Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	0.11 - 2.0		0.38	0.38
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 18		0.77	0.77
3 3-Oxoglutaric	≤ 0.11	H	0.24	0.24
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 13		1.1	1.1
5 Furancarbonylglycine *(Aspergillus)*	≤ 2.3		0.20	0.20
6 Tartaric *(Aspergillus)*	≤ 5.3		0.84	0.84
7 Arabinose	≤ 20		16	16
8 Carboxycitric	≤ 20		2.4	2.4
9 Tricarballylic *(Fusarium)*	≤ 0.58		0.04	0.04
Bacterial Markers				
10 Hippuric	≤ 241	H	403	403
11 2-Hydroxyphenylacetic	0.03 - 0.47		0.24	0.24
12 4-Hydroxybenzoic	≤ 0.73		0.23	0.23
13 4-Hydroxyhippuric	≤ 14		1.8	1.8
14 DHPPA (Beneficial Bacteria)	≤ 0.23	H	0.24	0.24
Clostridia Bacterial Markers				
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	≤ 18		3.4	3.4
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 102	H	124	124
17 4-Cresol *(C. difficile)*	≤ 39		8.6	8.6
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	≤ 6.8		0.58	0.58

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, however, does comply with CLIA regulations for clinical use.

The results should be interpreted in conjunction with the complete clinical picture, given patient history and presentation, and at the discretion of the medical provider.

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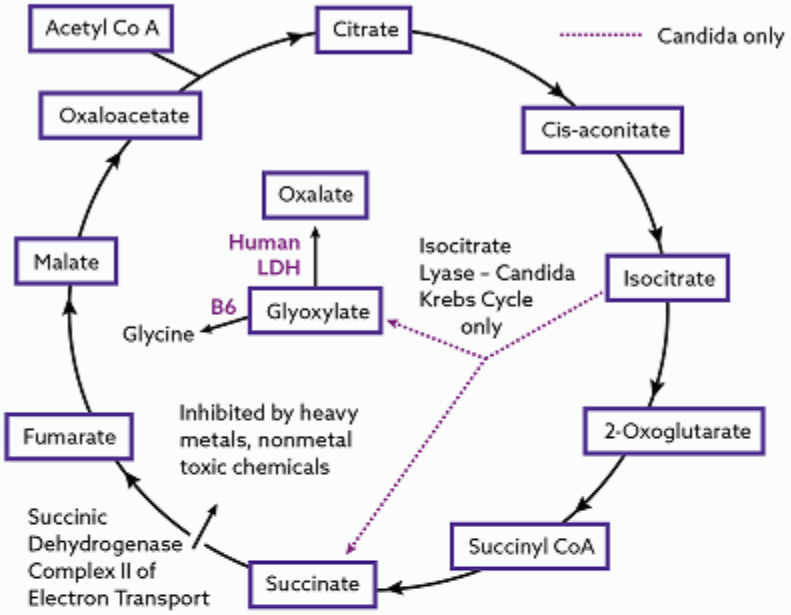
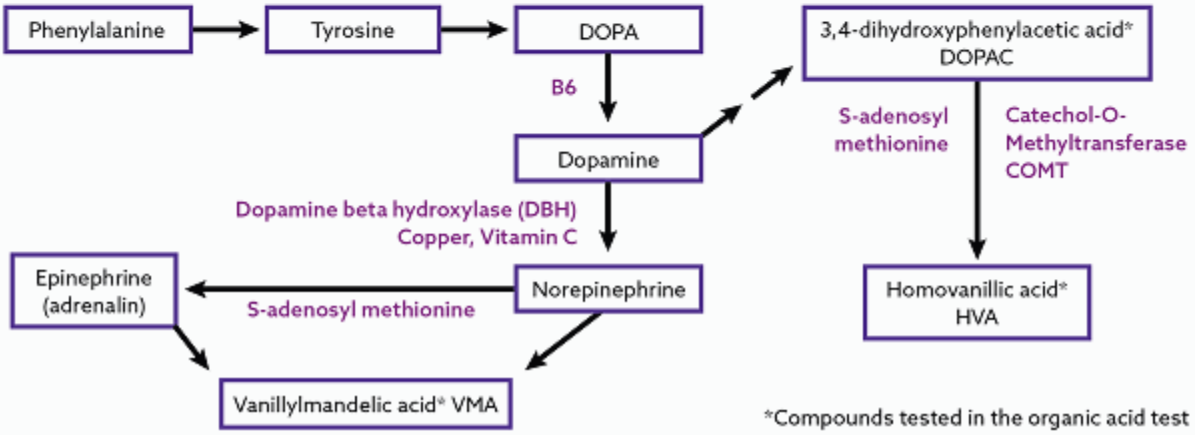
Human Krebs Cycle showing Candida Krebs Cycle variant that causes excess Oxalate via Glyoxylate



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



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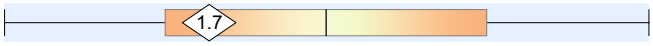
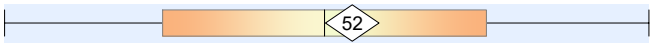
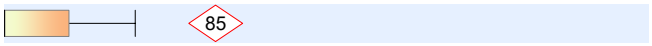
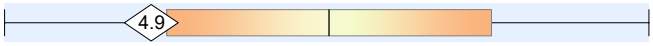
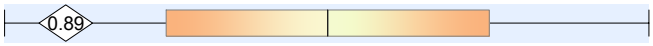
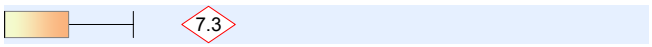
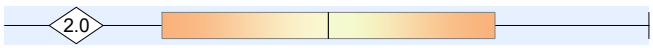
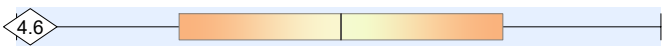
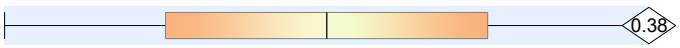
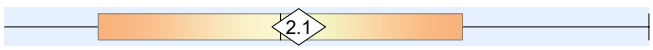
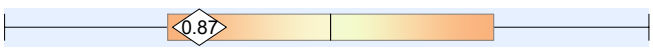
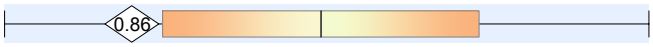
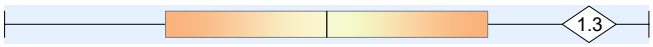
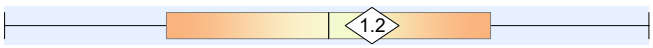
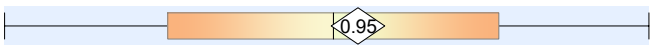
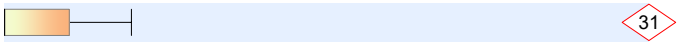
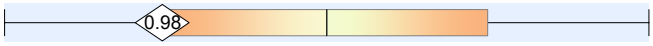
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)			Patient Value	Reference Population - Males Age 13 and Over
Oxalate Metabolites					
19 Glyceric	0.21	-	4.9	1.7	
20 Glycolic	18	-	81	52	
21 Oxalic	8.9	-	67	H 85	
Glycolytic Cycle Metabolites					
22 Lactic	0.74	-	19	4.9	
23 Pyruvic	0.28	-	6.7	0.89	
Mitochondrial Markers - Krebs Cycle Metabolites					
24 Succinic		≤	5.3	H 7.3	
25 Fumaric		≤	0.49	0.11	
26 Malic		≤	1.1	0.32	
27 2-Oxoglutaric		≤	18	2.0	
28 Aconitic	4.1	-	23	4.6	
29 Citric	2.2	-	260	130	
Mitochondrial Markers - Amino Acid Metabolites					
30 3-Methylglutaric	0.02	-	0.38	0.38	
31 3-Hydroxyglutaric		≤	4.6	2.1	
32 3-Methylglutaconic	0.38	-	2.0	0.87	
Neurotransmitter Metabolites					
Phenylalanine and Tyrosine Metabolites					
33 Homovanillic (HVA) *(dopamine)*	0.39	-	2.2	1.2	
34 Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53	-	2.2	0.86	
35 HVA / VMA Ratio	0.32	-	1.4	1.3	
36 Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.27	-	1.9	1.2	
37 HVA/ DOPAC Ratio	0.17	-	1.6	0.95	
Tryptophan Metabolites					
38 5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*		≤	2.9	H 31	
39 Quinolinic	0.52	-	2.4	0.98	
40 Kynurenic		≤	1.8	0.56	

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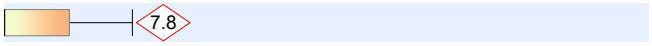
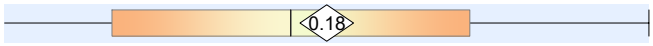
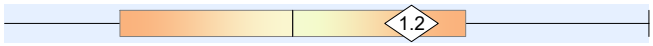
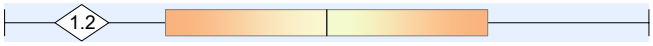
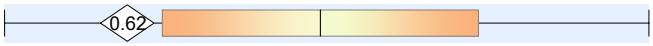
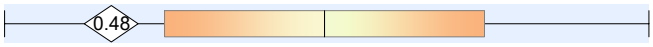
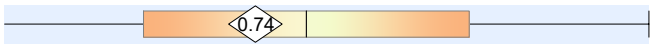
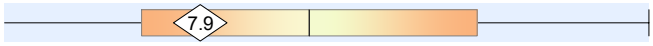
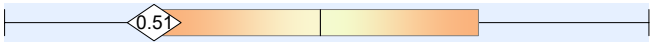
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Pyrimidine Metabolites - Folate Metabolism			
41 Uracil	≤ 6.9	H 7.8	
42 Thymine	≤ 0.36	0.18	
Ketone and Fatty Acid Oxidation			
43 3-Hydroxybutyric	≤ 1.9	1.2	
44 Acetoacetic	≤ 10	1.2	
45 Ethylmalonic	0.13 - 2.7	0.62	
46 Methylsuccinic	≤ 2.3	0.49	
47 Adipic	≤ 2.9	0.48	
48 Suberic	≤ 1.9	0.74	
49 Sebacic	≤ 0.14	0.05	
Nutritional Markers			
Vitamin B12			
50 Methylmalonic ✱	≤ 2.3	0.66	
Vitamin B6			
51 Pyridoxic (B6)	≤ 26	3.4	
Vitamin B5			
52 Pantothenic (B5)	≤ 5.4	1.2	
Vitamin B2 (Riboflavin)			
53 Glutaric ✱	≤ 0.43	0.13	
Vitamin C			
54 Ascorbic	10 - 200	H 326	
Vitamin Q10 (CoQ10)			
55 3-Hydroxy-3-methylglutaric ✱	≤ 26	7.9	
Glutathione Precursor and Chelating Agent			
56 N-Acetylcysteine (NAC)	≤ 0.13	0	
Biotin (Vitamin H)			
57 Methylcitric ✱	0.15 - 1.7	0.51	

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

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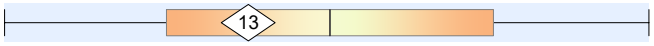
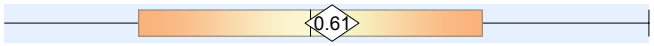
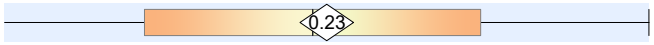
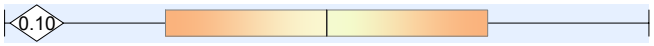
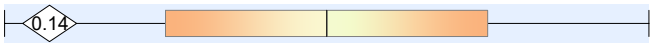
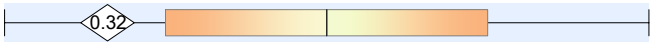
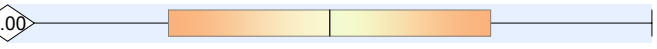
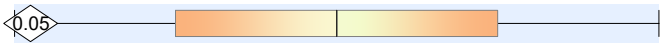
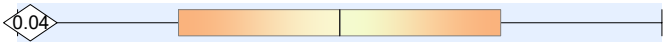
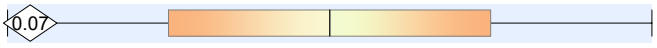
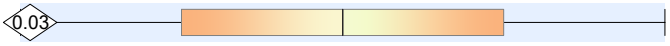
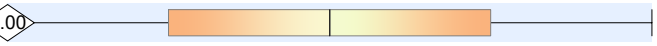
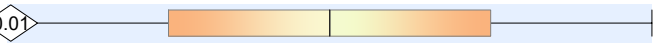
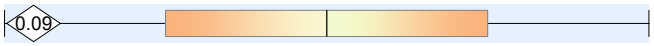
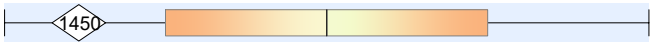
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Indicators of Detoxification			
Glutathione			
58 Pyroglutamic *	5.7 - 25	13	
Methylation, Toxic exposure			
59 2-Hydroxybutyric **	≤ 1.2	0.61	
Ammonia Excess			
60 Orotic	≤ 0.46	0.23	
Aspartame, salicylates, or GI bacteria			
61 2-Hydroxyhippuric	≤ 0.86	0.22	

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

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

Amino Acid Metabolites

Low values are not associated with inadequate protein intake and have not been demonstrated to indicate specific amino acid deficiencies.

62 2-Hydroxyisovaleric	≤ 2.0	0.10	
63 2-Oxoisovaleric	≤ 2.0	0.14	
64 3-Methyl-2-oxovaleric	≤ 2.0	0.32	
65 2-Hydroxyisocaproic	≤ 2.0	0	
66 2-Oxoisocaproic	≤ 2.0	0.05	
67 2-Oxo-4-methiolbutyric	≤ 2.0	0.04	
68 Mandelic	≤ 2.0	0.07	
69 Phenyllactic	≤ 2.0	0.03	
70 Phenylpyruvic	≤ 2.0	0	
71 Homogentisic	≤ 2.0	0.01	
72 4-Hydroxyphenyllactic	≤ 2.0	0.09	
73 N-Acetylaspartic	≤ 38	2.2	
74 Malonic	≤ 9.9	2.3	
75 4-Hydroxybutyric	≤ 4.3	0.51	
Mineral Metabolism			
76 Phosphoric	1,000 - 4,900	1,450	

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Indicator of Fluid Intake

77	*Creatinine	147	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.

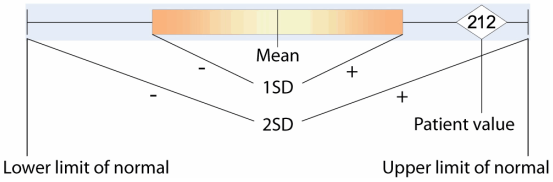
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

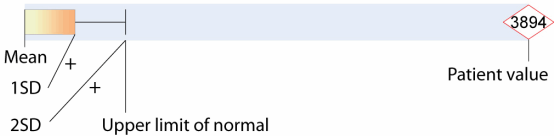
Example of Value Within Reference Range

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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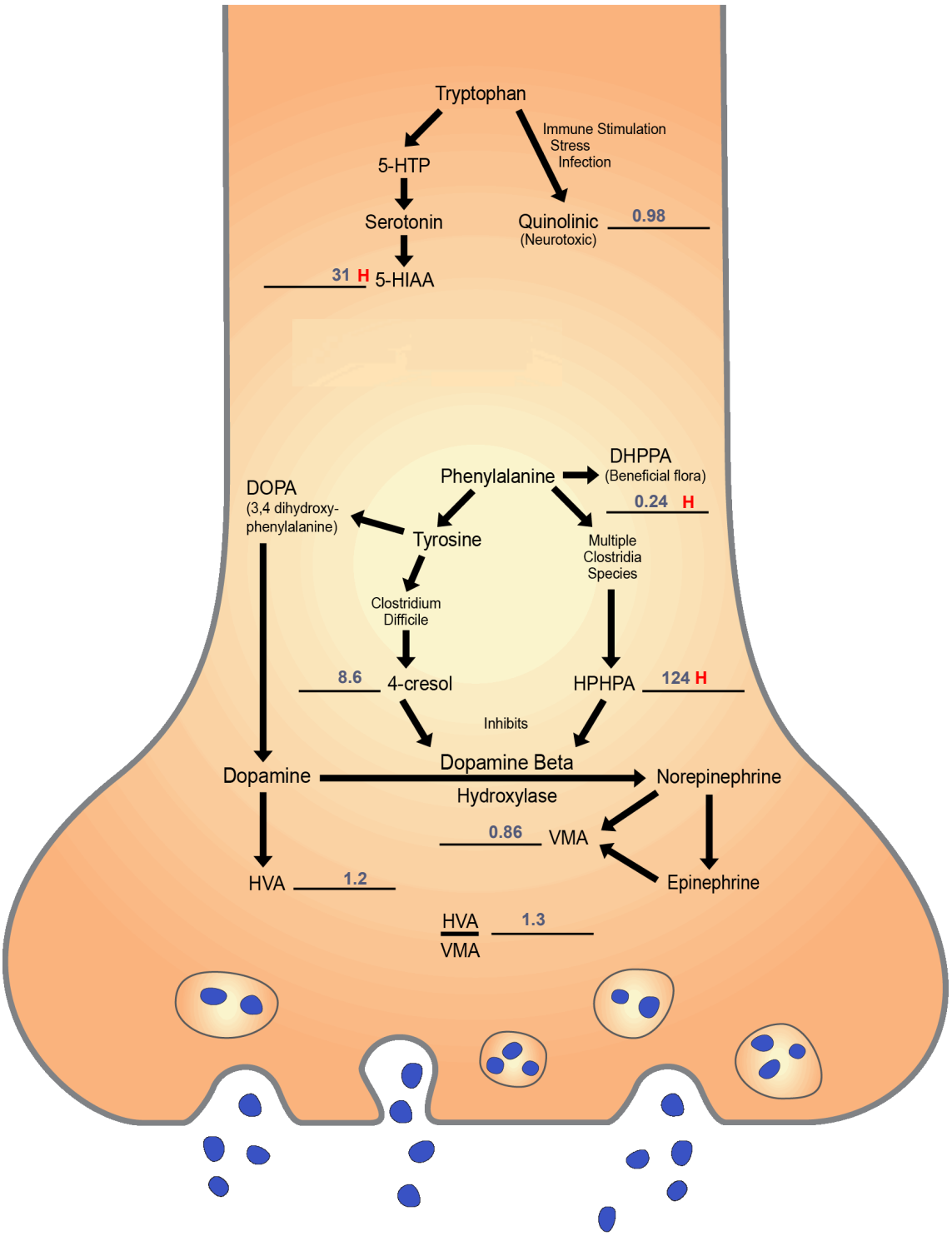
Neurotransmitter Metabolism Markers



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

Slightly high 3-oxoglutaric acid(3) indicates a possible yeast overgrowth. Prescription or natural (botanical) anti-fungals, along with supplementation with high potency multi-strain probiotics is recommended.

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 HPHPA (3-(3-hydroxyphenyl)-3-hydroxypropionic acid) (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 close to 100% effective at killing parent 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 *Corebiotic*, *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 (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.

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

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

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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.

Homovanillic acid (HVA) levels (33) below the mean indicate low production and/or decreased metabolism of the neurotransmitter dopamine. Homovanillic acid is a metabolite of the neurotransmitter dopamine. Low production of HVA can be due to decreased intake or absorption of dopamine's precursor amino acids such as phenylalanine and/or tyrosine, decreased quantities of cofactors needed for biosynthesis of dopamine such as tetrahydrobiopterin and vitamin B6 coenzyme or decreased amounts of cofactors such as S-adenosylmethionine (Sam-e) needed to convert dopamine to HVA. In addition, a number of genetic variations such as single nucleotide polymorphisms (SNPs) or mutations can cause reduced production of HVA due to enzymes with decreased function. HVA values below the mean but which are much higher than VMA values are usually due to impairment of dopamine beta hydroxylase due to excessive Clostridia metabolites, the mold metabolite fusaric acid, pharmaceuticals such as disulfiram, or food additives like aspartame or deficiencies of cofactors such as vitamin C or copper. Values may also be decreased in patients on monoamine oxidase (MAO) inhibitors. In addition, a number of genetic variations such as single nucleotide polymorphisms (SNPs) or mutations in MAO or COMT genes can cause reduced production of HVA. Such SNPs are available on **The Great Plains DNA methylation pathway test** which can be performed on a cheek swab.

Vanillylmandelic acid (VMA) levels (34) below the mean indicate low production and/or decreased metabolism of the neurotransmitters norepinephrine and epinephrine. Vanillylmandelic acid is a metabolite of the neurotransmitters norepinephrine and epinephrine. Low production of VMA can be due to decreased intake or absorption of norepinephrine's and epinephrine's precursor amino acids such as phenylalanine and/or tyrosine, decreased quantities of cofactors needed for biosynthesis of norepinephrine and epinephrine such as tetrahydrobiopterin and vitamin B6 coenzyme or decreased amounts of cofactors such as S-adenosylmethionine (Sam-e) needed to convert norepinephrine and epinephrine to VMA. In addition, a number of genetic variations such as single nucleotide polymorphisms (SNPs) or mutations in MAO or COMT genes can cause reduced production of VMA. Such SNPs are available on **The Great Plains DNA methylation pathway test** which can be performed on a cheek swab. VMA values below the mean but which are much lower than HVA values are usually due to impairment of dopamine beta hydroxylase due to Clostridia metabolites, the mold metabolite fusaric acid, pharmaceuticals such as disulfiram, or food additives like aspartame or deficiencies of cofactors such as vitamin C or copper. Values may be decreased in patients on monoamine oxidase (MAO) inhibitors. Another cause for a low VMA value is a genetic variation (single nucleotide polymorphism or SNP) of the DBH enzyme. Patients with low VMA due to Clostridia metabolites or genetic DBH deficiency should not be supplemented with phenylalanine, tyrosine, or L-DOPA.

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High 5-hydroxyindoleacetic acid (5-HIAA) (38) may occur in celiac or tropical sprue, carcinoid tumors, or from ingestion of foods high in serotonin, such as avocado, banana, tomato, plum, walnut, pineapple or eggplant. Ingesting bananas the day before urine collection may also increase HVA. Elevated values may also result from supplementing with tryptophan itself or 5-hydroxy-tryptophan (5HTP); if this is the case, a high value does not necessarily indicate the need to reduce or eliminate supplementation. It is possible that excessive tryptophan intake can lead to overproduction of the neurotoxic and inflammatory metabolite quinolinic acid. (See quinolinic acid value and interpretation).

High uracil (41) can be associated with disorders of folate metabolism, folate deficiency, and genetic disorders of pyrimidine metabolism. Genetic disorders of pyrimidine metabolism are more common when uracil exceeds 50 mmol/mol creatinine and thymine is also elevated. An autistic child with a uracil value >300 mmol/ mol creatinine and diffuse demyelination of the brain was treated with high levels of folate which normalized the uracil but did not improve the clinical symptoms.

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.

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

High ascorbic acid (vitamin C) (54) may be the result of supplementation. An elevated value of ascorbic acid does not mean that this amount of vitamin C is not beneficial.

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