤ 0.43		0.34	0.34
Vitamin C					
53	Ascorbic good	10 - 200	H	689	689
Vitamin Q10 (CoQ10)					
54	3-Hydroxy-3-methylglutaric ✱	≤ 26		9.5	9.5
Glutathione Precursor and Chelating Agent					
55	N-Acetylcysteine (NAC)	≤ 0.13		0.07	0.07
Biotin (Vitamin H)					
56	Methylcitric ✱	0.15 - 1.7		0.55	0.55

✱ ***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	Reference Population - Males Age 13 and Over
Indicators of Detoxification				
Glutathione				
57	Pyroglutamic ✸	5.7 - 25	23	23
Ammonia Excess				
58	Orotic	≤ 0.46	0.21	0.21
59	2-Hydroxyhippuric	≤ 0.86	0.34	0.34
Amino Acid Metabolites				
60	2-Hydroxyisovaleric	≤ 0.41	0	0.00
61	2-Oxoisovaleric	≤ 1.5	0	0.00
62	3-Methyl-2-oxovaleric	≤ 0.56	0.20	0.20
63	2-Hydroxyisocaproic	≤ 0.39	0.02	0.02
64	2-Oxoisocaproic	≤ 0.34	0.07	0.07
65	2-Oxo-4-methiolbutyric	≤ 0.14	0.03	0.03
66	Mandelic	≤ 0.09	0	0.00
67	Phenyllactic	≤ 0.10	0.02	0.02
68	Phenylpyruvic	0.02 - 1.4	0.57	0.57
69	Homogentisic	≤ 0.23	0.02	0.02
70	4-Hydroxyphenyllactic	≤ 0.62	0.28	0.28
71	N-Acetylaspartic	≤ 2.5	1.0	1.0
72	Malonic	≤ 9.9	6.4	6.4
73	3-Methylglutaric	0.02 - 0.38	0.28	0.28
74	3-Hydroxyglutaric	≤ 4.6	1.0	1.0
75	3-Methylglutaconic	0.38 - 2.0	0.64	0.64
Bone Metabolites				
76	Phosphoric	1 000 - 4 900	2 331	2331

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

Indicator of Fluid Intake

77	*Creatinine	119	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.

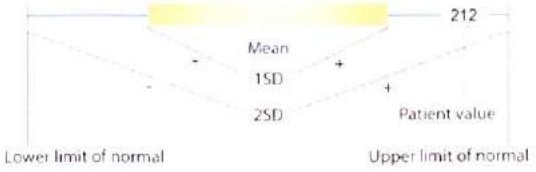
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

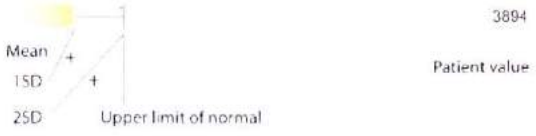
Example of Value Within Reference Range

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	



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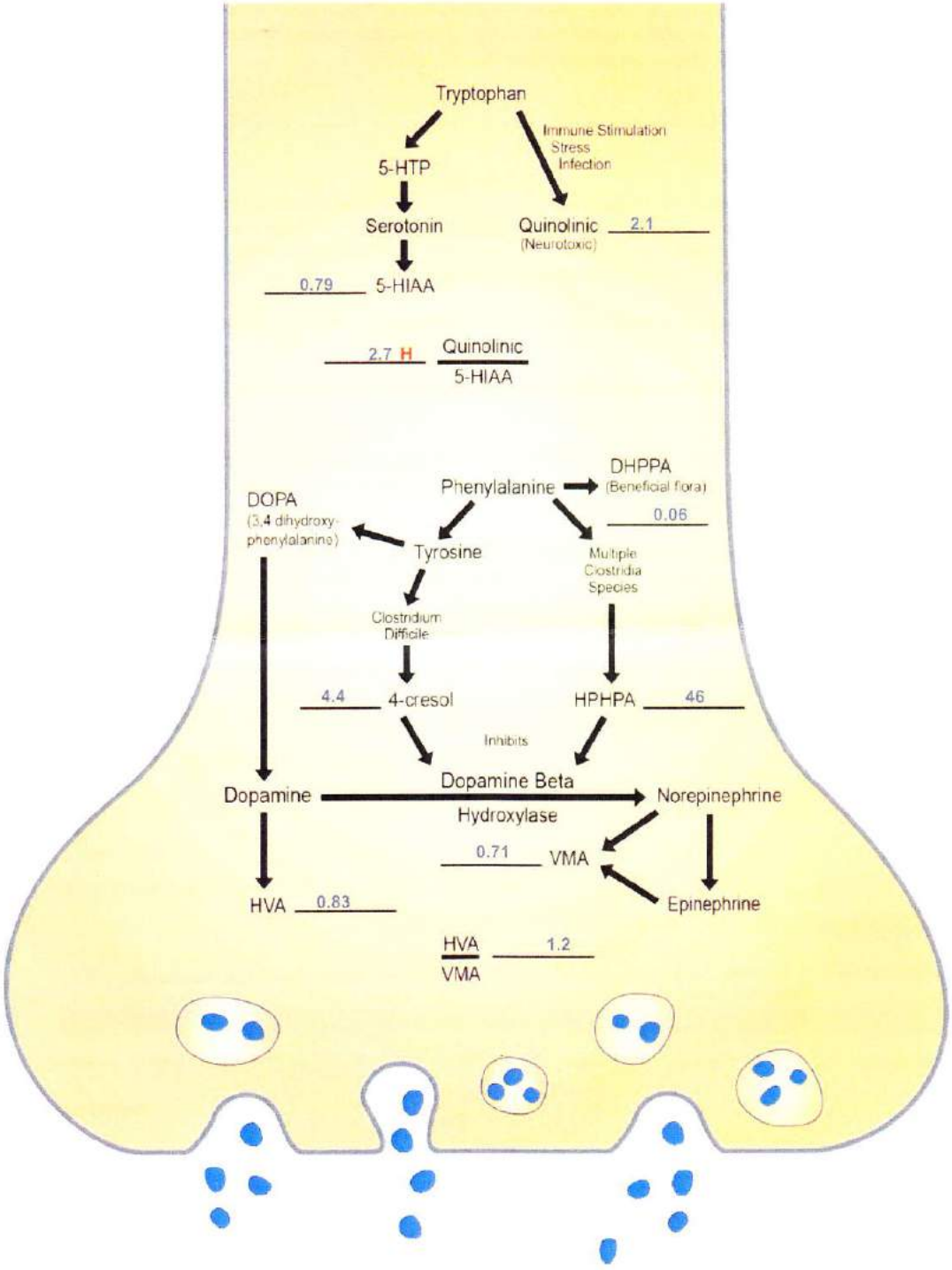
Neurotransmitter Metabolism Markers



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.

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.

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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>.

HVA levels below the mean (Marker 32) 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 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 quinolinic acid / 5-HIAA ratio (Marker 38) 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.

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.

High pantothenic acid (B5) (Marker 51) indicates high recent intake of pantothenic acid. Pantothenic acid is an essential B vitamin. Since some individuals may require very high doses of pantothenic acid, high values do not necessarily indicate the need to reduce pantothenic acid intake.

High ascorbic acid (vitamin C) (Marker 53) may be elevated as a result of supplementation. An elevated value of ascorbic acid does not mean that this amount of vitamin C is not beneficial.

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.