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 #:	235220	**Physician Name:**	
Patient Name:	Jonathan Barnett	**Date of Collection:**	04/06/2011
Patient Age:	54	**Time of Collection:**	03:30 AM
Sex:	M	**Print Date:**	04/12/2011

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	0.11 - 2.0		1.4	1.4
2 5-Hydroxymethyl-2-furoic	≤ 18	H	24	24
3 3-Oxoglutaric	≤ 0.11	H	0.33	0.33
4 Furan-2,5-dicarboxylic	≤ 13	H	23	23
5 Furancarbonylglycine	≤ 2.3		0.16	0.16
6 Tartaric	≤ 5.3	H	6.6	6.6
7 Arabinose	≤ 20	H	89	89
8 Carboxycitric	≤ 20		5.3	5.3
Malabsorption and Bacterial Markers				
9 2-Hydroxyphenylacetic	0.03 - 0.47		0.39	0.39
10 4-Hydroxyphenylacetic	≤ 18		10	10
11 4-Hydroxybenzoic	0.01 - 0.73		0.43	0.43
12 4-Hydroxyhippuric	≤ 14		4.1	4.1
13 Hippuric	≤ 241	H	610	610
14 3-Indoleacetic	≤ 6.8		1.8	1.8
15 Succinic	≤ 5.3		4.9	4.9
16 HPHPA (Clostridia marker)	≤ 102	H	109	109
17 DHPPA (Beneficial bacteria)	≤ 0.23		0.10	0.10

The Great Plains Laboratory, Inc.

Requisition #: 235220 **Physician Name:**

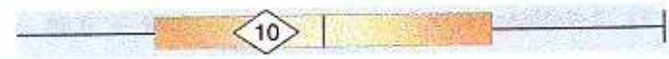
Patient Name: Jonathan Barnett **Date of Collection:** 4/6/2011

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Oxalate Metabolites				
18 Glyceric	0.21 - 4.9		3.0	
19 Glycolic	18 - 81		41	
20 Oxalic	8.9 - 67	H	118	
Glycolytic Cycle Metabolites				
21 Lactic	0.74 - 19		15	
22 Pyruvic	0.28 - 6.7		2.7	
23 2-Hydroxybutyric	≤ 1.2		0.50	
Krebs Cycle Metabolites				
24 Succinic	≤ 5.3		4.9	
25 Fumaric	≤ 0.49		0.21	
26 Malic	≤ 1.1		0.71	
27 2-Oxoglutaric	≤ 18		4.9	
28 Aconitic	4.1 - 23		11	
29 Citric	2.2 - 260		99	
Neurotransmitter Metabolites				
30 Homovanillic (HVA) *(dopamine)*	0.39 - 2.2		1.7	
31 Vanillylmandelic (VMA) *(norepinephrine, epinephrin*	0.53 - 2.2		1.7	
32 HVA/VMA Ratio	0.32 - 1.4		0.99	
33 5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 2.9		0.66	
34 Quinolinic	0.52 - 2.4	H	7.4	
35 Kynurenic	0.12 - 1.8	H	4.7	
36 Quinolinic/5-HIAA Ratio	≤ 2.5	H	11	

The Great Plains Laboratory, Inc.

Requisition #: 235220 **Physician Name:**

Patient Name: Jonathan Barnett **Date of Collection:** 4/6/2011

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Pyrimidines - Folate Metabolism			
37 Uracil	≤ 6.9	3.3	
38 Thymine	≤ 0.36	0.11	
Ketone and Fatty Acid Oxidation			
39 3-Hydroxybutyric	≤ 1.9	0.71	
40 Acetoacetic	≤ 10	1.1	
41 4-Hydroxybutyric	≤ 4.3	0.91	
42 Ethylmalonic	0.13 - 2.7	1.5	
43 Methylsuccinic	≤ 2.3	1.6	
44 Adipic	≤ 2.9	1.5	
45 Suberic	≤ 1.9	H 4.0	
46 Sebacic	≤ 0.14	0.11	
Nutritional Markers			
Vitamin B12			
47 Methylmalonic	≤ 2.3	0.88	
Vitamin B6			
48 Pyridoxic (B6)	≤ 26	H 31	
Vitamin B5			
49 Pantothenic (B5)	≤ 5.4	H 185	
Vitamin B2 (Riboflavin)			
50 Glutaric	≤ 0.43	H 0.56	
Vitamin C			
51 Ascorbic	10 - 200	H 8 761	
Vitamin Q10 (CoQ10)			
52 3-Hydroxy-3-methylglutaric	≤ 26	10	
Glutathione Precursor and Chelating Agent			
53 N-Acetylcysteine (NAC)	≤ 0.13	0.04	

The Great Plains Laboratory, Inc.

Requisition #: 235220 **Physician Name:**

Patient Name: Jonathan Barnett **Date of Collection:** 4/6/2011

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Nutritional Markers				
Biotin (Vitamin H)				
54 Methylcitric	0.15 - 1.7		0.57	0.57
Indicators of Detoxification				
55 Pyroglutamic	5.7 - 25		24	24
56 Orotic	≤ 0.46		0.26	0.26
57 2-Hydroxyhippuric	≤ 0.86		0.78	0.78
Amino Acid Metabolites				
58 2-Hydroxyisovaleric	≤ 0.41		0	0.00
59 2-Oxoisovaleric	≤ 1.5		0	0.00
60 3-Methyl-2-oxovaleric	≤ 0.56		0	0.00
61 2-Hydroxyisocaproic	≤ 0.39		0.06	0.06
62 2-Oxoisocaproic	≤ 0.34		0.06	0.06
63 2-Oxo-4-methiolbutyric	≤ 0.14		0.09	0.09
64 Mandelic	≤ 0.09	H	0.12	0.12
65 Phenyllactic	≤ 0.10		0.08	0.08
66 Phenylpyruvic	0.02 - 1.4		0.79	0.79
67 Homogentisic	≤ 0.23		0.11	0.11
68 4-Hydroxyphenyllactic	≤ 0.62		0.50	0.50
69 N-Acetylaspartic	≤ 2.5		0.42	0.42
70 Malonic	≤ 9.9		4.3	4.3
71 3-Methylglutaric	0.02 - 0.38		0.30	0.30
Bone Metabolites				
72 Phosphoric	332 - 5 040	H	7 877	7877

The Great Plains Laboratory, Inc.

Requisition #:	235220	***Physician Name:***	
Patient Name:	Jonathan Barnett	***Date of Collection:***	4/6/2011

Indicator of Fluid Intake

73	*Creatinine	88	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.

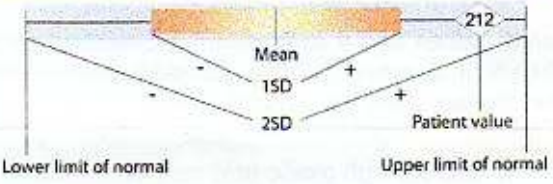
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

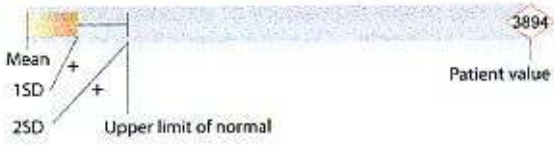
Example of Value Within Reference Range

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	



Interpretation

High yeast/fungal metabolites 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 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 HPHPA (3-(3-hydroxyphenyl)-3-hydroxypropionic acid) is associated with behavioral, GI, and/or neuropsychiatric effects. GI symptoms may include diarrhea or constipation. Neuropsychiatric effects are more common when values exceed 500 mmol/mol creatinine. HPHPA is an abnormal phenylalanine metabolite produced by GI bacteria of the *Clostridia* genus, including *C. sporogenes, C. botulinum, C. caloritolerans, C. mangenoti, C. ghoni, C. bifermentans, C. difficile, and C. sordelli.* Phenylalanine or tyrosine supplements should be avoided because of the possibility of conversion to HPHPA or other toxic byproducts. In most cases, *Clostridia* overgrowth can be controlled by probiotics supplementation, with 30 billion cfu's/day or more of *Lactobacillus rhamnosus GG* (Culturelle) and/or at least 2-6 billion cfu's/day of *Saccharomyces boulardii.*

High oxalic with or without elevated glyceric or glycolic acids 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.

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.

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.

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/eng/oxalates.asp>.

5-hydroxyindoleacetic acid (5-HIAA) levels below the mean 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 may be a sign of inflammation and/or neural excitotoxicity. Quinolinic acid is derived from the amino acid tryptophan and is neurotoxic at high levels. As an excitotoxic stimulant of certain brain cells that have NMDA-type receptors, high quinolinic acid may cause nerve cell death with continuous stimulation. 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. High levels of quinolinic acid may inhibit heart contractions, cause lipid peroxidation in the brain, and increase apoptosis (programmed cell death) of astrocytes in human brain. The level of quinolinic acid is also highly correlated with the degree of arthritis impairment.

Quinolinic acid is also a metal chelator, and inhibits enzymes that allow the body to produce glucose when needed. Excessive immune stimulation and chronic inflammation, resulting in overproduction of cytokines like interferon, stimulates overproduction of quinolinic acid. However, quinolinic acid is an important intermediate in making the essential nutritional cofactor nicotinamide adenine dinucleotide (NAD), which is also derived from niacin (B3). Phthalates inhibit the conversion of quinolinic acid to NAD.

Treatment of excessive levels of quinolinic acid can be achieved by multiple approaches: reducing tryptophan supplements, preventing repeated infections and subsequent immune overstimulation by: supplementation with colostrum, transfer factor and probiotics; reducing the use of immune modulators like interferon that increase quinolinic acid production; or reducing the numbers of vaccines given at one time or increasing the interval between vaccinations. In addition, 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. A high quinolinic acid/ 5-hydroxyindoleacetic acid ratio or high quinolinic/kynurenic acid ratio would be indicative of immune overstimulation and/or phthalate toxicity.

High quinolinic acid / 5-HIAA ratio 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.

High kynurenic acid may result from vitamin B-6 (pyridoxine) deficiency, immune stimulation or ingestion of tryptophan supplements. The kynurenine pathway is the main path of tryptophan metabolism. Although kynurenic acid may be elevated in vitamin B-6 (pyridoxine) deficiency, excretion of pyridoxic acid itself, as the major metabolite of B-6, is a much better marker for deficiency. Kynurenine (KYN) is the central compound of the pathway which splits into two separate branches: to kynurenic acid and to quinolinic acid, the precursor of the coenzyme NAD. Endogenous kynurenic acid is an antagonist to the excitatory amino acid alpha 7-nicotinic acetylcholine and to N-methyl-D-aspartate (NMDA) receptors. In several studies, kynurenic acid has been protective against the neurotoxic effects of quinolinic acid, which is a specific agonist of NMDA receptors and a potent producer of free radicals. The pathogenesis of several neurodegenerative disorders has been demonstrated to involve imbalances in the kynurenine pathway, including Alzheimer's disease, Parkinson disease, multiple sclerosis, and amyotrophic laterosclerosis (ALS).

Slight elevation in suberic acid is consistent with overnight fasting or increased fat in the diet. Regardless of cause, supplementation with L-carnitine or acetyl-L-carnitine (500-1000 mg per day) may be beneficial.

High pyridoxic acid indicates high recent intake of vitamin B6. Pyridoxic acid is a major metabolite of vitamin B6. Because some individuals may require very high doses of vitamin B6, high values do not necessarily indicate the need to reduce vitamin B6 intake.

High pantothenic acid (B5) 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 glutaric acid 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.

High ascorbic acid (vitamin C) 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.

High mandelic acid usually results from exposure to styrene. Mandelic acid in urine samples of people exposed to styrene ranges from less than 4 to 2200 mmol/mol creatinine. Mandelic acid is the major metabolite of styrene. Styrene (vinylbenzene) is used as an intermediate in plastic synthesis. Values less than 5 mg/L are due to normal metabolism of phenylalanine or tyrosine. High concentrations of styrene cause central nervous system depression, nausea, headache, fatigue, and liver damage. When exposed to 100 ppm of styrene in air, mandelic acid in urine was found to average 1700 mmol/mol creatinine. Mandelic acid is also a metabolite of ethylbenzene, and some antispasmodic and vasodilator drugs. Normal phenyllactic and phenylpyruvic acids indicate that styrene or drug exposure is more likely than PKU as a cause of these abnormalities. Dopamine metabolism is a target for the neurotoxic effects of some monocyclic aromatic hydrocarbons and their metabolites. Reduce exposure by eliminating plastic and styrofoam containers for cooking, reheating, eating or drinking (especially warm or hot) food or beverages. Replace these containers with glass, paper, or stainless steel whenever possible. Elimination of styrene can be accelerated by sauna treatment, reduced glutathione supplementation (oral, intravenous, transdermal, precursors such as N-acetyl cysteine [NAC]). High values of mandelic acid also occur in phenylketonuria (PKU). Normal values of phenyllactic and phenylpyruvic acids may rule out PKU; a mild or heterozygous form of PKU might be present. Measuring serum phenylalanine will rule out PKU. Other causes may be increased dietary phenylalanine or phenylalanine supplements. Ascorbic acid deficiency may also be related to this abnormality since ascorbic acid is a cofactor for phenylalanine hydroxylase. Supplementation with ascorbic acid (vitamin C) at 1000 mg/day or more may be beneficial.

High phosphoric acid or its base conjugate phosphate is associated with hyperparathyroidism, vitamin D-resistant rickets, vitamin D intoxication, blood lead levels above 1.5 ppm, renal tubular damage, familial hypophosphatemia, immobilization following paraplegia or fracture due to bone resorption, high nutritional intake of phosphate, and metabolic acidosis. Phosphate excretion is directly proportional to dietary intake. Foods high in phosphate include sodas, candy, ice cream, chocolate, mayonnaise, frozen pizza and commercially processed cakes, cookies and meats. Phosphate excretion is diurnal with lowest values occurring in the early morning.

Low values for amino acid metabolites have no known clinical significance and do not indicate insufficient intake of protein.

These laboratory tests have not been evaluated by the FDA and are not intended for diagnosis. 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.