The Great Plains Laboratory, Inc.

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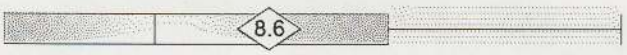
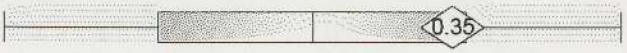
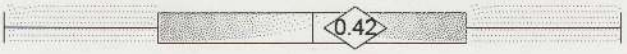
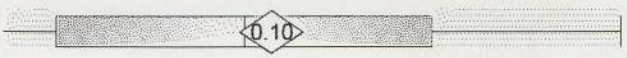
Requisition #:	245892	*Physician Name:*	
Patient Name:	Jonathan D Barnett	*Date of Collection:*	08/22/2011
Patient Age:	55	*Time of Collection:*	06:00 AM
Sex:	M	*Print Date:*	08/29/2011

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	0.85		
2 5-Hydroxymethyl-2-furoic	≤	18	8.0		
3 3-Oxoglutaric	≤	0.11	0		
4 Furan-2,5-dicarboxylic	≤	13	9.0		
5 Furancarbonylglycine	≤	2.3	1.2		
6 Tartaric	≤	5.3	0.30		
7 Arabinose	≤	20	H	114	
8 Carboxycitric	≤	20	8.6		
Malabsorption and Bacterial Markers					
9 2-Hydroxyphenylacetic	0.03	- 0.47	0.35		
10 4-Hydroxyphenylacetic	≤	18	H	22	
11 4-Hydroxybenzoic	0.01	- 0.73	0.42		
12 4-Hydroxyhippuric	≤	14	5.3		
13 Hippuric	≤	241	H	261	
14 3-Indoleacetic	≤	6.8	1.9		
15 Succinic	≤	5.3	H	7.6	
16 HPHPA (Clostridia marker)	≤	102	H	141	
17 DHPPA (Beneficial bacteria)	≤	0.23	0.10		

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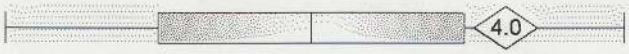
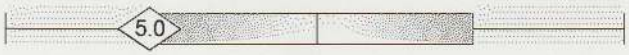
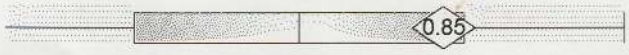
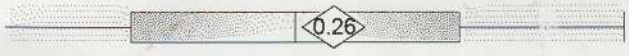
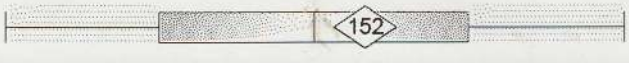
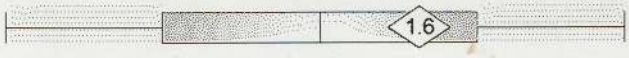
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Oxalate Metabolites			
18 Glyceric	0.21 - 4.9	4.0	
19 Glycolic	18 - 81	66	
20 Oxalic	8.9 - 67	H 115	
Glycolytic Cycle Metabolites			
21 Lactic	0.74 - 19	5.0	
22 Pyruvic	0.28 - 6.7	1.9	
23 2-Hydroxybutyric	≤ 1.2	0.85	
Krebs Cycle Metabolites			
24 Succinic	≤ 5.3	H 7.6	
25 Fumaric	≤ 0.49	0.26	
26 Malic	≤ 1.1	0.37	
27 2-Oxoglutaric	≤ 18	14	
28 Aconitic	4.1 - 23	19	
29 Citric	2.2 - 260	152	
Neurotransmitter Metabolites			
30 Homovanillic (HVA) *(dopamine)*	0.39 - 2.2	1.6	
31 Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53 - 2.2	1.9	
32 HVA/VMA Ratio	0.32 - 1.4	0.82	
33 5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 2.9	0.72	
34 Quinolinic	0.52 - 2.4	H 8.7	
35 Kynurenic	0.12 - 1.8	1.5	
36 Quinolinic/5-HIAA Ratio	≤ 2.5	H 12	

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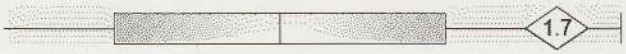
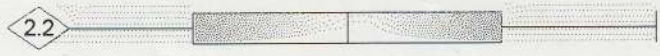
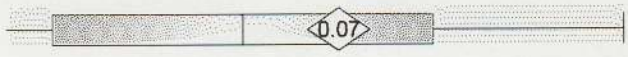
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Pyrimidines - Folate Metabolism				
37 Uracil	≤ 6.9		5.3	
38 Thymine	≤ 0.36		0.21	
Ketone and Fatty Acid Oxidation				
39 3-Hydroxybutyric	≤ 1.9		1.7	
40 Acetoacetic	≤ 10		0.49	
41 4-Hydroxybutyric	≤ 4.3		0.49	
42 Ethylmalonic	0.13 - 2.7		2.5	
43 Methylsuccinic	≤ 2.3	H	3.5	
44 Adipic	≤ 2.9	H	5.5	
45 Suberic	≤ 1.9	H	4.7	
46 Sebacic	≤ 0.14		0.11	
Nutritional Markers				
Vitamin B12				
47 Methylmalonic	≤ 2.3		2.0	
Vitamin B6				
48 Pyridoxic (B6)	≤ 26		4.1	
Vitamin B5				
49 Pantothenic (B5)	≤ 5.4	H	16	
Vitamin B2 (Riboflavin)				
50 Glutaric	≤ 0.43	H	0.70	
Vitamin C				
51 Ascorbic	10 - 200	L	2.2	
Vitamin Q10 (CoQ10)				
52 3-Hydroxy-3-methylglutaric	≤ 26		22	
Glutathione Precursor and Chelating Agent				
53 N-Acetylcysteine (NAC)	≤ 0.13		0.07	

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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	1.1	1.1
Indicators of Detoxification			
55 Pyroglutamic	5.7 - 25	H 30	30
56 Orotic	≤ 0.46	H 0.48	0.48
57 2-Hydroxyhippuric	≤ 0.86	0.50	0.50
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	0.13	0.13
62 2-Oxoisocaproic	≤ 0.34	0	0.00
63 2-Oxo-4-methiolbutyric	≤ 0.14	0.02	0.02
64 Mandelic	≤ 0.09	H 0.28	0.28
65 Phenyllactic	≤ 0.10	0.06	0.06
66 Phenylpyruvic	0.02 - 1.4	0.16	0.16
67 Homogentisic	≤ 0.23	0.04	0.04
68 4-Hydroxyphenyllactic	≤ 0.62	0.42	0.42
69 N-Acetylaspartic	≤ 2.5	0.74	0.74
70 Malonic	≤ 9.9	0	0.00
71 3-Methylglutaric	0.02 - 0.38	H 0.66	0.66
Bone Metabolites			
72 Phosphoric	332 - 5 040	H 12 466	12466

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Indicator of Fluid Intake

73	*Creatinine	144	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.

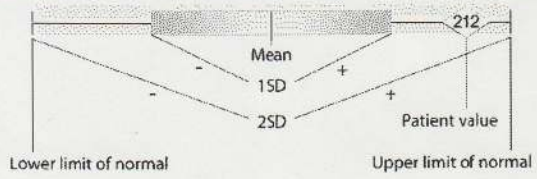
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

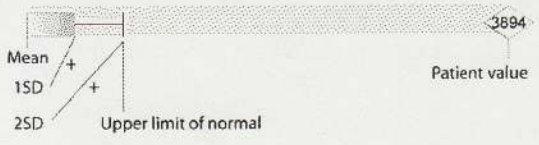
Example of Value Within Reference Range

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Result
Intestinal Microbial Overgrowth		
HPHPA (Clostridia marker)	< 219 .9	212



Example of Elevated Value

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Result
Intestinal Microbial Overgrowth		
HPHPA (Clostridia marker)	< 219 .9	H 3894



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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 4-hydroxyphenylacetic acid is a tyrosine product of GI bacteria that is associated with bacterial overgrowth and small bowel disease (Chalmers et al, Clin Chem 25:1791,1979). Elevated values may also indicate celiac disease. Suggest supplementation with 20-30 billion cells per day of probiotics and evaluation for celiac disease.

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 succinic acid may indicate a relative deficiency of riboflavin and/or coenzyme Q10 (cofactors for succinic dehydrogenase in the Krebs cycle). Supplementation with a minimum of 20 mg riboflavin (which could be provided through a high quality multivitamin) and/or 50 mg/day of coenzyme Q10 is recommended. Clinical observation suggests that succinic acid levels also decrease after treatment for GI dysbiosis.

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. 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.

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Requisition #:	245892	*Physician Name:*	
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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

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.

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Requisition #:	245892	*Physician Name:*	
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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 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 ethylmalonic, methylsuccinic, adipic, suberic, or sebacic acids may be due to fatty acid oxidation disorders, carnitine deficiency, fasting, or to increased intake of the medium-chain triglycerides found in coconut oil, MCT oil, and some infant formulas. The fatty acid oxidation defects are associated with hypoglycemia, apnea episodes, lethargy, and coma. [An acyl carnitine profile (Duke University Biochemical Genetics Laboratory, http://medgenetics.pediatrics.duke.edu) can rule out fatty acid oxidation defects.] Regardless of cause, supplementation with L-carnitine or acetyl-L-carnitine (500-1000 mg per day) may be beneficial.

Pyridoxic acid (B6) levels below the mean 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) 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.

The Great Plains Laboratory, Inc.

Requisition #:	245892	*Physician Name:*	
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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.

Ascorbic acid (vitamin C) levels below the mean 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.

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Requisition #:	245892	*Physician Name:*	
Patient Name:	Jonathan D Barnett	*Date of Collection:*	8/22/2011

High or Low Pyroglutamic acid

High pyroglutamic acid

Pyroglutamic acid is formed from intracellular gamma-glutamylcysteine conversion to pyroglutamic acid. This conversion is regulated by **intracellular** glutathione. When intracellular glutathione is low or there is a deficiency of glutathione synthetase, **greater** amounts of gamma-glutamylcysteine and pyroglutamic acid are formed. Intracellular glutathione deficiency and high pyroglutamic acid are commonly caused by moderate doses of acetaminophen (paracetamol), vigabatrin or antibiotics (flucloxacillin, netimicin). **High** pyroglutamic acid may also be caused by genetic deficiency of the enzyme oxoprolinase which breaks down pyroglutamic acid (5-oxoproline) and may also be associated with: urea cycle disorders; propionic acidemia; hawkinsinuria; Stevens-Johnson syndrome with severe burns; homocystinuria; prematurity; glycine deficiency; or infants on synthetic formulas. High pyroglutamic acid due to intracellular glutathione deficiency because of genetic deficiency or acetaminophen toxicity can be treated with the supplement N-acetyl cysteine (NAC). Administration of NAC is beneficial in preventing or mitigating hepatic injury caused by acetaminophen through stimulation of glutathione synthesis, enhancement of nontoxic routes of acetaminophen metabolism, detoxifying the toxic acetaminophen metabolite, and free radical scavenging. Individuals using acetaminophen on a regular basis may wish to take prophylactic doses of NAC with acetaminophen.

Low pyroglutamic acid

Other gamma-glutamyl amino acid conjugates (peptides) are formed from the condensation of **extracellular** glutathione with extracellular amino acids, forming gamma-glutamyl amino acid conjugates that are transferred into the cells, utilizing the cell membrane enzyme gamma-glutamyl transpeptidase. Once inside the cells, these gamma glutamyl conjugates may be converted to pyroglutamic acid. A low level of **extracellular** glutathione or a deficiency of gamma-glutamyl transpeptidase may result in a **deficiency** of pyroglutamic acid. Deficiency of the enzyme gammaglutamyl cyclotransferase may also cause deficiency of pyroglutamic acid.

Summary of both low and high pyroglutamic acid

An intracellular **deficiency of glutathione** raises pyroglutamic acid while extracellular **deficiency** of glutathione may **lower** pyroglutamic acid. Genetic disorders of glutathione metabolism and/or drug toxicity may result in pyroglutamic acid at concentrations of 1000 mmol/mol creatinine or higher. Even at therapeutic values, acetaminophen commonly elevates pyroglutamic acid to values 100 times the upper limit of normal due to depletion of intracellular glutathione.

Slightly elevated orotic acid levels (less than 5 mmol/mol creatinine) are commonly associated with dysbiosis. In this case, the use of probiotics may be beneficial. Elevated orotic acid may also indicate a disorder of ammonia metabolism. It is also possible, but unlikely, that this individual may have an undiagnosed inborn error of metabolism of the urea cycle.

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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 3-methylglutaric acid 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-generic 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 with the 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.

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 indicate the absence of genetic disorders of amino acid metabolism.

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.