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 #:	631729	***Physician:***	RON YAFFE
Patient Name:	Yosef Avisrur	***Date of Collection:***	10/15/2018
Patient Age:	30	***Time of Collection:***	00:00 AM
Patient Sex:	M	***Print Date:***	11/13/2018

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	H	2.9	2.9
2 5-Hydroxymethyl-2-furoic	≤ 18		11	11
3 3-Oxoglutaric	≤ 0.11		0	0.00
4 Furan-2,5-dicarboxylic	≤ 13		7.9	7.9
5 Furancarbonylglycine	≤ 2.3		0.17	0.17
6 Tartaric	≤ 5.3		1.1	1.1
7 Arabinose	≤ 20	H	55	55
8 Carboxycitric	≤ 20		0.03	0.03
9 Tricarballylic	≤ 0.58		0.29	0.29
Bacterial Markers				
10 Hippuric	≤ 241		1.7	1.7
11 2-Hydroxyphenylacetic	0.03 - 0.47		0.40	0.40
12 4-Hydroxybenzoic	0.01 - 0.73	H	8.4	8.4
13 4-Hydroxyhippuric	≤ 14		0.08	0.08
14 DHPPA (Beneficial Bacteria)	≤ 0.23		0.05	0.05
Clostridia Bacterial Markers				
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	≤ 18		6.7	6.7
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 102		15	15
17 4-Cresol *(C. difficile)*	≤ 39		5.6	5.6
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	≤ 6.8		0.25	0.25

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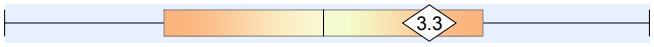
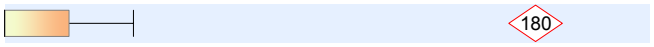
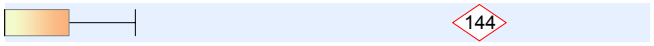
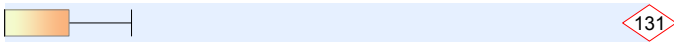
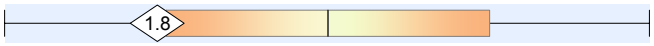
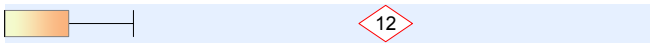
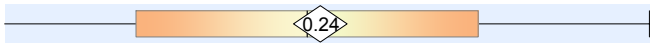
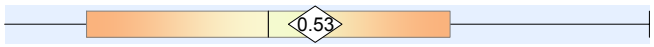
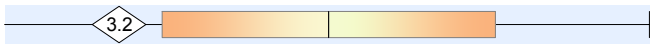
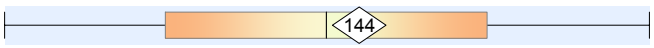
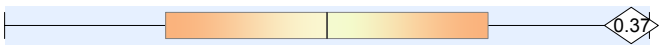
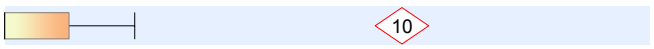
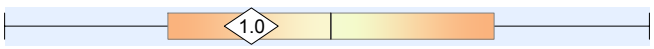
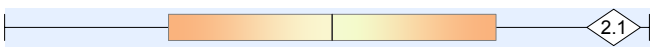
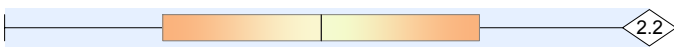
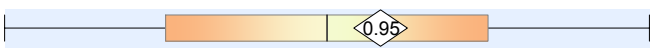
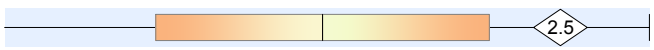
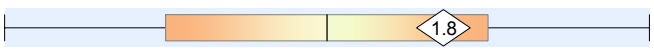
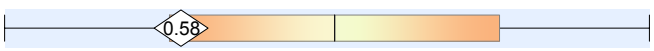
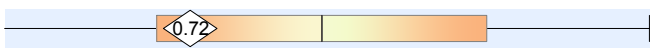
Metabolic Markers in Urine		Reference Range *(mmol/mol creatinine)*		Patient Value	Reference Population - Males Age 13 and Over
Oxalate Metabolites					
19	Glyceric	0.21 - 4.9		3.3	
20	Glycolic	18 - 81	H	180	
21	Oxalic	8.9 - 67	H	144	
Glycolytic Cycle Metabolites					
22	Lactic	0.74 - 19	H	131	
23	Pyruvic	0.28 - 6.7		1.8	
Mitochondrial Markers - Krebs Cycle Metabolites					
24	Succinic	≤ 5.3	H	12	
25	Fumaric	≤ 0.49		0.24	
26	Malic	≤ 1.1		0.53	
27	2-Oxoglutaric	≤ 18		3.2	
28	Aconitic	4.1 - 23		23	
29	Citric	2.2 - 260		144	
Mitochondrial Markers - Amino Acid Metabolites					
30	3-Methylglutaric	0.02 - 0.38		0.37	
31	3-Hydroxyglutaric	≤ 4.6	H	10	
32	3-Methylglutaconic	0.38 - 2.0		1.0	
Neurotransmitter Metabolites					
Phenylalanine and Tyrosine Metabolites					
33	Homovanillic (HVA) *(dopamine)*	0.39 - 2.2		2.1	
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53 - 2.2		2.2	
35	HVA / VMA Ratio	0.32 - 1.4		0.95	
Tryptophan Metabolites					
36	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 2.9		2.5	
37	Quinolinic	0.52 - 2.4		1.8	
38	Kynurenic	0.12 - 1.8		0.58	
39	Quinolinic / 5-HIAA Ratio	≤ 2.5		0.72	

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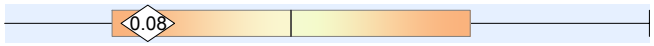
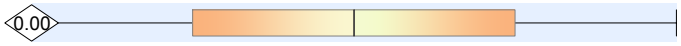
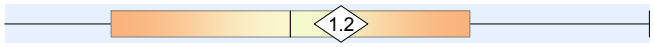
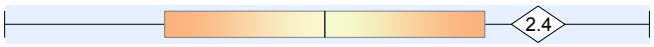
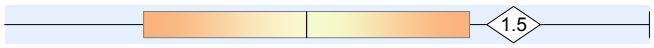
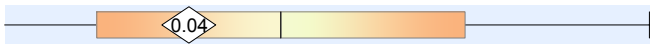
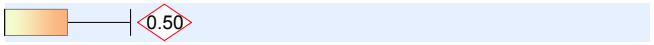
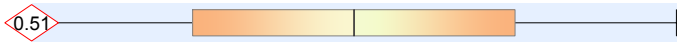
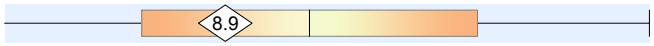
Patient Name:	Yosef Avisrur	***Date of Collection:***	10/15/2018

Metabolic Markers in Urine		Reference Range *(mmol/mol creatinine)*		Patient Value		Reference Population - Males Age 13 and Over
Pyrimidine Metabolites - Folate Metabolism						
40	Uracil	≤ 6.9		2.0		
41	Thymine	≤ 0.36		0.08		
Ketone and Fatty Acid Oxidation						
42	3-Hydroxybutyric	≤ 1.9		0.74		
43	Acetoacetic	≤ 10		0		
44	4-Hydroxybutyric	≤ 4.3		1.7		
45	Ethylmalonic	0.13 - 2.7	H	4.2		
46	Methylsuccinic	≤ 2.3		1.2		
47	Adipic	≤ 2.9		2.4		
48	Suberic	≤ 1.9		1.5		
49	Sebacic	≤ 0.14		0.04		
Nutritional Markers						
Vitamin B12						
50	Methylmalonic ✱	≤ 2.3		1.8		
Vitamin B6						
51	Pyridoxic (B6)	≤ 26		5.9		
Vitamin B5						
52	Pantothenic (B5)	≤ 5.4		1.8		
Vitamin B2 (Riboflavin)						
53	Glutaric ✱	≤ 0.43	H	0.50		
Vitamin C						
54	Ascorbic	10 - 200	L	0.51		
Vitamin Q10 (CoQ10)						
55	3-Hydroxy-3-methylglutaric ✱	≤ 26		8.9		
Glutathione Precursor and Chelating Agent						
56	N-Acetylcysteine (NAC)	≤ 0.13		0		
Biotin (Vitamin H)						
57	Methylcitric ✱	0.15 - 1.7		1.6		

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

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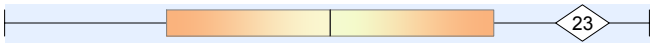
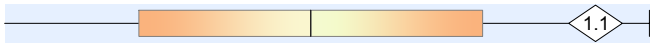
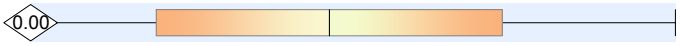
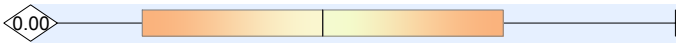
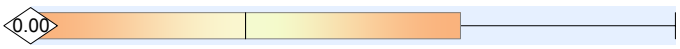
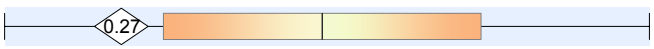
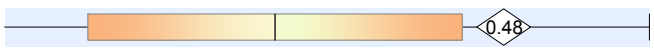
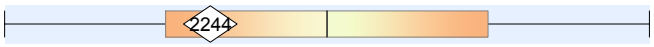
Metabolic Markers in Urine		Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Males Age 13 and Over
Indicators of Detoxification				
Glutathione				
58	Pyroglutamic ✱	5.7 - 25	23	
59	2-Hydroxybutyric ✱	≤ 1.2	1.1	
Ammonia Excess				
60	Orotic	≤ 0.46	0.36	
Aspartame, salicylates, or GI bacteria				
61	2-Hydroxyhippuric	≤ 0.86	0.01	

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

Amino Acid Metabolites				
62	2-Hydroxyisovaleric	≤ 0.41	0	
63	2-Oxoisovaleric	≤ 1.5	0	
64	3-Methyl-2-oxovaleric	≤ 0.56	0.05	
65	2-Hydroxyisocaproic	≤ 0.39	0	
66	2-Oxoisocaproic	≤ 0.34	0.05	
67	2-Oxo-4-methiolbutyric	≤ 0.14	0	
68	Mandelic	≤ 0.09	0	
69	Phenyllactic	≤ 0.10	0	
70	Phenylpyruvic	0.02 - 1.4	0.27	
71	Homogentisic	≤ 0.23	0.01	
72	4-Hydroxyphenyllactic	≤ 0.62	0.48	
73	N-Acetylaspartic	≤ 2.5	2.2	
74	Malonic	≤ 9.9	4.6	
Mineral Metabolism				
75	Phosphoric	1 000 - 4 900	2 244	

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Patient Name:	Yosef Avisrur	***Date of Collection:***	10/15/2018

Indicator of Fluid Intake

76	***Creatinine**	**96**	**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.

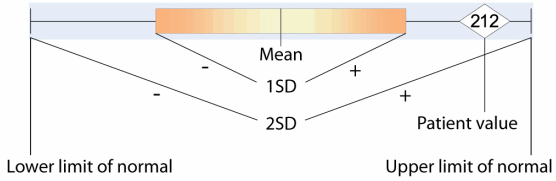
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

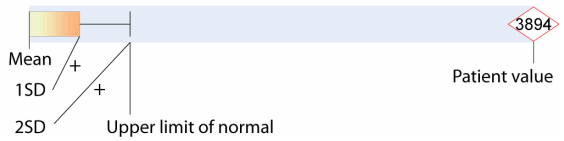
Example of Value Within Reference Range

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	

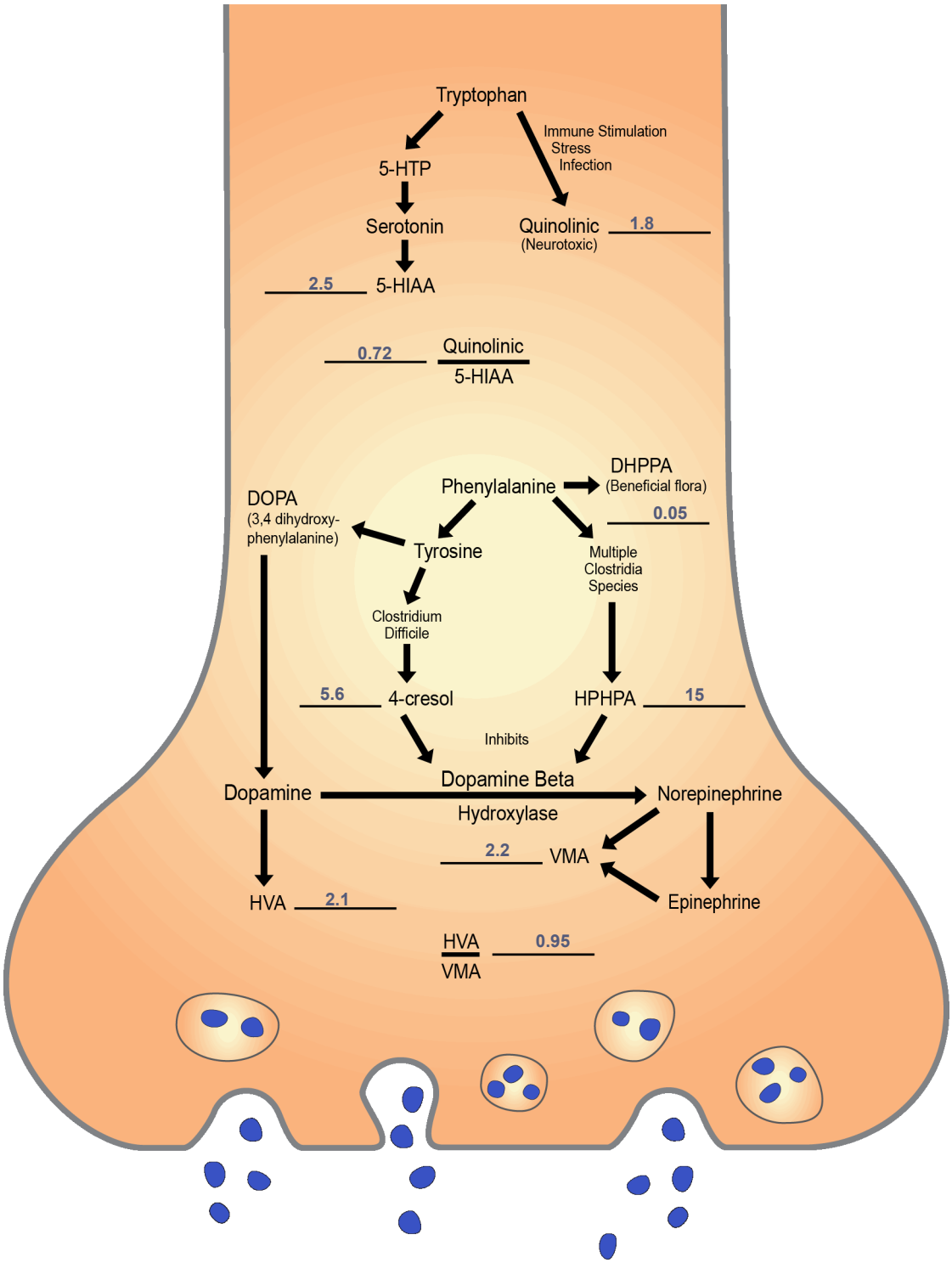


Example of Elevated Value

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 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 lactic acid and/or high pyruvic acid (Markers 22,23) may be caused by many nonspecific factors, such as vigorous exercise, bacterial overgrowth of the GI tract, shock, poor perfusion, anemia, mitochondrial dysfunction or damage, and many other causes. Conversion of pyruvic acid to acetyl-CoA requires the cofactors coenzyme A (derived from pantothenic acid), lipoic acid, FAD derived from riboflavin, and thiamine. However, the possibility of an inborn error of metabolism increases as the value exceeds 300 mmol/mol creatinine. Values greater than 1000 mmol/mol creatinine indicate a much higher likelihood of an inborn error of metabolism. There are many inborn errors of metabolism that present elevated lactic acid, including disorders of sugar metabolism and pyruvate dehydrogenase deficiency.

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 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).

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.

Pyridoxic acid (B6) levels below the mean (Marker 51) 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.

Pantothenic acid (B5) levels below the mean (Marker 52) may be associated with less than optimum health conditions. Supplementation with B5 (250 mg/day) or a multivitamin may be beneficial.

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.

Ascorbic acid (vitamin C) levels below the mean (Marker 54) 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.

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.