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 #:		***Physician:***	KURT WOELLER DO
Patient Name:		***Date of Collection:***	3/2017
Patient Age:	2	***Time of Collection:***	03:30 PM
Patient Sex:	F	***Print Date:***	

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*		Patient Value	Reference Population - Females Under Age 13
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	≤ 5.3		4.1	
2 5-Hydroxymethyl-2-furoic	≤ 30	H	65	
3 3-Oxoglutaric	≤ 0.52		0	
4 Furan-2,5-dicarboxylic	≤ 22		16	
5 Furancarbonylglycine	≤ 3.6		0.44	
6 Tartaric	≤ 3.9	H	21	
7 Arabinose	≤ 56	H	354	
8 Carboxycitric	≤ 34		4.9	
9 Tricarballylic	≤ 0.86		0.33	
Bacterial Markers				
10 Hippuric	≤ 717		569	
11 2-Hydroxyphenylacetic	≤ 1.1		0.89	
12 4-Hydroxybenzoic	0.09 - 2.0	H	2.1	
13 4-Hydroxyhippuric	≤ 27		20	
14 DHPPA (Beneficial Bacteria)	≤ 0.73		0.31	
Clostridia Bacterial Markers				
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	≤ 30		30	
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 227	H	542	
17 4-Cresol *(C. difficile)*	≤ 76		6.3	
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	≤ 11		2.1	

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.

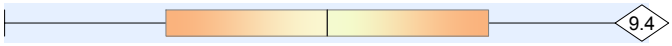
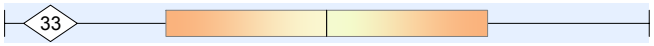
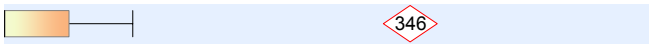
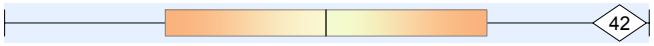
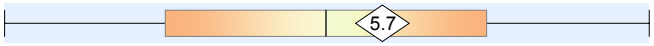
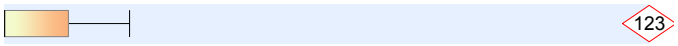
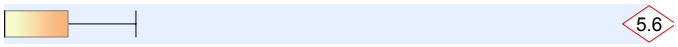
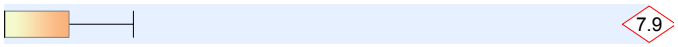
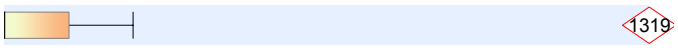
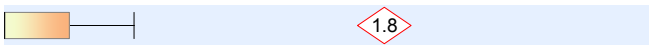
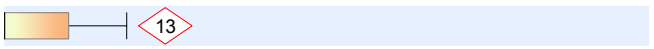
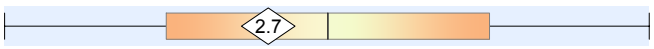
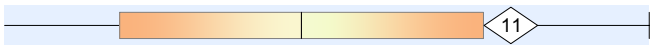
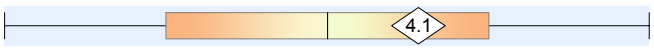
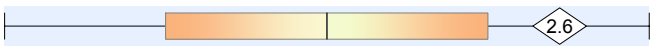
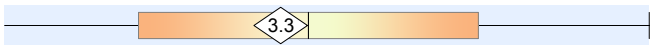
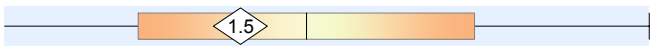
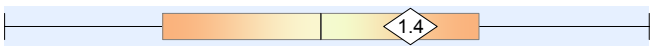
The Great Plains Laboratory, Inc.

Requisition #:

Patient Name:

Physician: KURT WOELLER DO

Date of Collection: 3/2017

Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Females Under Age 13
Oxalate Metabolites					
19	Glyceric	0.71 - 9.5		9.4	
20	Glycolic	20 - 202		33	
21	Oxalic	15 - 174	H	346	
Glycolytic Cycle Metabolites					
22	Lactic	0.18 - 44		42	
23	Pyruvic	0.88 - 9.1		5.7	
Mitochondrial Markers - Krebs Cycle Metabolites					
24	Succinic	≤ 15	H	123	
25	Fumaric	0.04 - 1.3	H	5.6	
26	Malic	≤ 2.2	H	7.9	
27	2-Oxoglutaric	≤ 81		8.7	
28	Aconitic	11 - 35		35	
29	Citric	59 - 440	H	1 319	
Mitochondrial Markers - Amino Acid Metabolites					
30	3-Methylglutaric	0.07 - 0.95	H	1.8	
31	3-Hydroxyglutaric	≤ 11	H	13	
32	3-Methylglutaconic	≤ 6.4		2.7	
Neurotransmitter Metabolites					
Phenylalanine and Tyrosine Metabolites					
33	Homovanillic (HVA) *(dopamine)*	≤ 14		11	
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.87 - 5.9		4.1	
35	HVA / VMA Ratio	0.12 - 3.0		2.6	
Tryptophan Metabolites					
36	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 7.7		3.3	
37	Quinolinic	0.63 - 6.7		4.5	
38	Kynurenic	≤ 4.1		1.5	
39	Quinolinic / 5-HIAA Ratio	0.04 - 2.2		1.4	

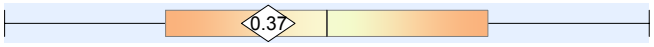
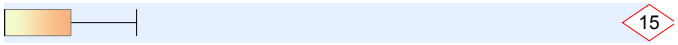
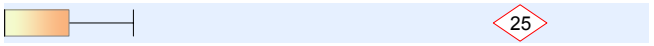
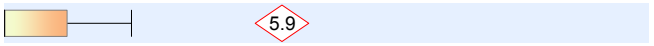
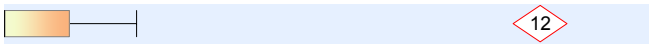
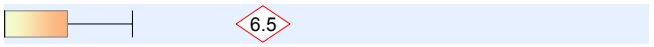
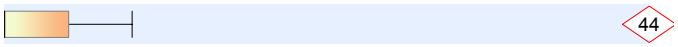
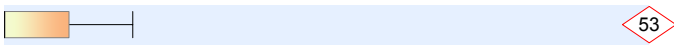
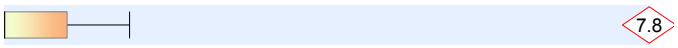
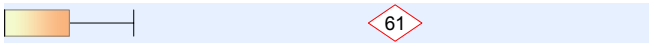
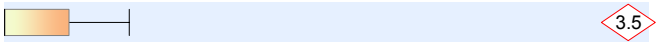
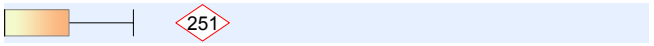
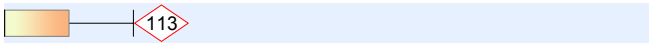
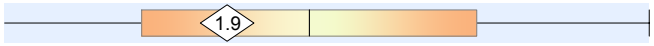
The Great Plains Laboratory, Inc.

Requisition #:

Patient Name:

Physician: KURT WOELLER DO

Date of Collection: 3/2017

Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Females Under Age 13
Pyrimidine Metabolites - Folate Metabolism					
40	Uracil	≤ 19		7.2	
41	Thymine	0.01 - 0.89		0.37	
Ketone and Fatty Acid Oxidation					
42	3-Hydroxybutyric	≤ 4.1	H	15	
43	Acetoacetic	≤ 10	H	25	
44	4-Hydroxybutyric	≤ 3.4	H	5.9	
45	Ethylmalonic	≤ 4.6	H	12	
46	Methylsuccinic	≤ 4.3	H	6.5	
47	Adipic	≤ 9.7	H	44	
48	Suberic	≤ 9.5	H	53	
49	Sebacic	≤ 0.37	H	7.8	
Nutritional Markers					
Vitamin B12					
50	Methylmalonic ✱	≤ 6.2		6.1	
Vitamin B6					
51	Pyridoxic (B6)	≤ 59		46	
Vitamin B5					
52	Pantothenic (B5)	≤ 26	H	61	
Vitamin B2 (Riboflavin)					
53	Glutaric ✱	≤ 1.1	H	3.5	
Vitamin C					
54	Ascorbic	10 - 200	H	251	
Vitamin Q10 (CoQ10)					
55	3-Hydroxy-3-methylglutaric ✱	≤ 101	H	113	
Glutathione Precursor and Chelating Agent					
56	N-Acetylcysteine (NAC)	≤ 0.41		0	
Biotin (Vitamin H)					
57	Methylcitric ✱	≤ 5.5		1.9	

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

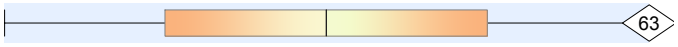
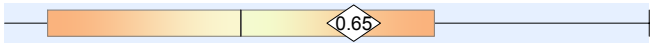
The Great Plains Laboratory, Inc.

Requisition #:

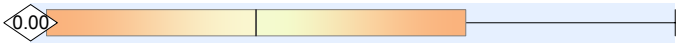
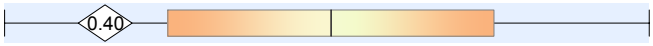
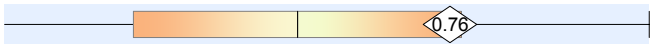
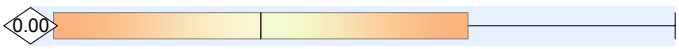
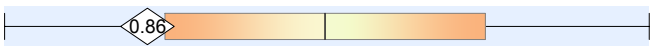
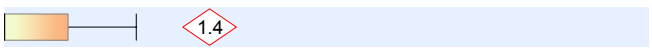
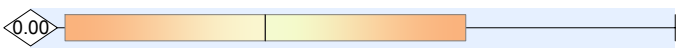
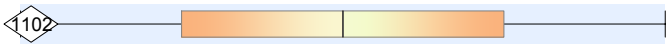
Patient Name:

Physician: KURT WOELLER DO

Date of Collection: 3/2017

Metabolic Markers in Urine		Reference Range (mmol/mol creatinine)				Patient Value	Reference Population - Females Under Age 13
Indicators of Detoxification							
Glutathione							
58	Pyroglutamic ✱	7.0	-	63		63	
59	2-Hydroxybutyric ✱		≤	2.2	H	3.6	
Ammonia Excess							
60	Orotic		≤	0.88	H	1.4	
Aspartame, salicylates, or GI bacteria							
61	2-Hydroxyhippuric		≤	1.2		0.65	

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

Amino Acid Metabolites							
62	2-Hydroxyisovaleric		≤	1.2		0	
63	2-Oxoisovaleric	0.03	-	2.4		0.40	
64	3-Methyl-2-oxovaleric		≤	1.1		0.76	
65	2-Hydroxyisocaproic		≤	0.70		0	
66	2-Oxoisocaproic		≤	0.54		0.14	
67	2-Oxo-4-methiolbutyric		≤	0.30		0.06	
68	Mandelic		≤	0.28		0	
69	Phenyllactic		≤	0.27		0.17	
70	Phenylpyruvic	0.45	-	2.3		0.86	
71	Homogentisic		≤	0.51		0.10	
72	4-Hydroxyphenyllactic	0.04	-	1.1	H	1.4	
73	N-Acetylaspartic		≤	8.1		0	
74	Malonic		≤	12		0	
Mineral Metabolism							
75	Phosphoric	1 000	-	7 300		1 102	

The Great Plains Laboratory, Inc.

Requisition #:		*Physician:*	KURT WOELLER DO
Patient Name:		*Date of Collection:*	3/2017

Indicator of Fluid Intake

76	*Creatinine	55	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.

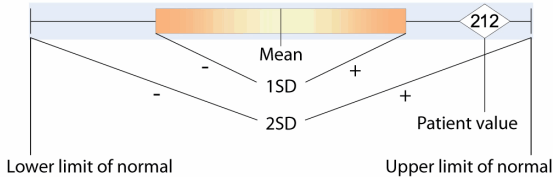
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

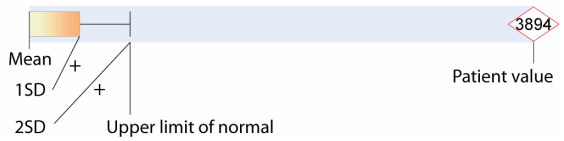
Example of Value Within Reference Range

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	

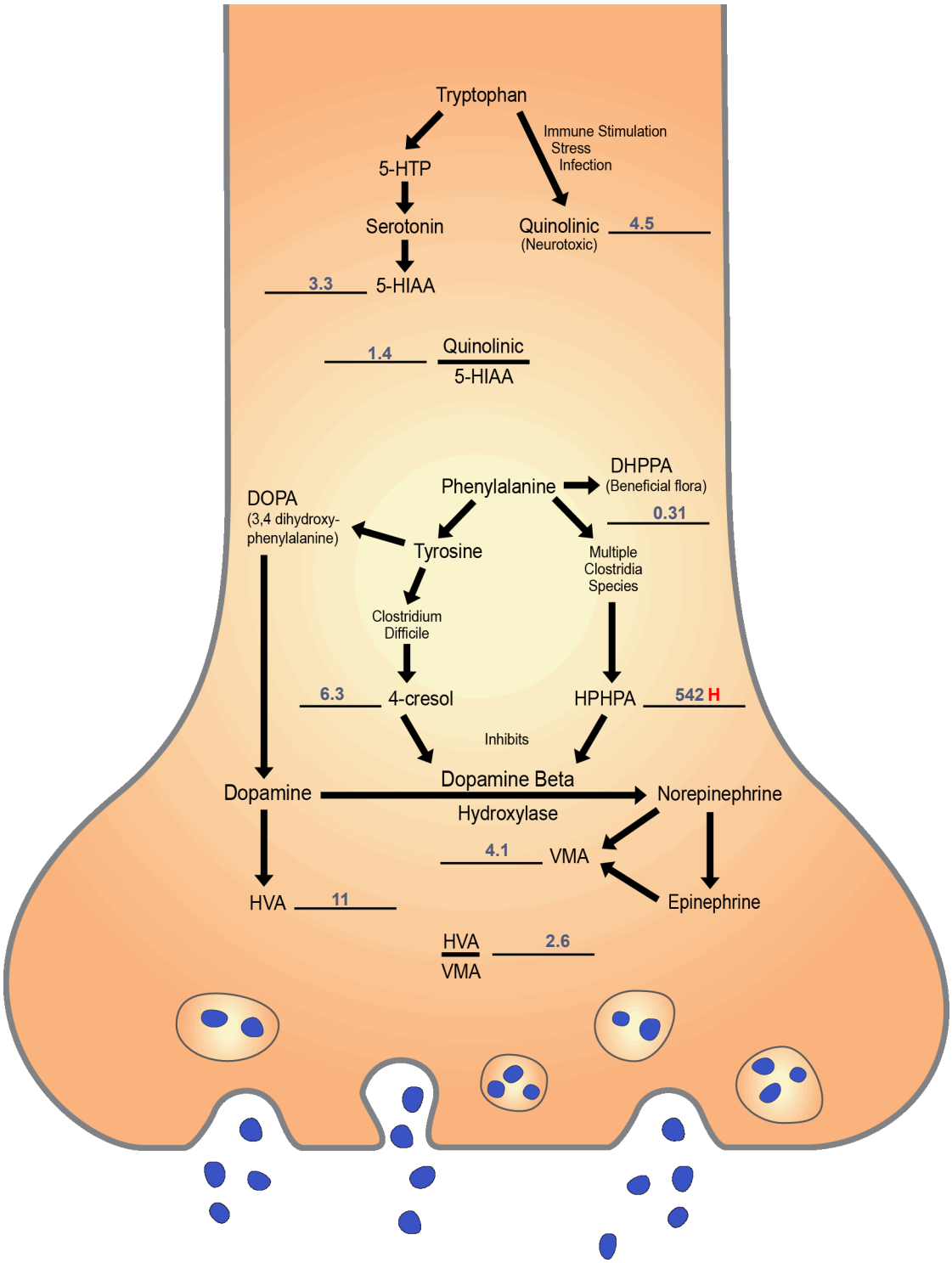


Example of Elevated Value

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.

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 4-hydroxybenzoic acid and/or 4-hydroxyhippuric acid (Markers 12,13) may be due to bacterial overgrowth of the GI tract, intake of fruits such as blueberries rich in polyphenols (anthocyanins, flavonols, and hydroxycinnamates), or may be from paraben additive exposure. Parabens are 4-hydroxybenzoic acid alkyl esters with antimicrobial properties. 4-Hydroxybenzoic acid may be excreted as its glycine conjugate 4-hydroxyhippuric acid. High levels of these paraben metabolites in urine (>10 mmol /mol creatinine) may result from excessive exposure to parabens. Parabens are common preservatives allowed in foods, drugs, cosmetics and toiletries, but they also have a long history of use in a variety of pharmaceutical products for injection, inhalation, oral, topical, rectal or vaginal administration. Some individuals experience skin reactions as most parabens are readily and completely absorbed through the skin and the GI tract. Parabens have been considered safe because of their low toxicity profile and their long history of safe use; however, recent studies challenge this view. In 1998, Routledge *et.al*., (Toxicol.Appl.Pharmacol. **153**,12-19), reported parabens having estrogenic activity *in vitro*. A number of *in vivo* studies have further elucidated potential endocrine disruption by parabens affecting reproduction or promote tumor growth . Parabens have been found at high levels in breast cancer biopsies, although a definitive relationship with breast cancer has not been demonstrated. Parabens may contribute to mitochondrial failure by uncoupling oxidative phosphorylation and depleting cellular ATP . 4-Hydroxyhippuric acid has been found to be an inhibitor of Ca2+- ATPase in end-stage renal failure. Eliminate all sources of parabens. To accelerate paraben excretion , use sauna therapy, the Hubbard detoxification protocol employing niacin supplementation, or glutathione supplementation (oral, intravenous, transdermal, or precursors such as N-acetyl cysteine [NAC]).

High HPHPA (3-(3-hydroxyphenyl)-3-hydroxypropionic acid) (Marker 16) is an abnormal phenylalanine metabolite produced when byproducts of *Clostridium* bacteria combine with human metabolites. High concentrations of this compound cause abnormal behavior by inhibiting metabolism of dopamine to epinephrine, resulting in high levels of the dopamine metabolite homovanillic acid (HVA) in the urine and insufficient epinephrine/norepinephrine in the body. It is associated with behavioral, gastrointestinal, and neuropsychiatric symptoms including tic disorders, depression, autism, schizophrenia, aggression, seizures, anorexia, obsessive compulsive disorder, and hyperactivity. Neuropsychiatric effects are more common when values exceed 500 mmol/mol creatinine.

The *Clostridia* species that cause the greatest quantities of urinary HPHPA are *C. sporogenes, C. caloritolerans,* and *C. botulinum*. Additionally, *C. mangenoti, C. ghoni, C. bifermentans, C. caproicum, and C. sordellii* are also capable of causing elevated urinary levels of HPHPA.

HPHPA precursors are **not** produced by *C.perfringens* -types A-F*, C.tetani, C.subterminale C.capitovale, C.septicum, C.difficile, C.histolyticum,* or *C.tertium.*

C. botulinum would appear to be an unlikely source unless clinical symptoms of botulism are present. The botulinum toxin can cause a severe flaccid paralytic <http://en.wikipedia.org/wiki/Flaccid_paralysis> disease in humans and animals and is the most potent toxin known to humankind, with a lethal dose of less than 1 µg in humans. Symptoms of botulism include weakness, impaired vision, fatigue, and impaired speech. This may then be followed by weakness of the arms, chest muscles and legs. Surprisingly, symptoms may sometimes be mild and the severity of symptoms appears to be modulated by the amount of beneficial flora in the intestinal tract. In food borne botulism, symptoms generally begin 18 to 36 hours after eating contaminated food, but they can occur as early as 6 hours or as late as 10 days. *C. caloritolerans* is so named because it can survive at the boiling point for 8 hours. Its extreme resistance to heat may allow common food borne transmission. *C. sporogenes* is the name given to strains of *Clostridium botulinum* that do not produce botulinum <http://en.wikipedia.org/wiki/Botulinum> neurotoxins. *C. sporogenes* differs from C. botulinum by a single gene. C. sporogenes is ubiquitous in nature and is commonly found in the flora of humans. *C. sordellii* can be pathogenic and has been implicated in fatal toxic shock syndrome among women of child bearing age.

Treatment with Metronidazole or Vancomycin is almost 100% effective in killing parent *Clostridia* organisms but not their spores. At least three months of probiotic therapy is recommended after antimicrobial treatment due to spore formation by *Clostridia* species. *Clostridia* overgrowth can sometimes be controlled by supplementation with *Lactobacillus rhamnosus GG* (Culturelle) or *Saccharomyces boulardii.* Phenalalanine or tyrosine supplements should be avoided because of the possibility of conversion to HPHPA or other toxic byproducts.

High oxalic with or without elevated glyceric or glycolic acids (Markers 19,20,21) 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 succinic acid (Marker 24) 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 fumaric acid (Marker 25) may be due to impaired Krebs cycle function, defect of the enzyme fumarase or a defect in mitochondrial function. Recommendations for supporting mitochondrial function include supplementation with coenzyme Q-10 (300-600 mg), NAD (25-50mg), L-carnitine or 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. All of these supplements are known to benefit mitochondrial dysfunction.

High malic acid (Marker 26) indicates a greater requirement for nutrients such as niacin (25-50mg) and coenzyme Q-10 (300-600mg). If malic acid is simultaneously elevated with citric, fumaric and alpha-ketoglutaric acids, a possible Cytochrome C Oxidase deficiency would strongly indicate mitochondrial energy pathway dysfunction.

High citric acid (Marker 29) may be due to increased intake of citric acid-containing foods or as a result of intestinal yeast that either produce citric acid or perhaps inhibit the human citric acid cycle. Increased citric acid may also indicate depletion of glutathione, which is required for the enzyme aconitase to metabolize both aconitic and citric acids. If pyroglutamic acid is also high, consider supplements of reduced glutathione, n-acetyl cysteine (NAC), or lipoic acid.

High 3-methylglutaric and/or high 3-methylglutaconic acids (Markers 30,32) 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.

High 3-hydroxyglutaric (Marker 31) is a metabolite associated with the genetic disease glutaric aciduria type I, which is due to a deficiency of glutaryl CoA dehydrogenase, an enzyme involved in the breakdown of lysine, hydroxylysine, and tryptophan. Other elevated organic acids may include glutaric and glutaconic acids. 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 have developed bleeding in the brain or eyes that may be mistaken for the effects of child abuse. This abnormality should be confirmed by additional testing of enzyme deficiencies and/or DNA at a pediatric medical genetics center (Morton et al., Am J. Med. Genetics **41**: 89-95, 1991). Elevated values may also be found in hepatic carnitine palmitoyltransferase I deficiency, short-chain acyl dehydrogenase deficiency (SCAD), or ketosis. Mitochondrial dysfunction induced by glutaric acid metabolites causes astrocytes to adopt a proliferative phenotype, which may underlie neuronal loss, white matter abnormalities and macrocephalia. Values in glutaric aciduria type I range from 60-3000 mmol/mol creatinine. Values higher than normal but less than 60 mmol/mol creatinine may be due to mild glutaric acidemia type I or to the other causes indicated above. Treatment of this disorder includes special diets low in lysine and supplementation with carnitine or acetyl-L-carnitine (1000-2000 mg/day).

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

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

Slightly high 4-hydroxybutyric acid (Marker 44) may be due to the interference from closely related compounds or due to the use of 4-hydroxybutric acid (also called gamma-hydroxy butyric acid) as a supplement.

High ethylmalonic, methylsuccinic, adipic, suberic, or sebacic acids (Markers 45,46,47,48,49) 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.

High pantothenic acid (B5) (Marker 52) 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 (Marker 53) can result from glutaric acidemias, fatty acid oxidation defects, riboflavin deficiency, ingestion of medium-chain triglycerides, metabolic effects of valproic acid (Depakene), and celiac disease. The genetic disorders are usually diagnosed in children but have occasionally been detected in adults. The probability of a genetic disease is higher when values exceed 10 mmol/mol creatinine but such diseases may also be present with lower urine values. DNA tests have been developed for the confirmation of both types of genetic disorders but may not be commercially available. This compound may be elevated in about 10% of children with autism. Regardless of the cause, supplementation with riboflavin (20-100 mg/day) and coenzyme Q-10 (50-100 mg/day) may be beneficial.

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

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

High ascorbic acid (vitamin C) (Marker 54) 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 3-hydroxy-3-methylglutaric acid (Marker 55) is seen in the genetic disease 3-hydroxy 3-methylglutaric aciduria. Typical values observed in the genetic disease are 200-11,000mmol/mol creatinine. The cause of less significant increases in this urinary metabolite is unknown. 3-Hydroxy-3-methylglutaric aciduria may cause vomiting, lethargy, hypotonia, and apnea, sometimes evolving to coma. Laboratory tests reveal metabolic acidosis with severe hypoketotic hypoglycemia on fasting or during acute illness, hyperammonemia, and abnormal liver function. Preliminary diagnosis is based on a pattern of organic acids in urine which includes 3-hydroxy-3-methylglutaric, 3-hydroxyisovaleric, 3-methylglutaconic, 3-methylglutaric, and 3-methylcrotonic acids. Because yeast also produces this compound and yeast metabolites are frequently elevated along with this compound; slight increases may be yeast-related. Reduced activity of 3-hydroxy 3-methylglutaryl Co A reductase, a critical enzyme at the beginning of the cholesterol synthesis pathway, may also elevate this compound. Check cholesterol values when this compound is elevated up to 300 mmol/mol creatinine. Slight elevations may result from coenzyme Q10 deficiency. Supplementation with coenzyme Q10 at 50 - 120 mg/day may be beneficial.

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

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

Slightly elevated orotic acid (Marker 60) 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.

High 4-hydroxyphenyllactic acid (Marker 72) is associated with tyrosinemia, which can be due to immature development of enzymes in infants or to genetic deficiencies. Even a mild case would have levels at least of 100 mmol/mol creatinine. Values between the upper limit of normal and 100 mmol creatinine may be due to the heterozygous genetic carrier state, or mild disease or unknown physiological conditions.

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

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

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.