Requisition #:	1155602			*Practitioner:*	RN LABS
Patient Name:	Lynette Blake			*Date of Collection:*	01/23/2023
Date of Birth:	09/09/1949	*Patient Age:*	73	*Time of Collection:*	03:00 AM
Patient Sex:	F			*Print Date:*	02/23/2023
Specimen Id.:	1155602-2				

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	0.49	0.49
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 14	5.3	5.3
3 3-Oxoglutaric	≤ 0.33	0	0.00
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 16	3.7	3.7
5 Furancarbonylglycine *(Aspergillus)*	≤ 1.9	0.07	0.07
6 Tartaric *(Aspergillus)*	≤ 4.5	0.21	0.21
7 Arabinose	≤ 29	16	16
8 Carboxycitric	≤ 29	0.01	0.01
9 Tricarballylic *(Fusarium)*	≤ 0.44	0.07	0.07
Bacterial Markers			
10 Hippuric	≤ 613	482	482
11 2-Hydroxyphenylacetic	0.06 - 0.66	0.17	0.17
12 4-Hydroxybenzoic	≤ 1.3	0.26	0.26
13 4-Hydroxyhippuric	0.79 - 17	1.4	1.4
14 DHPPA (Beneficial Bacteria)	≤ 0.38	0.11	0.11
Clostridia Bacterial Markers			
15 4-Hydroxyphenylacetic *(C. difficile, C. stricklandii, C. lituseburense & others)*	≤ 19	4.0	4.0
16 HPHPA *(C. sporogenes, C. caloritolerans, C. botulinum & others)*	≤ 208	40	40
17 4-Cresol *(C. difficile)*	≤ 75	17	17
18 3-Indoleacetic *(C. stricklandii, C. lituseburense, C. subterminale & others)*	≤ 11	0.05	0.05

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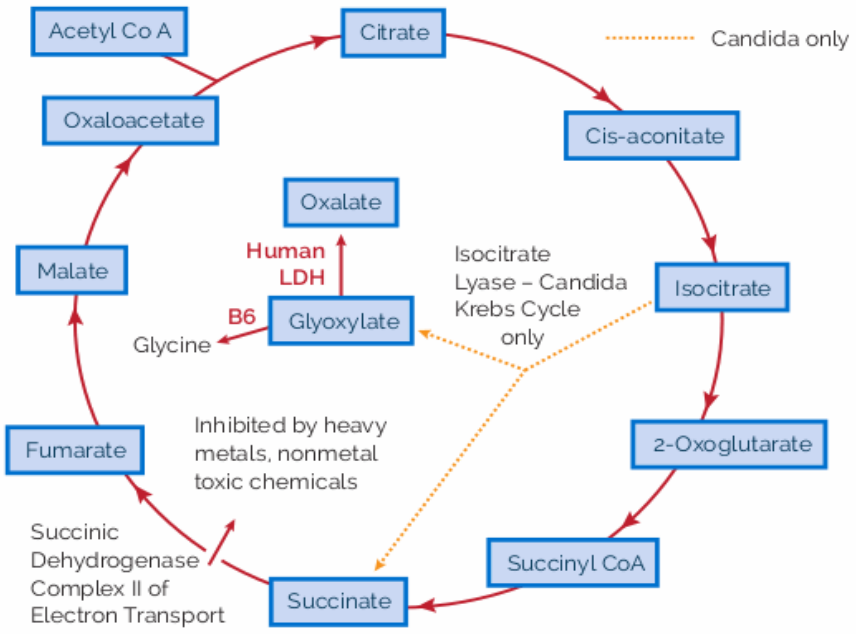
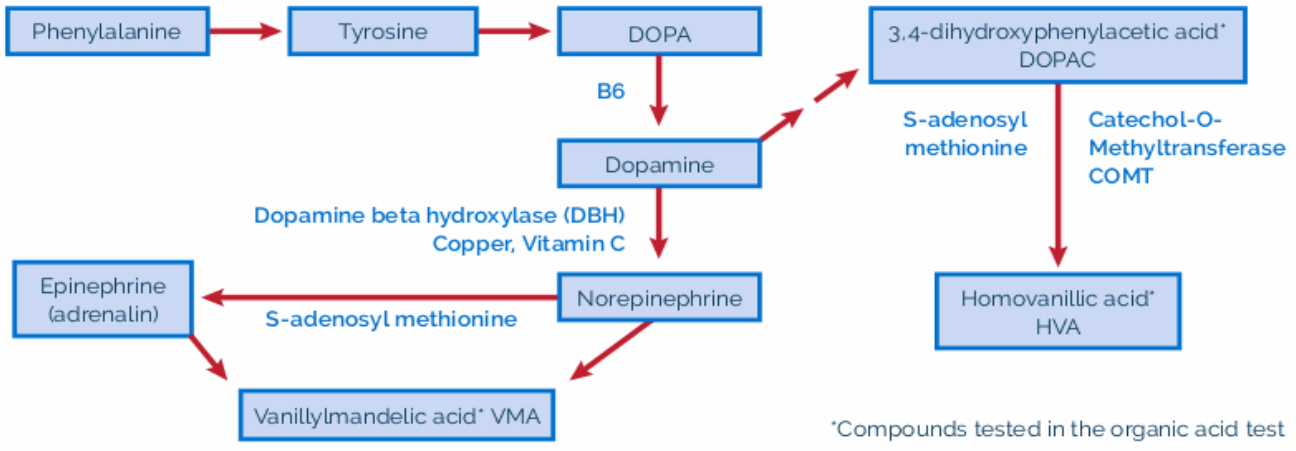
Requisition #:	1155602	***Practitioner:***	RN LABS
Patient Name:	Lynette Blake	***Date of Collection:***	01/23/2023
Specimen Id.:	1155602-2		

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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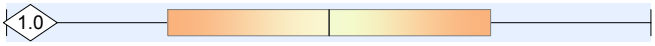
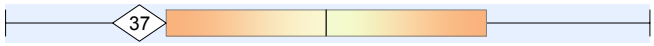
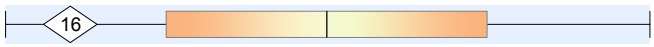
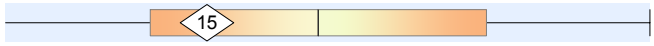
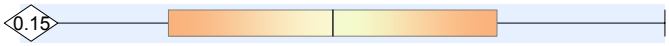
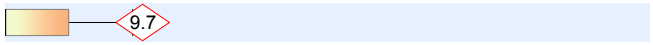
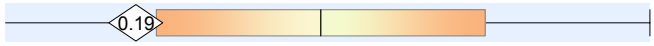
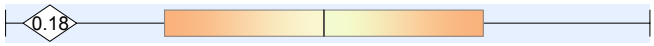
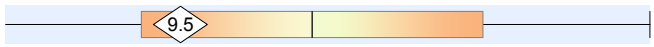
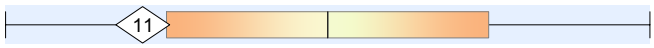
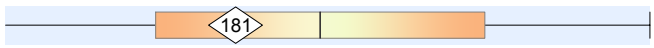
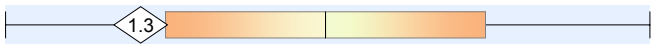
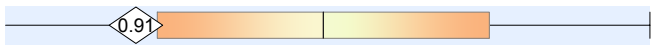
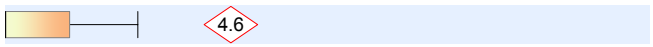
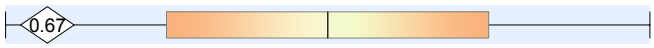
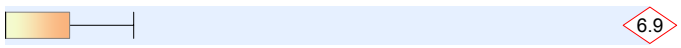
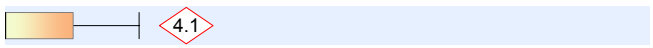
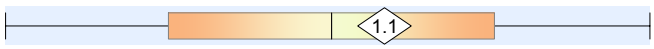
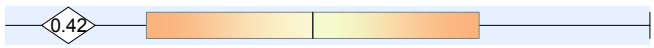
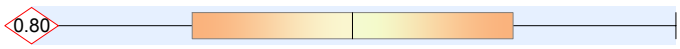
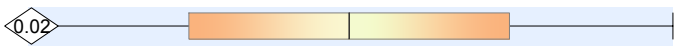
Requisition #:	1155602	*Practitioner:*	RN LABS
Patient Name:	Lynette Blake	*Date of Collection:*	01/23/2023
Specimen Id.:	1155602-2		

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	1.0	
20 Glycolic	16 - 117	37	
21 Oxalic	6.8 - 101	16	
Glycolytic Cycle Metabolites			
22 Lactic	≤ 48	15	
23 Pyruvic	≤ 9.1	0.15	
Mitochondrial Markers - Krebs Cycle Metabolites			
24 Succinic	≤ 9.3	H 9.7	
25 Fumaric	≤ 0.94	0.19	
26 Malic	0.06 - 1.8	0.18	
27 2-Oxoglutaric	≤ 35	9.5	
28 Aconitic	6.8 - 28	11	
29 Citric	≤ 507	181	
Mitochondrial Markers - Amino Acid Metabolites			
30 3-Methylglutaric	≤ 0.76	0.35	
31 3-Hydroxyglutaric	≤ 6.2	1.3	
32 3-Methylglutaconic	≤ 4.5	0.91	
Neurotransmitter Metabolites			
Phenylalanine and Tyrosine Metabolites			
33 Homovanillic (HVA) *(dopamine)*	0.80 - 3.6	H 4.6	
34 Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.46 - 3.7	0.67	
35 HVA / VMA Ratio	0.16 - 1.8	H 6.9	
36 Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.08 - 3.5	H 4.1	
37 HVA/ DOPAC Ratio	0.10 - 1.8	1.1	
Tryptophan Metabolites			
38 5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤ 4.3	0.42	
39 Quinolinic	0.85 - 3.9	L 0.80	
40 Kynurenic	≤ 2.2	0.02	

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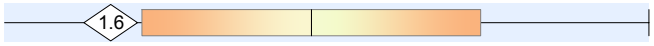
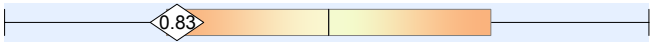
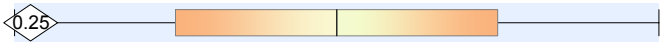
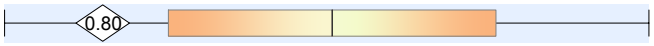
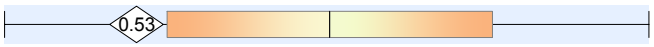
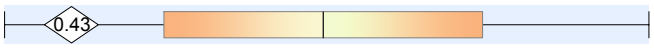
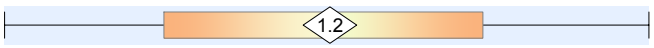
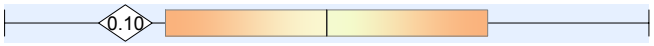
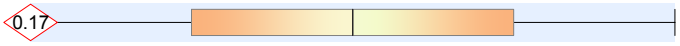
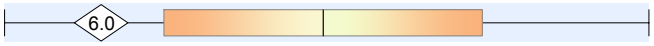
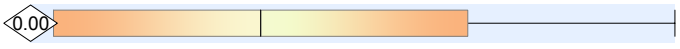
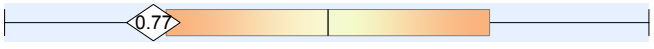
Requisition #:	1155602	*Practitioner:*	RN LABS
Patient Name:	Lynette Blake	*Date of Collection:*	01/23/2023
Specimen Id.:	1155602-2		

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	1.6	
42 Thymine	≤ 0.56	0.06	
Ketone and Fatty Acid Oxidation			
43 3-Hydroxybutyric	≤ 3.1	0.83	
44 Acetoacetic	≤ 10	0.25	
45 Ethylmalonic	0.44 - 2.8	0.80	
46 Methylsuccinic	0.10 - 2.2	0.53	
47 Adipic	0.04 - 3.8	0.43	
48 Suberic	0.18 - 2.2	1.2	
49 Sebacic	≤ 0.24	0.04	
Nutritional Markers			
Vitamin B12			
50 Methylmalonic ✱	≤ 2.3	0.48	
Vitamin B6			
51 Pyridoxic (B6)	≤ 34	0.77	
Vitamin B5			
52 Pantothenic (B5)	≤ 10	0.86	
Vitamin B2 (Riboflavin)			
53 Glutaric ✱	0.04 - 0.36	0.10	
Vitamin C			
54 Ascorbic	10 - 200	L 0.17	
Vitamin Q10 (CoQ10)			
55 3-Hydroxy-3-methylglutaric ✱	0.17 - 39	6.0	
Glutathione Precursor and Chelating Agent			
56 N-Acetylcysteine (NAC)	≤ 0.28	0	
Biotin (Vitamin H)			
57 Methylcitric ✱	0.19 - 2.7	0.77	

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

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Requisition #:	1155602	*Practitioner:*	RN LABS
Patient Name:	Lynette Blake	*Date of Collection:*	01/23/2023
Specimen Id.:	1155602-2		

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	L	6.1	6.1

Methylation, Toxic exposure

59	2-Hydroxybutyric ✱✱	0.03	- 1.8		0.59	0.59

Ammonia Excess

60	Orotic	0.06	- 0.54		0.09	0.09

Aspartame, salicylates, or GI bacteria

61	2-Hydroxyhippuric		≤ 1.3		0.03	0.03

✱ ***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		0.04	0.04
63	2-Oxoisovaleric		≤ 2.1		0	0.00
64	3-Methyl-2-oxovaleric		≤ 2.0		0	0.00
65	2-Hydroxyisocaproic		≤ 2.0		0	0.00
66	2-Oxoisocaproic		≤ 2.0		0	0.00
67	2-Oxo-4-methiolbutyric		≤ 2.0		0.03	0.03
68	Mandelic		≤ 2.0		0.04	0.04
69	Phenyllactic		≤ 2.0		0.14	0.14
70	Phenylpyruvic		≤ 2.0		0	0.00
71	Homogentisic		≤ 2.0		0.03	0.03
72	4-Hydroxyphenyllactic		≤ 2.0		0.13	0.13
73	N-Acetylaspartic		≤ 38		1.4	1.4
74	Malonic		≤ 9.7		0.60	0.60
75	4-Hydroxybutyric		≤ 4.8		0.71	0.71

Mineral Metabolism

76	Phosphoric	1,000	- 5,000		1,121	1121

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Requisition #:	1155602	*Practitioner:*	RN LABS
Patient Name:	Lynette Blake	*Date of Collection:*	01/23/2023
Specimen Id.:	1155602-2		

Indicator of Fluid Intake

77	*Creatinine	61	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.

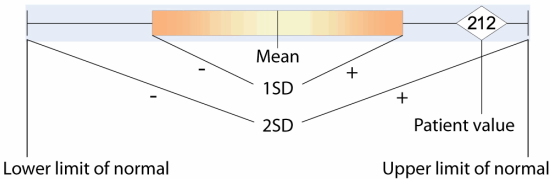
The first graph will occur when the value of the patient is within the reference (normal) range, defined as the mean plus or minus two standard deviations.

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.

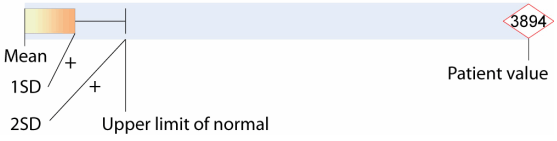
Example of Value Within Reference Range

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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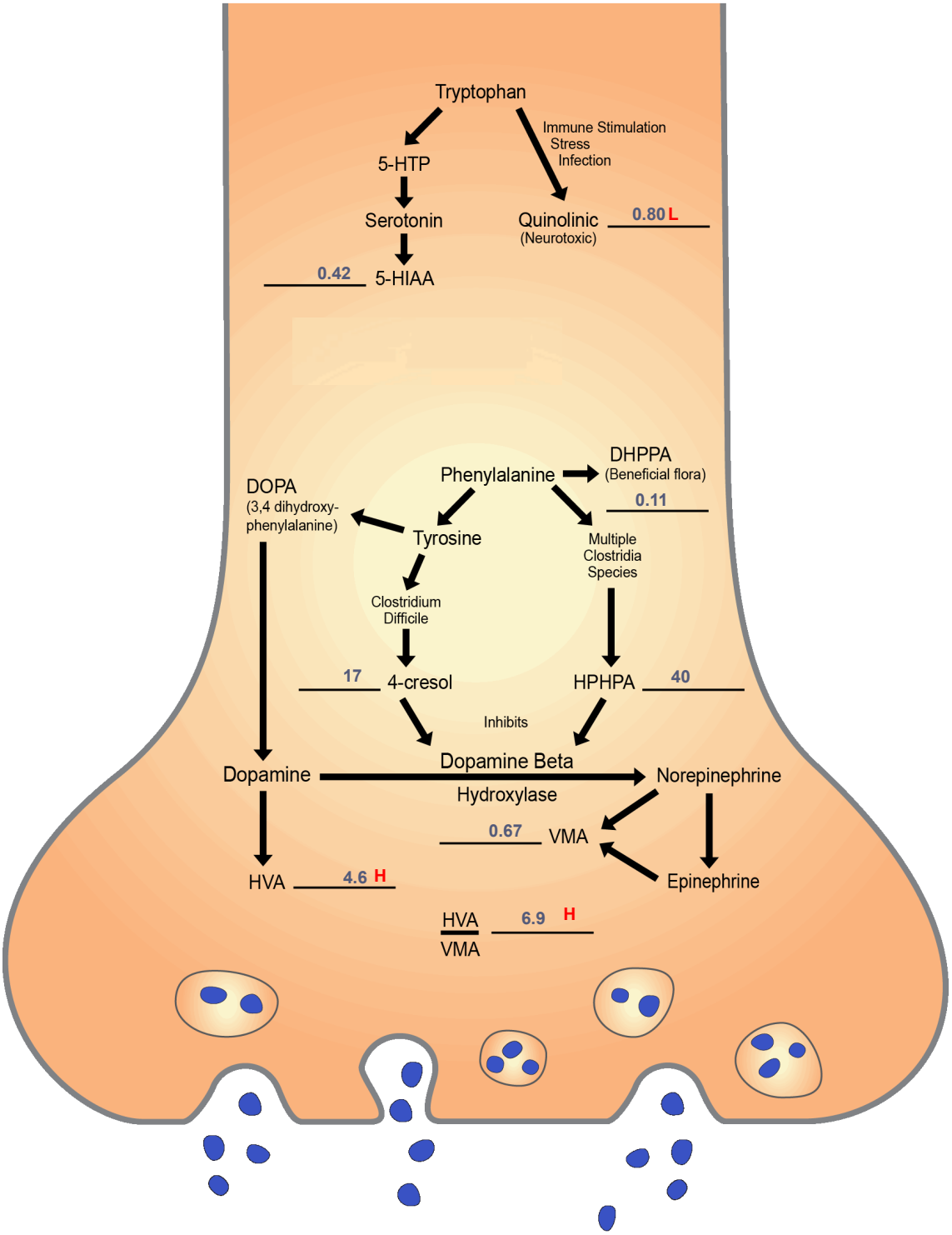
Patient Name:	Lynette Blake	***Date of Collection:***	01/23/2023
Specimen Id.:	1155602-2		

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 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.

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.

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High HVA (33) High HVA is usually associated with Clostridia colonization or excess fusaric acid from fungus of the gastrointestinal tract and/or deficiencies of dopamine-beta-hydroxylase (DBH) activity due to single nucleotide polymorphisms (SNPs) or genetic deletions that code for enzymes with low activity. The genetic deficiencies of DBH can be treated with the drug Droxidopa (L-*threo*-dihydroxyphenylserine). Droxidopa has the ability to cross the blood brain barrier and be converted to norepinephrine by an alternate biochemical pathway that bypasses the DBH genetic block. Individuals with genetic deficiencies of DBH may have orthostatic hypertension and hypoglycemia and may be more susceptible to attention deficit disorder, Alzheimer's disease, and Parkinson's disease, depression, and bipolar depression. The severity of ADHD symptoms is related to decreased DBH enzyme activity. Cocaine abusers with low-activity DBH SNPs have increased sensitivity to cocaine-induced paranoia and euphoria. The drugs disulfiram and Etamicastat inhibit DBH and the inhibition of alcohol, drug, and gambling addictions by disulfiram may be mediated by DBH inhibition.

If HVA is elevated and VMA is normal and the patient has elevated Clostridia markers, avoid supplementation with L-DOPA, phenylalanine or tyrosine until *Clostridia* is treated. Homovanillic acid (HVA), a dopamine metabolite, is often elevated due to stress-induced catecholamine output from the adrenal gland which depletes vitamin C. Supplementation with vitamin C (ascorbate) may be helpful in such cases.* Elevated HVA can result from the intake of L-DOPA, dopamine, phenylalanine, or tyrosine. Elevated HVA may also result from ingestion of aspartame (Nutrasweet®), salicylates (aspirin), and dietary salicylates. For more information about salicylates in foods go to <http://www.feingold.org/salicylate.php>. Elevated HVA may also result from toxic metal exposure (including lead, aluminum, manganese,arsenic, and mercury), presumably due to DBH inhibition. Heavy metal testing (blood or hair) might be useful to determine if such exposure is significant.

If values are more than double the upper limit of normal, toxoplasmosis and tumors such as neuroblastoma, or other catecholamine-secreting tumors should be ruled out. Catecholamine-secreting tumors can be ruled out by 24- hour VMA and/or HVA testing in urine. Even in this subgroup, the incidence of tumors is extremely rare.

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 HVA/VMA ratio (35) the HVA/VMA ratio reflects the balance between dopamine and norepinephrine/epinephrine production by catecholamine producing neurons in the central nervous system, sympathetic nervous system, and adrenal gland. The most common reason for an elevation of the HVA/VMA ratio is a decreased conversion of dopamine to norepinephrine. The enzyme responsible for this conversion, dopamine beta-hydroxylase (DBH), is copper and vitamin C dependent so an elevated ratio could be due to deficiencies of these cofactors. **The most common reason** for this elevated ratio is inhibition of this enzyme by Clostridia byproducts including HPHPA, 4-cresol, or 4-hydroxyphenylacetic acid. Other causes of an increased ratio include inhibition of DBH by the mold metabolite fusaric acid, pharmaceuticals such as disulfiram, or food additives like aspartame. Another cause for an elevated ratio is a genetic variation (single nucleotide polymorphism or SNP) of the DBH enzyme. Alternatively, the activity of the DBH enzyme can be measured on blood serum. Individuals with low DBH activity can be treated with the drug Droxidopa™, which provides adequate norepinephrine by an alternate biochemical pathway. High ratios are common in a large number of neuropsychiatric diseases regardless of the reason for DBH deficiency.

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.

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 5HIAA 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.

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.

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 pyroglutamic acid (58) the diagnostic significance of low pyroglutamic acid is unclear.

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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