MOSAIC DIAGNOSTICS

OAT ORGANIC ACIDS TEST

Requisition #:	9900001			*Practitioner:*	NO PHYSICIAN
Patient Name:	Report Sample			*Date of Collection:*	12/01/2022
Date of Birth:	03/09/1960	*Patient Age:*	62	*Time of Collection:*	Not Given
Patient Sex:	F			*Report Date:*	11/09/2023

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Females Age 13 and Over
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	≤ 3.6		1.6	1.6
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 14		14	14
3 3-Oxoglutaric	≤ 0.33		0.23	0.23
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 16		8.1	8.1
5 Furancarbonylglycine *(Aspergillus)*	≤ 1.9	H	15	15
6 Tartaric *(Aspergillus)*	≤ 4.5	H	6.2	6.2
7 Arabinose	≤ 29	H	69	69
8 Carboxycitric	≤ 29		12	12
9 Tricarballylic *(Fusarium)*	≤ 0.44	H	0.55	0.55
Bacterial Markers				
10 Hippuric	≤ 613	H	1,340	1340
11 2-Hydroxyphenylacetic	0.06 - 0.66		0.53	0.53
12 4-Hydroxybenzoic	≤ 1.3		1.2	1.2
13 4-Hydroxyhippuric	0.79 - 17		8.7	8.7
14 DHPPA (Beneficial Bacteria)	≤ 0.38	H	0.57	0.57
Clostridia Bacterial Markers				
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	≤ 19		15	15
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 208		162	162
17 4-Cresol *(C. difficile)*	≤ 75		37	37
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	≤ 11		2.9	2.9

This test was developed, and its performance characteristics determined by Mosaic Diagnostics Laboratory. It has not been cleared or approved by the US Food and Drug Administration.

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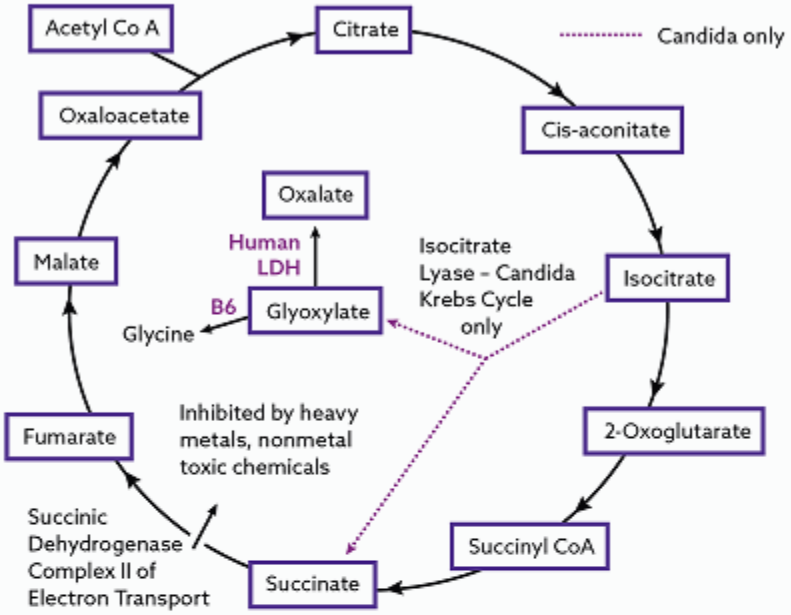
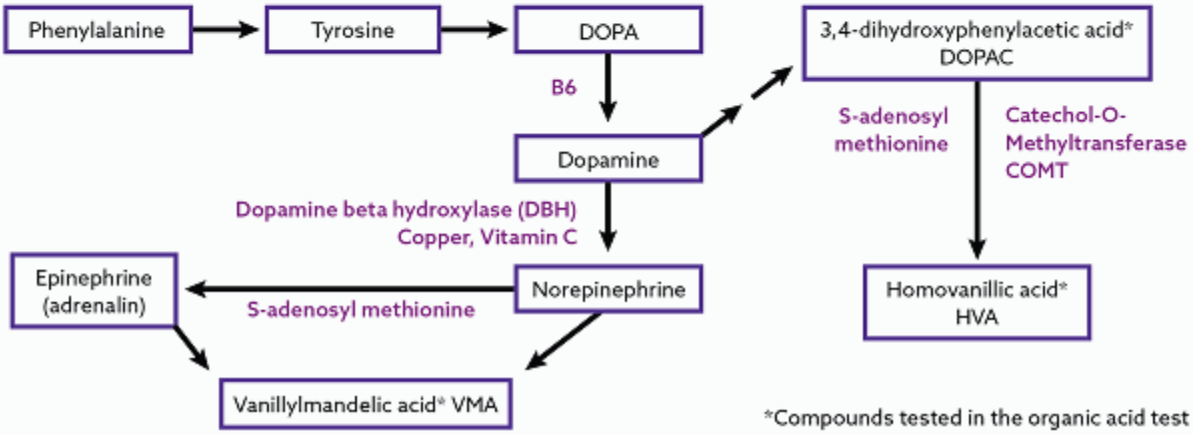
Human Krebs Cycle showing Candida Krebs Cycle variant that causes excess Oxalate via Glyoxylate



Major pathways in the synthesis and breakdown of **catecholamine neurotransmitters** in the absence of microbial inhibitors



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Patient Name:	Report Sample	***Date of Collection:***	12/01/2022

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Females Age 13 and Over
Oxalate Metabolites			
19 Glyceric	0.77 - 7.0	H 7.6	7.6
20 Glycolic	16 - 117	89	89
21 Oxalic	6.8 - 101	H 224	224
Glycolytic Cycle Metabolites			
22 Lactic	≤ 48	22	22
23 Pyruvic	≤ 9.1	2.4	2.4
Mitochondrial Markers - Krebs Cycle Metabolites			
24 Succinic	≤ 9.3	H 18	18
25 Fumaric	≤ 0.94	0.82	0.82
26 Malic	0.06 - 1.8	1.7	1.7
27 2-Oxoglutaric	≤ 35	11	11
28 Aconitic	6.8 - 28	14	14
29 Citric	≤ 507	H 610	610
Mitochondrial Markers - Amino Acid Metabolites			
30 3-Methylglutaric	≤ 0.76	0.35	0.35
31 3-Hydroxyglutaric	≤ 6.2	5.4	5.4
32 3-Methylglutaconic	≤ 4.5	1.4	1.4
Neurotransmitter Metabolites			
Phenylalanine and Tyrosine Metabolites			
33 Homovanillic (HVA) *(dopamine)*	0.80 - 3.6	3.5	3.5
34 Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.46 - 3.7	2.5	2.5
35 HVA / VMA Ratio	0.16 - 1.8	1.4	1.4
36 Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.08 - 3.5	H 4.6	4.6
37 HVA/ DOPAC Ratio	0.10 - 1.8	0.77	0.77
Tryptophan Metabolites			
38 5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 4.3	1.9	1.9
39 Quinolinic	0.85 - 3.9	2.4	2.4
40 Kynurenic	≤ 2.2	1.4	1.4

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Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Females Age 13 and Over
Pyrimidine Metabolites - Folate Metabolism			
41 Uracil	≤ 9.7	4.5	
42 Thymine	≤ 0.56	0.19	
Ketone and Fatty Acid Oxidation			
43 3-Hydroxybutyric	≤ 3.1	1.7	
44 Acetoacetic	≤ 10	1.3	
45 Ethylmalonic	0.44 - 2.8	2.1	
46 Methylsuccinic	0.10 - 2.2	H 4.1	
47 Adipic	0.04 - 3.8	2.0	
48 Suberic	0.18 - 2.2	H 3.2	
49 Sebacic	≤ 0.24	0.21	
Nutritional Markers			
Vitamin B12			
50 Methylmalonic ✱	≤ 2.3	H 2.8	
Vitamin B6			
51 Pyridoxic (B6)	≤ 34	3.7	
Vitamin B5			
52 Pantothenic (B5)	≤ 10	H 23	
Vitamin B2 (Riboflavin)			
53 Glutaric ✱	0.04 - 0.36	H 0.89	
Vitamin C			
54 Ascorbic	10 - 200	L 0.56	
Vitamin Q10 (CoQ10)			
55 3-Hydroxy-3-methylglutaric ✱	0.17 - 39	29	
Glutathione Precursor and Chelating Agent			
56 N-Acetylcysteine (NAC)	≤ 0.28	0.04	
Biotin (Vitamin H)			
57 Methylcitric ✱	0.19 - 2.7	1.1	

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

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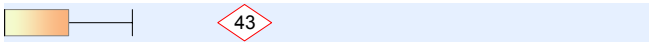
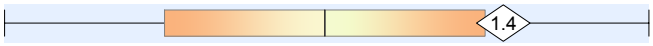
Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Females Age 13 and Over

Indicators of Detoxification

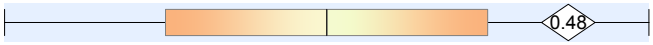
Glutathione

58	Pyroglutamic ✱	10 - 33	H	43	

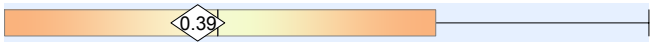
Methylation, Toxic exposure

59	2-Hydroxybutyric ✱✱	0.03 - 1.8		1.4	

Ammonia Excess

60	Orotic	0.06 - 0.54		0.48	

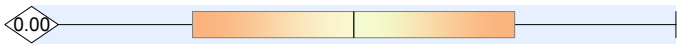
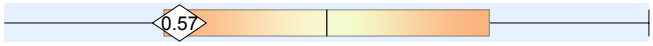
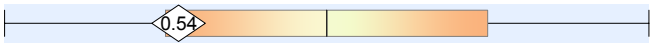
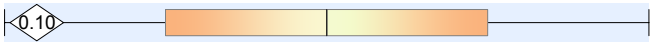
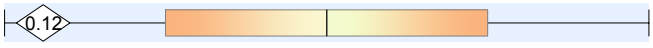
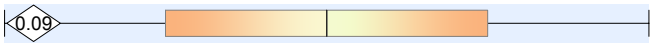
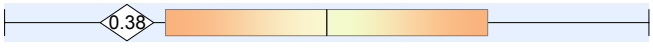
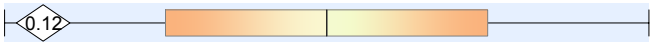
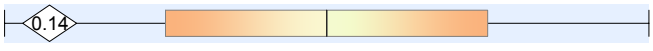
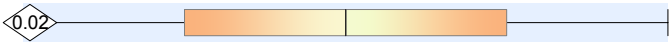
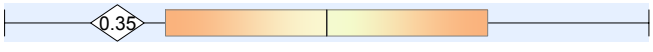
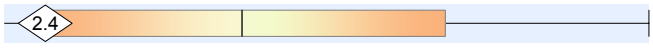
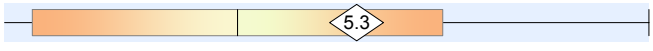
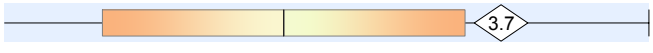
Aspartame, salicylates, or GI bacteria

61	2-Hydroxyhippuric	≤ 1.3		0.39	

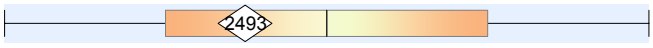
✱ ***A high value for this marker may indicate a Glutathione deficiency.***

✱✱ ***High values may indicate methylation defects and/or toxic exposures.***

Amino Acid Metabolites

62	2-Hydroxyisovaleric	≤ 2.0		0	
63	2-Oxoisovaleric	≤ 2.1		0.57	
64	3-Methyl-2-oxovaleric	≤ 2.0		0.54	
65	2-Hydroxyisocaproic	≤ 2.0		0.10	
66	2-Oxoisocaproic	≤ 2.0		0.12	
67	2-Oxo-4-methiolbutyric	≤ 2.0		0.09	
68	Mandelic	≤ 2.0		0.38	
69	Phenyllactic	≤ 2.0		0.12	
70	Phenylpyruvic	≤ 2.0		0.14	
71	Homogentisic	≤ 2.0		0.02	
72	4-Hydroxyphenyllactic	≤ 2.0		0.35	
73	N-Acetylaspartic	≤ 38		2.4	
74	Malonic	≤ 9.7		5.3	
75	4-Hydroxybutyric	≤ 4.8		3.7	

Mineral Metabolism

76	Phosphoric	1,000 - 5,000		2,493	

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Indicator of Fluid Intake

77	***Creatinine**	**100**	**mg/dL**	

*The creatinine test is performed to adjust metabolic marker results for differences in fluid intake. Urinary creatinine has limited diagnostic value due to variability as a result of recent fluid intake. Samples are rejected if creatinine is below 20 mg/dL unless the client requests results knowing of our rejection criteria.

Explanation of Report Format

The reference ranges for organic acids were established using samples collected from typical individuals of all ages with no known physiological or psychological disorders. The ranges were determined by calculating the mean and standard deviation (SD) and are defined as ± 2SD of the mean. Reference ranges are age and gender specific, consisting of Male Adult (≥13 years), Female Adult (≥13 years), Male Child (<13 years), and Female Child (<13 years).

There are two types of graphical representations of patient values found in the new report format of both the standard Organic Acids Test and the Microbial Organic Acids Test.

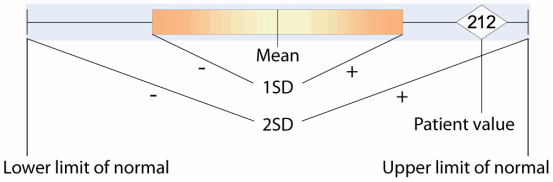
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

The second graph will occur when the value of the patient exceeds the upper limit of normal. In such cases, the graphical reference range is “shrunk” so that the degree of abnormality can be appreciated at a glance. In this case, the lower limits of normal are not shown, only the upper limit of normal is shown.

In both cases, the value of the patient is given to the left of the graph and is repeated on the graph inside a diamond. If the value is within the normal range, the diamond will be outlined in black. If the value is high or low, the diamond will be outlined in red.

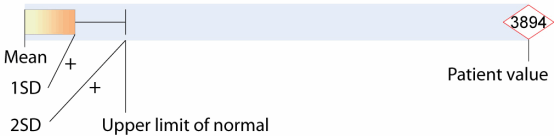
Example of Value Within Reference Range

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth				
HPHPA (Clostridia marker)	<	219 .9	212	



Example of Elevated Value

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Result	Reference Range - Males Age 13 and Under
Intestinal Microbial Overgrowth				
HPHPA (Clostridia marker)	<	219 .9	H 3894	



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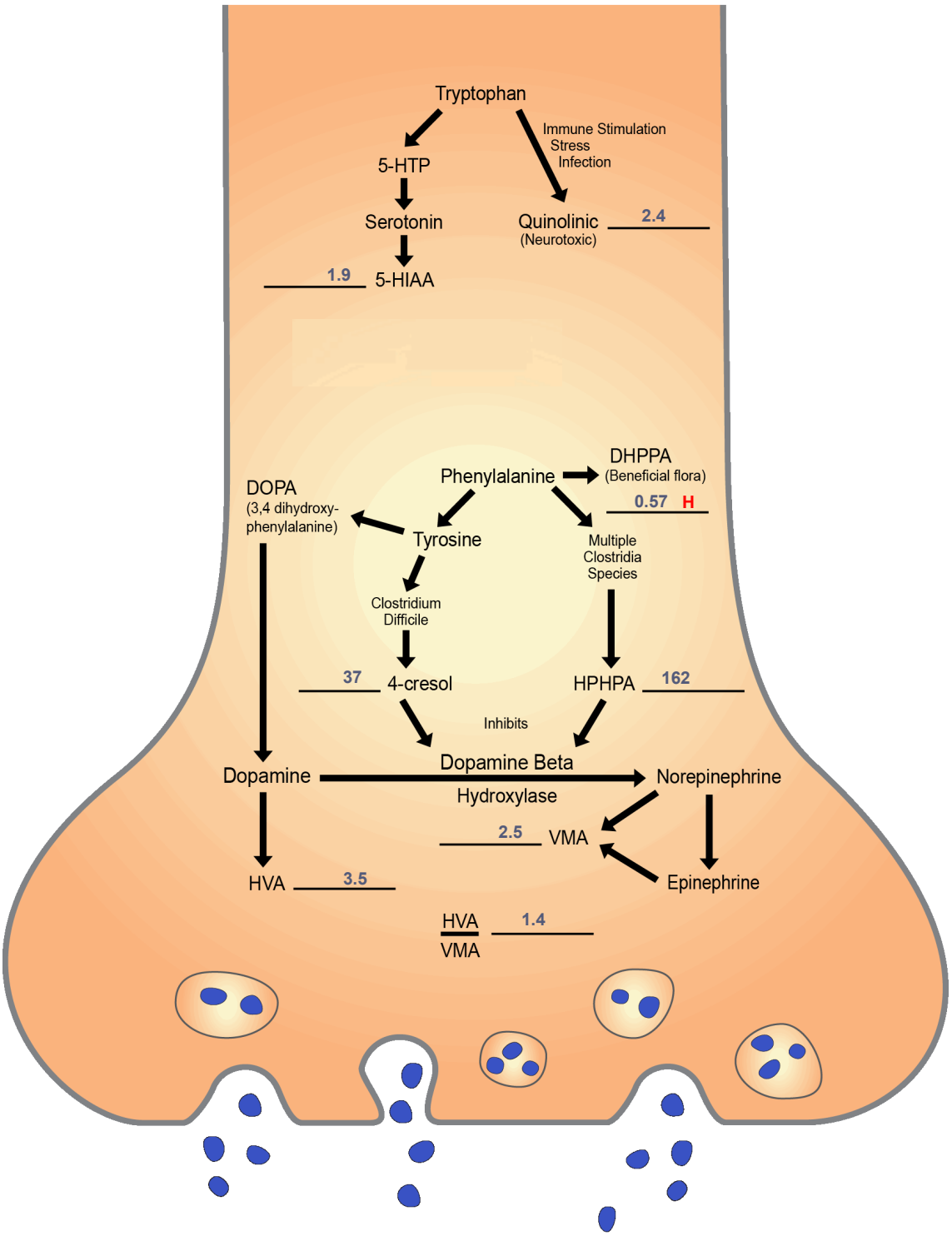
Neurotransmitter Metabolism Markers



The diagram contains the patient's test results for neurotransmitter metabolites and shows their relationship with key biochemical pathways within the axon terminal of nerve cells. The effect of microbial byproducts on the blockage of the conversion of dopamine to norepinephrine is also indicated.

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Interpretation

High yeast/fungal metabolites (1-8) Elevations of one or more metabolites indicate a yeast/fungal overgrowth of the gastrointestinal (GI) tract. Prescription or natural (botanical) anti-fungals, along with supplementation of high potency multi-strain probiotics, may reduce yeast/fungal levels.

High 5-hydroxymethyl-2-furoic acid (2), furan-2,5-dicarboxylic acid (4), or furancarbonylglycine (5). High 5-hydroxymethyl-2-furoic acid, furan-2,5-dicarboxylic acid, and furancarbonylglycine have been reported to be byproducts of fungi such as Aspergillus species. Tartaric acid and oxalic acid have also been reported as fungal byproducts. Values of these compounds in urine decreased after antifungal treatment so high values may indicate fungal colonization of the gastrointestinal tract. Individuals with high values may want to followup with The Great Plains Laboratory urine Mycotoxin test.

High tricarballylic acid (propane-1,2,3-tricarboxylic acid) (9) could be caused by the intake of corn or corn-based food contaminated with fumonisins, a group of mycotoxins produced primarily by *F. verticillioides*, and other related species. Tricarballylic acid is released from fumonisins during passage through the gastrointestinal tract. Tricarballylic acid is an inhibitor of the enzyme aconitase and therefore interferes with the Krebs cycle. The main symptoms of aconitase deficiency are myopathy and exercise intolerance. It may also act as a magnesium chelator. Tricarballylic acid is also metabolite of a component of a substance in modified corn starch, octenylsuccinic acid, found in a number of infant formulas such as Nutramigen, Vivonex, and Pregestimil. In addition, tricarballylic acid is a byproduct of beet sugar and maple sugar refining and might appear after ingestion of these sugars. Tricarballylic acid is also released from fumonisins upon certain food processing conditions. Clinical syndromes due to the intact mycotoxin are rare and characterized by abdominal pain and diarrhea. A specific role for fumonisins in the development of neural tube defects was suggested after the appearance of a cluster of such defects in Texas associated with consumption of corn from the heavily fumonisin-contaminated 1989 corn crop. More recent studies have shown that fumonisin B1 inhibits folate metabolism in cultured cells. Confirmation of Fusarium species can be done by the urine Mycotoxin test of The Great Plains Laboratory.

High hippuric acid (10) 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 DHPPA (3,4 dihydroxyphenylpropionic acid) (14) indicates excessive intake of chlorogenic acid, a common substance found 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. Harmless or beneficial bacteria such as Lactobacilli, Bifidobacteria, and E. coli mediate the breakdown of chlorogenic acid to 3,4-dihydroxyphenylpropionic acid (DHPPA), and high values may indicate increased amounts of these species in the GI tract. In addition, one *Clostridia* species, *C. orbiscindens*, can convert the flavanoids luteolin and eriodictyol, occurring only in a relatively small food group that includes parsley, thyme, celery, and sweet red pepper to 3,4-dihydroxyphenylpropionic acid. The quantity of *Clostridia orbiscindens* in the GI tract is negligible (approximately 0.1% of the total bacteria) compared to the predominant flora of *Lactobacilli, Bifidobacteria,* and *E. coli*. Consequently, this marker is essentially useless as a general *Clostridia* marker but may be a good indicator of the presence of beneficial flora.

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High glyceric (19): may be due to microbial sources such as yeast (Aspergillus, Penicillium, Candida) or due to dietary sources containing glycerol/glycerine.

High oxalic (21) with or without elevated glyceric (19) or glycolic acids (20) may be associated with the genetic hyperoxalurias, autism, women with vulvar pain, fibromyalgia, and may also be due to high vitamin C intake. However, kidney stone formation from oxalic acid was not correlated with vitamin C intake in a very large study. Besides being present in varying concentrations in most vegetables and fruits, oxalates, the mineral conjugate base forms of oxalic acid, are also byproducts of molds such as *Aspergillus* and *Penicillium* and probably *Candida*. If yeast or fungal markers are elevated, antifungal therapy may reduce excess oxalates. High oxalates may cause anemia that is difficult to treat, skin ulcers, muscles pains, and heart abnormalities. Elevated oxalic acid is also the result of anti-freeze (ethylene glycol) poisoning. Oxalic acid is a toxic metabolite of trichloroacetic acid and other environmental pollutants. In addition, decomposing vitamin C may form oxalates during transport or storage.

Elevated oxalate values with a concomitant increase in glycolic acid may indicate genetic hyperoxaluria (type I), whereas increased glyceric acid may indicate a genetic hyperoxaluria (type II). Elevated oxalic acid with normal levels of glyceric or glycolic metabolites rules out a genetic cause for high oxalate. However, elevated oxalates may be due to a new genetic disorder, hyperoxaluria type III.

Regardless of its source, high oxalic acid may contribute to kidney stones and may also reduce ionized calcium. Oxalic acid absorption from the GI tract may be reduced by calcium citrate supplementation before meals. Vitamin B6, arginine, vitamin E, chondroitin sulfate, taurine, selenium, omega-3 fatty acids and/or N-acetyl glucosamine supplements may also reduce oxalates and/or their toxicity. Excessive fats in the diet may cause elevated oxalate if fatty acids are poorly absorbed because of bile salt deficiency. Unabsorbed free fatty acids bind calcium to form insoluble soaps, reducing calcium's ability to bind oxalate and increase its absorption. If taurine is low in a plasma amino acid profile, supplementation with taurine (1000 mg/day) may help stimulate bile salt production (taurocholic acid), leading to better fatty acid absorption and diminished oxalate absorption.

High levels of oxalates are common in autism. Malabsorption of fat and intestinal *Candida* overgrowth are probably the major causes for elevated oxalates in this disorder. Even individuals with elevated glyceric or glycolic acids may not have a genetic disease. To rule out genetic diseases in those people with abnormally high markers characteristic of the genetic diseases, do the following steps: (1) Follow the nutritional steps indicated in this interpretation for one month; (2) If *Candida* is present, treat *Candida* for at least one month; (3) Repeat the organic acid test after abstaining from vitamin C supplements for 48 hours; (4) If the biochemical markers characteristic of genetic oxalate disorders are still elevated in the repeat test, consider DNA tests for the most common mutations of oxalate metabolism. DNA testing for type I hyperoxaluria is available from the Mayo Clinic, Rochester, MN as test #89915 "*AGXT* Gene, Full Gene Analysis" and, for the p.Gly170Arg mutation only, as # 83643 "Alanine:Glyoxylate Aminotransferase [*AGXT*] Mutation Analysis [G170R], Blood"). Another option to confirm the genetic disease is a plasma oxalate test, also available from the Mayo Clinic (Phone 507.266.5700). Plasma oxalate values greater than 50 micromol/L are consistent with genetic oxalate diseases and may serve as an alternate confirmation test.

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Bone tends to be the major repository of excess oxalate in patients with primary hyperoxaluria. Bone oxalate levels are negligible in healthy subjects. Oxalate deposition in the skeleton tends to increase bone resorption and decrease osteoblast activity.

Oxalates may also be deposited in the kidneys, joints, eyes, muscles, blood vessels, brain, and heart and may contribute to muscle pain in fibromyalgia. Oxalate crystal formation in the eyes may be a source of severe eye pain in individuals with autism who may exhibit eye-poking behaviors. High oxalates in the GI tract also may significantly reduce absorption of essential minerals such as calcium, magnesium, zinc, and others. In addition, oxalate deposits in the breast have been associated with breast cancer.

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.

People with abnormally high markers characteristic of the genetic diseases should do the following:
1. Avoid spinach, soy, nuts, and berries for one month.
2. If *Candida* is present, treat *Candida* for at least one month.
3. Repeat the organic acid test having abstained 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.

High succinic acid (24) The most common cause of elevated succinic acid is exposure to toxic chemicals which impairs mitochondria function. The most useful tests for confirming toxic chemical exposure are **The Great Plains Laboratory GPL-TOX test** on urine for 172 chemicals and the hair metals test. Succinic acid is metabolized by the mitochondrial enzyme succinic dehydrogenase, which is significant in that it is both a Krebs cycle enzyme and a component- complex 2-of the mitochondrial electron transport chain, making this metabolite a marker of mitochondrial complex 2 as well as Krebs cycle dysfunction. A sampling of toxic chemicals that have been associated with mitochondrial dysfunction include glyphosate, 2, 4-dichlorophenoxyacetic acid (2, 4-D), organophosphate pesticides, mercury, and lead. Approximately 95% of elevated succinic acid results are associated with toxic chemical exposure. Succinic acid in the organic acid test and tiglylglycine in the **GPLTOX test** are two of the most useful markers for mitochondrial dysfunction. Tiglylglycine is a marker for mitochondrial respiratory chain complex I dysfunction while elevated succinic acid indicates respiratory complex 2 dysfunction. Occasionally both succinic acid and tiglylglycine may be elevated in mitochondrial dysfunction. Other Krebs cycle markers may also be elevated when severe chemical toxicity is present. In general, the severity of the chemical toxicity is correlated with higher values of succinic acid.

Less common causes of elevated succinic acid are mitochondrial mutations which may be due to mutations in the nuclear or the mitochondrial DNA for mitochondrial proteins such as Kearns-Sayres disorder. Succinic acid is a metabolite of gamma aminobutyric acid (GABA) so supplementation with GABA may also increase succinic acid.

High citric acid (29) may be due to increased intake of foods containing citric acid or as a result of intestinal yeast that either produce citric acid or perhaps inhibit the human citric acid cycle.

High 3,4-dihydroxyphenylacetic acid (DOPAC) (36) 3,4-dihydroxyphenylacetic acid (DOPAC) is an intermediate in the metabolism of dopamine. Values may be elevated due to increased intake of amino acid precursors of DOPAC such as phenylalanine, tyrosine, or DOPA. Values may be elevated due to factors that inhibit dopamine beta hydroxylase (DBH) like Clostridia metabolites, the mold metabolite fusaric acid, pharmaceuticals such as disulfiram, or food additives like aspartame, or to deficiencies of the DBH enzyme due to copper deficiency, vitamin C deficiency, or malic acid deficiency. Single nucleotide polymorphisms (SNPs) of DBH or catechol-O-methyltransferase (COMT) that result in reduced enzyme activities also result in increased amounts of DOPAC. SNPs of COMT are available on **The Great Plains Laboratory DNA methylation pathway test** which can be performed on a cheek swab. Deficiencies of S-adenosylmethionine (S-ame) also are associated with high amounts of DOPAC. DOPAC may also be increased when bananas are ingested the day before urine collection.

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5-hydroxyindoleacetic acid (5HIAA) (38) levels below the mean may indicate lower production and/or decreased metabolism of the neurotransmitter serotonin. 5-hydroxy-indoleacetic acid is a metabolite of serotonin. Low values have been correlated with symptoms of depression. Low production of 5 HIAA can be due to decreased intake or absorption of serotonin's precursor amino acid tryptophan, decreased quantities of cofactors needed for biosynthesis of serotonin such as tetrahydrobiopterin and vitamin B6 coenzyme. In addition, a number of genetic variations such as single nucleotide polymorphisms (SNPs) or mutations can cause reduced production of 5HIAA. Such SNPs are available on **The Great Plains DNA methylation pathway test** which can be performed on a cheek swab. Values may be decreased in patients on monoamine oxidase (MAO) inhibitors that are drugs or foods that contain tyramine such such as Chianti wine and vermouth, fermented foods such as cheeses, fish, bean curd, sausage, bologna, pepperoni, sauerkraut, and salami.

High ethylmalonic, methylsuccinic, adipic, suberic, or sebacic acids (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 may be beneficial.

High methylmalonic acid (50) is seen in vitamin B12 deficiency, in defective absorption or transport of vitamin B12, and in the genetic disease methylmalonic acidemia. Values greater than 100 mmol/mol creatinine are more consistent with the genetic disease, while lower values are more commonly associated with nutritional deficiencies. Supplementation with vitamin B12 may be beneficial*.

Pyridoxic acid (B6) levels below the mean (51) may be associated with less than optimum health conditions (low intake, malabsorption, or dysbiosis). Supplementation with B6 or a multivitamin may be beneficial.

High pantothenic acid (B5) (52) most commonly indicates recent intake of pantothenic acid as a supplement. Pantothenic acid is an essential B vitamin that is converted to coenzyme A (unrelated to vitamin A). Coenzyme A is needed for the synthesis of fatty acids, cholesterol, and acetyl choline and is also needed for the Krebs cycle and fatty acid catabolism. Because some individuals may require high doses of pantothenic acid, high values do not necessarily indicate the need to reduce pantothenic acid intake. However, if a patient who **does not take B-vitamin** supplements has high values of pantothenic acid, especially if the values are 20 or more times the upper limit of normal, the individual may have a genetic deficiency in the conversion of pantothenic acid to pantothenic acid-phosphate, which is the first step in the production of coenzyme A. It may be useful to retest after one week off all B-vitamin supplementation; individuals with PKAN would be expected to still have very elevated pantothenic acid levels even with no supplementation. This disease is called pantothenate kinase-associated neurodegeneration (PKAN), an inborn error of metabolism characterized by iron accumulation in the basal ganglia and by the presence of dystonia, dysarthria, Parkinson symptoms, and retinal degeneration. In mild variants of this disease, psychiatric illnesses such as schizoaffective disorder, hallucinations, obsessive compulsive disorder, speech defects, and depression are common. Mutations in pantothenate kinase 2 (PANK2), the rate-limiting enzyme in mitochondrial coenzyme A biosynthesis, represent the most common genetic cause of this disorder. Other biochemical abnormalities commonly found on the organic acid test in this disorder include elevated lactate, pyruvate, and Krebs cycle intermediates. Confirmation of mutant DNA requires special genetic testing. The University of Chicago does testing for PANK2 deletion for a price of $1000 in 2017.
The link is: <http://dnatesting.uchicago.edu/tests/pank2-deletionduplication-analysis>

Treatment for the illness is currently focused on giving high doses of pantothenic acid to stimulate any residual enzyme. Doses as high as 10 g per day have been ingested with few side effects. Other suggested therapies are increased supplementation with cholesterol, fat soluble vitamins, and bile salts. Since Lactobacillus species produce pantothenic acid phosphate, supplementation with high doses of probiotics might also be beneficial.

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High glutaric acid (53) can result from glutaric acidemias, fatty acid oxidation defects, riboflavin deficiency, ingestion of medium-chain triglycerides, metabolic effects of valproic acid (Depakene), or celiac disease. The genetic disorders are usually diagnosed in children but occasionally have been detected in adults. The probability of a genetic disease is higher when values exceed 10 mmol/mol creatinine but these conditions are not ruled out by lower urine values. DNA testing has been developed for the confirmation of both types of genetic disorders but may not yet be commercially available. This compound may be elevated in about 10% of children with autism. Regardless of the cause, supplementation with riboflavin and coenzyme Q10 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 along with carnitine supplementation.

Glutaric academia type II, also called acyl-CoA dehydrogenase deficiency, is caused by a genetic defect in one of the mitochondrial electron transport proteins, and 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 (54) may indicate a less than optimum level of the antioxidant vitamin C. Individuals who consume large amounts of vitamin C can still have low values if the sample is taken 12 or more hours after intake. Supplementation with buffered vitamin C taken 2 or 3 times a day is suggested.

High pyroglutamic acid (58) Elevated pyroglutamic acid (5-oxoproline) is most commonly due to intracellular glutathione deficiency due to toxic exposures such as acetomenophen toxicity. Pyroglutamic acid (5-oxoproline) 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, high 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 (Sabril) or certain antibiotics (flucloxacillin, netimicin) or exposure to toxic environmental chemicals that deplete glutathione such as halogenated hydrocarbons (e.g. DDT, PCB's, and many others). High pyroglutamic acid may also be caused by genetic deficiency of the enzyme oxoprolinase which breaks down pyroglutamic acid 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. Treatment most often includes supplementation with either N-acetyl-cysteine or liposomal glutathione.

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.

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