Requisition #:	1174201			*Practitioner:*	DANE FLIEDNER
Patient Name:	Isaac Lobato Franca			*Date of Collection:*	03/18/2023
Date of Birth:	11/06/2018	*Patient Age:*	4	*Time of Collection:*	10:00 AM
Patient Sex:	M			*Print Date:*	04/04/2023
Specimen Id.:	1174201-2				

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range *(mmol/mol creatinine)*	Patient Value	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth			
Yeast and Fungal Markers			
1 Citramalic	≤ 5.0	1.0	1.0
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 28	6.5	6.5
3 3-Oxoglutaric	≤ 0.46	0	0.00
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 18	8.1	8.1
5 Furancarbonylglycine *(Aspergillus)*	≤ 3.1	0.69	0.69
6 Tartaric *(Aspergillus)*	≤ 6.5	H 21	21
7 Arabinose	≤ 50	H 71	71
8 Carboxycitric	≤ 25	2.7	2.7
9 Tricarballylic *(Fusarium)*	≤ 1.3	0.40	0.40
Bacterial Markers			
10 Hippuric	≤ 680	H 1,530	1530
11 2-Hydroxyphenylacetic	≤ 0.86	0.58	0.58
12 4-Hydroxybenzoic	≤ 3.0	0.92	0.92
13 4-Hydroxyhippuric	≤ 30	28	28
14 DHPPA (Beneficial Bacteria)	≤ 0.59	0.50	0.50
Clostridia Bacterial Markers			
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	2.0 - 32	15	15
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 220	H 471	471
17 4-Cresol *(C. difficile)*	≤ 84	11	11
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	0.60 - 14	3.2	3.2

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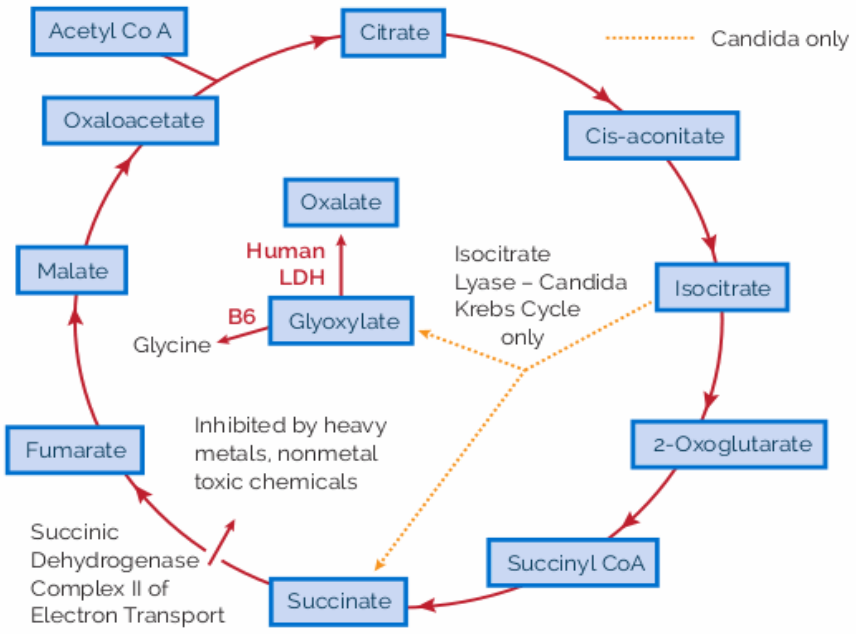
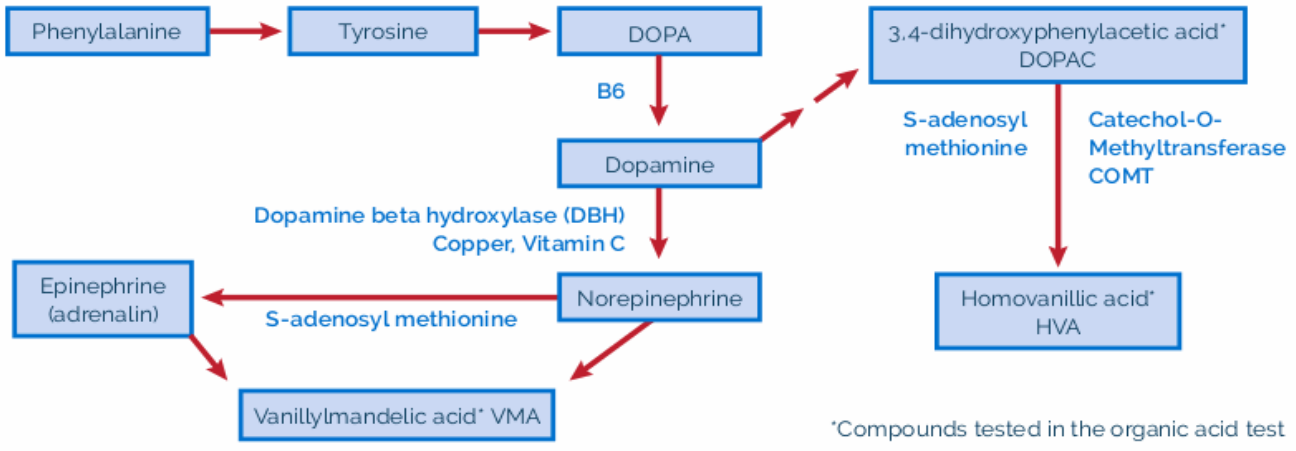
Specimen Id.:	1174201-2		

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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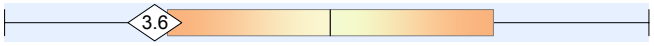
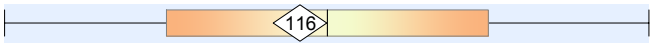
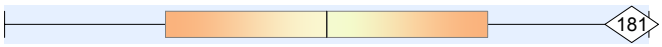
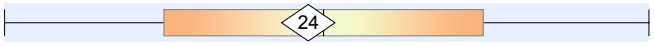
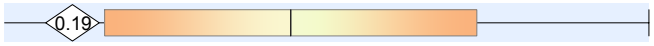
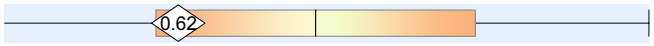
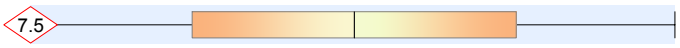
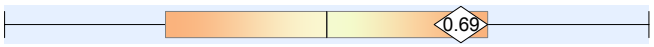
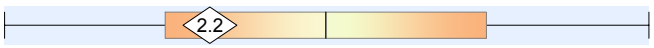
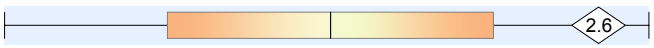
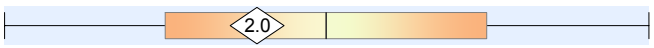
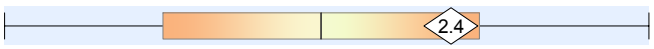
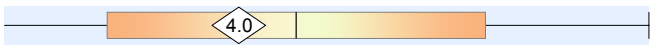
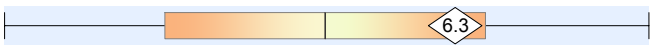
Requisition #:	1174201	*Practitioner:*	DANE FLIEDNER
Patient Name:	Isaac Lobato Franca	*Date of Collection:*	03/18/2023
Specimen Id.:	1174201-2		

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Under Age 13
Oxalate Metabolites			
19 Glyceric	0.74 - 13	3.6	
20 Glycolic	27 - 221	116	
21 Oxalic	35 - 185	181	
Glycolytic Cycle Metabolites			
22 Lactic	2.6 - 48	24	
23 Pyruvic	0.32 - 8.8	5.1	
Mitochondrial Markers - Krebs Cycle Metabolites			
24 Succinic	≤ 23	8.3	
25 Fumaric	≤ 1.8	0.19	
26 Malic	≤ 2.3	0.62	
27 2-Oxoglutaric	≤ 96	50	
28 Aconitic	9.8 - 39	L 7.5	
29 Citric	≤ 597	101	
Mitochondrial Markers - Amino Acid Metabolites			
30 3-Methylglutaric	0.01 - 0.97	0.69	
31 3-Hydroxyglutaric	≤ 16	7.4	
32 3-Methylglutaconic	≤ 6.9	2.2	
Neurotransmitter Metabolites			
Phenylalanine and Tyrosine Metabolites			
33 Homovanillic (HVA) *(dopamine)*	0.49 - 13	4.9	
34 Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.72 - 6.4	1.9	
35 HVA / VMA Ratio	0.23 - 2.8	2.6	
36 Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.13 - 4.9	2.0	
37 HVA/ DOPAC Ratio	0.37 - 3.3	2.4	
Tryptophan Metabolites			
38 5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 11	4.0	
39 Quinolinic	0.48 - 8.8	6.3	
40 Kynurenic	≤ 4.2	2.5	

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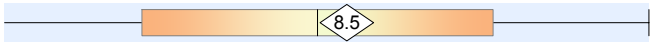
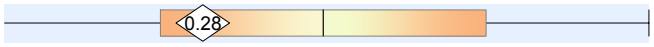
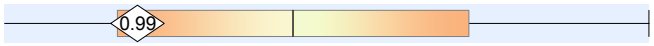
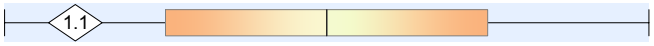
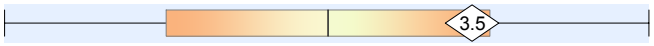
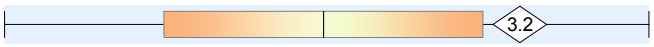
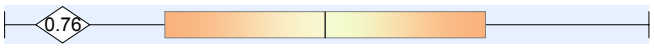
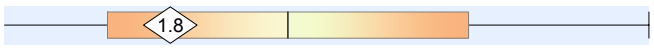
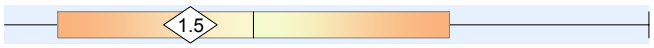
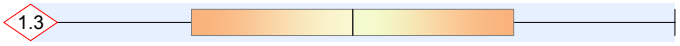
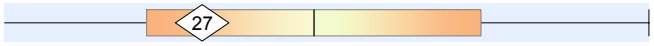
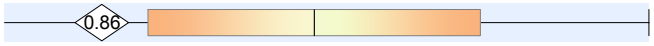
Requisition #:	1174201	*Practitioner:*	DANE FLIEDNER
Patient Name:	Isaac Lobato Franca	*Date of Collection:*	03/18/2023
Specimen Id.:	1174201-2		

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Under Age 13
Pyrimidine Metabolites - Folate Metabolism			
41 Uracil	≤ 16	8.5	
42 Thymine	≤ 0.91	0.28	
Ketone and Fatty Acid Oxidation			
43 3-Hydroxybutyric	≤ 4.8	0.99	
44 Acetoacetic	≤ 10	1.1	
45 Ethylmalonic	0.06 - 4.8	3.5	
46 Methylsuccinic	≤ 4.0	3.2	
47 Adipic	0.19 - 6.5	0.76	
48 Suberic	≤ 7.0	1.8	
49 Sebacic	≤ 0.61	0.05	
Nutritional Markers			
Vitamin B12			
50 Methylmalonic ✱	≤ 5.2	1.5	
Vitamin B6			
51 Pyridoxic (B6)	≤ 53	4.1	
Vitamin B5			
52 Pantothenic (B5)	≤ 14	7.8	
Vitamin B2 (Riboflavin)			
53 Glutaric ✱	≤ 1.4	0.53	
Vitamin C			
54 Ascorbic	10 - 200	L 1.3	
Vitamin Q10 (CoQ10)			
55 3-Hydroxy-3-methylglutaric ✱	≤ 88	27	
Glutathione Precursor and Chelating Agent			
56 N-Acetylcysteine (NAC)	≤ 0.34	0	
Biotin (Vitamin H)			
57 Methylcitric ✱	≤ 5.7	0.86	

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

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Requisition #:	1174201	*Practitioner:*	DANE FLIEDNER
Patient Name:	Isaac Lobato Franca	*Date of Collection:*	03/18/2023
Specimen Id.:	1174201-2		

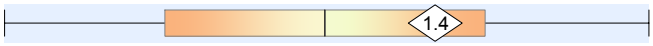
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Under Age 13

Indicators of Detoxification

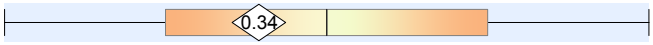
Glutathione

58	Pyroglutamic ✱	13 - 62	40	

Methylation, Toxic exposure

59	2-Hydroxybutyric ✱✱	0.19 - 2.0	1.4	

Ammonia Excess

60	Orotic	0.04 - 0.80	0.34	

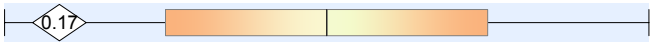
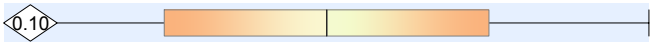
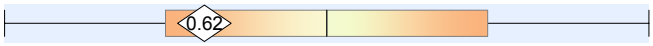
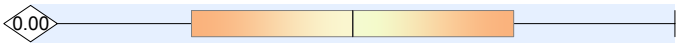
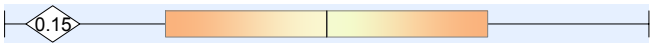
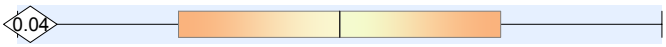
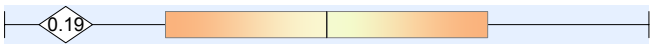
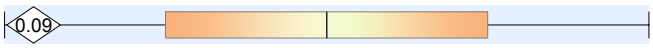
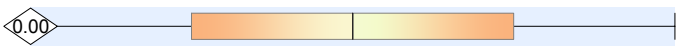
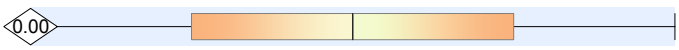
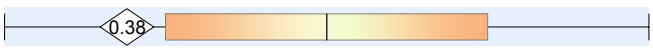
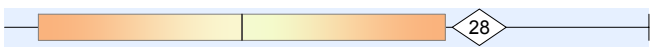
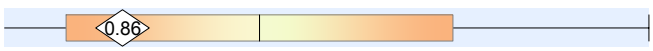
Aspartame, salicylates, or GI bacteria

61	2-Hydroxyhippuric	≤ 1.2	0.67	

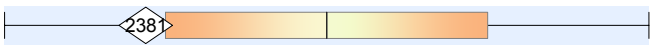
✱ ***A high value for this marker may indicate a Glutathione deficiency.***

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

Amino Acid Metabolites

62	2-Hydroxyisovaleric	≤ 2.0	0.17	
63	2-Oxoisovaleric	≤ 2.5	0.10	
64	3-Methyl-2-oxovaleric	≤ 2.0	0.62	
65	2-Hydroxyisocaproic	≤ 2.0	0	
66	2-Oxoisocaproic	≤ 2.0	0.15	
67	2-Oxo-4-methiolbutyric	≤ 2.0	0.04	
68	Mandelic	≤ 2.0	0.19	
69	Phenyllactic	≤ 2.0	0.09	
70	Phenylpyruvic	≤ 4.0	0	
71	Homogentisic	≤ 2.0	0	
72	4-Hydroxyphenyllactic	≤ 2.0	0.38	
73	N-Acetylaspartic	≤ 38	28	
74	Malonic	≤ 18	8.1	
75	4-Hydroxybutyric	≤ 4.7	0.86	

Mineral Metabolism

76	Phosphoric	1,000 - 7,300	2,381	

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Patient Name:	Isaac Lobato Franca	*Date of Collection:*	03/18/2023
Specimen Id.:	1174201-2		

Indicator of Fluid Intake

77	*Creatinine	73	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.

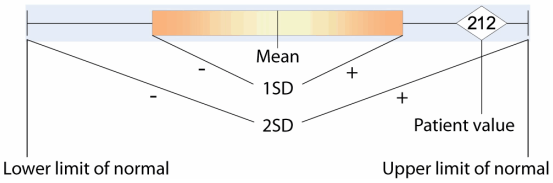
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

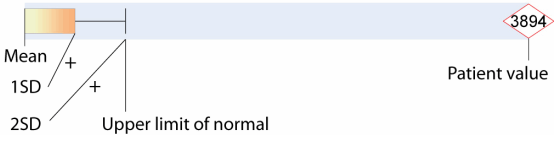
Example of Value Within Reference Range

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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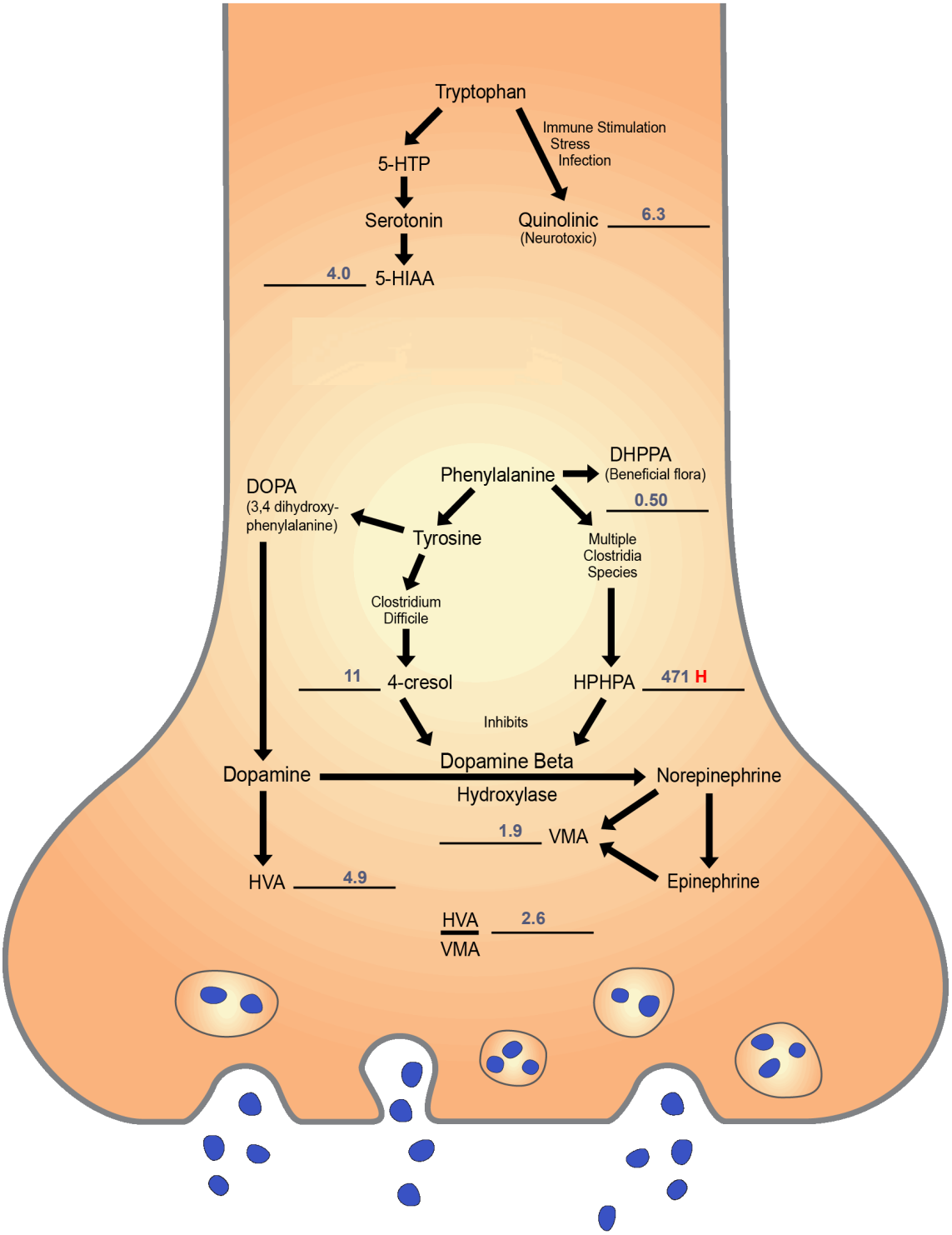
Neurotransmitter Metabolism Markers



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 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 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.

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Low or low normal citric acid (29) may be due to impaired function of the Krebs cycle, low dietary intake of citrate-containing foods such as citrus fruits and juices, potassium deficiency, acidosis (especially renal tubular acidosis), chronic kidney failure, diabetes, hypoparathyroidism, or excessive muscle activity. Low values may indicate increased risk of oxalate kidney stone formation, especially if oxalic acid is elevated also. Supplement with calcium or magnesium citrate if oxalic acid is elevated.

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.

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.

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.

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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.

Low citramalic, 2-hydroxyphenylacetic, 4-hydroxyphenylacetic, 4-hydroxybenzoic, 4-hydroxyhippuric, 3-indoleacetic, glyceric, glycolic, oxalic, lactic, pyruvic, 3-Methylglutaric, 3-methylglutaconic, 2-hydroxybutyric, fumaric, malic, aconitic, quinolinic, kynurenic, thymine, ethylmalonic, methylsuccinic, adipic, suberic, glutaric, 3-hydroxy-3-methylglutaric, methylcitric, or orotic values have no known clinical significance.

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