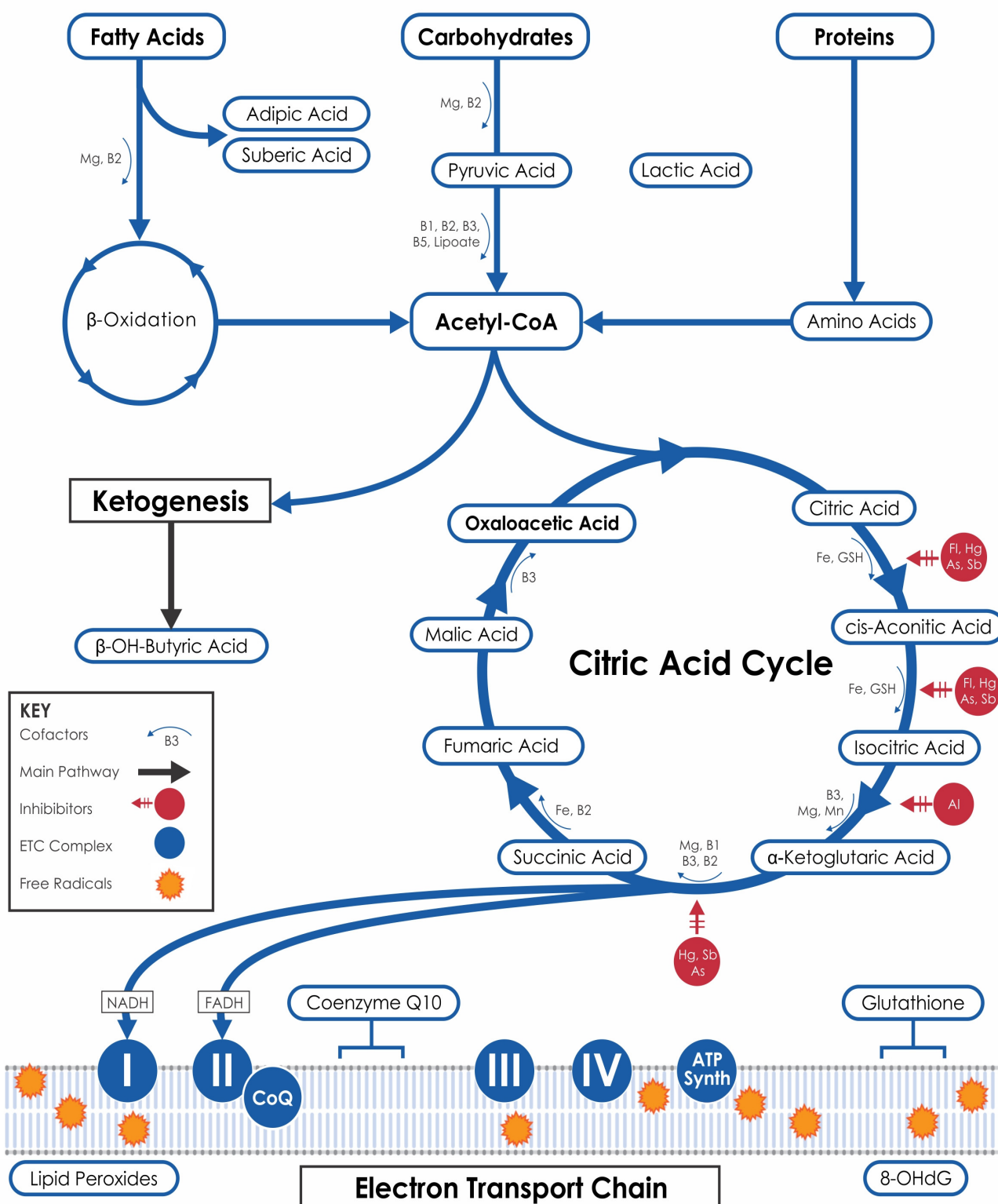


ORGANIC ACIDS METABOLOMIC MAPPING

Method: LCMS/MS/MS

Organic Acids Pathways



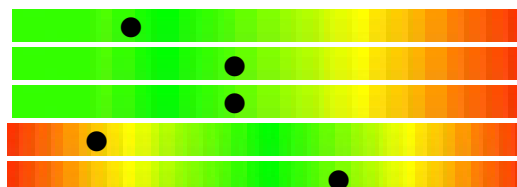
Nutrient Markers

URINE, SPOT

KETONE/FATTY ACID Metabolites

(Carnitine & B2)

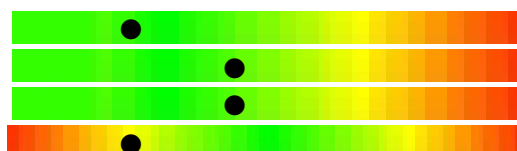
1. Adipic Acid.	1.02	0.00 - 11.10 ug/mgCR
2. Suberic Acid.	2.59	0.00 - 4.60 ug/mgCR
3. Ethylmalonic Acid	3.29	0.00 - 6.30 ug/mgCR
4. Pimelic Acid	6.4	5.9 - 31.8 ug/mgCR
5. Methyl-Succinic Acid	18.50	3.20 - 21.10 ug/mgCR



CARBOHYDRATE Metabolism/Glycolysis

(B1, B3, Cr, Lipoic Acid, CoQ10)

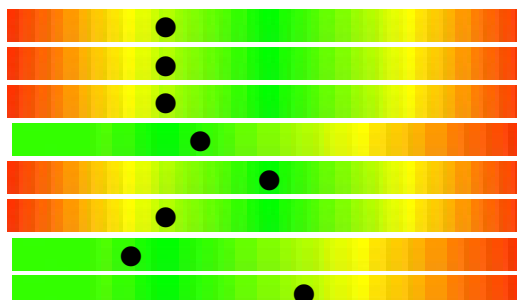
6. Pyruvic Acid.	0.61	0.00 - 6.40 ug/mgCR
7. Lactic Acid.	8.02	0.00 - 16.40 ug/mgCR
8. b-OH-Butyric Acid	5.33	0.00 - 9.90 ug/mgCR
9. Glucose (OA)	0.2	0.1 - 1.1 mmol/L



CITRIC ACID CYCLE Metabolites.

(B Comp., CoQ10, Amino Acids, Mg)

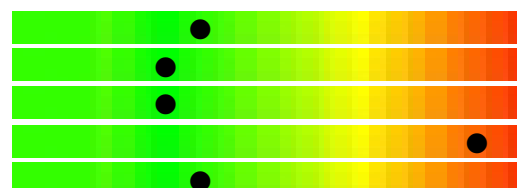
10. Citric Acid.	267.0	56.0 - 987.0 ug/mgCR
11. cis-Aconitic Acid.	31.5	18.0 - 78.0 ug/mgCR
12. Isocitric Acid.	58.1	35.0 - 143.0 ug/mgCR
13. a-Ketoglutaric Acid.	13.77	0.00 - 35.00 ug/mgCR
14. Succinic Acid	12.72	1.10 - 20.90 ug/mgCR
15. Fumaric Acid.	1.17	1.10 - 1.35 ug/mgCR
16. Malic Acid.	0.50	0.00 - 3.10 ug/mgCR
17. b-OH-b-Methylglutaric Acid	4.10	0.00 - 5.10 ug/mgCR



B-Complex Vitamins & Amino Acid Markers

(B1, B2, B3, B5, B6, Biotin)

18. a-Ketoisovaleric Acid	0.18	0.00 - 0.49 ug/mgCR
19. a-Ketoisocaproic Acid	0.13	0.00 - 0.52 ug/mgCR
20. a-Keto-b-Methylvaleric Acid	0.31	0.00 - 1.10 ug/mgCR
21. Xanthurenic Acid	0.78 *H	0.0 - 0.5 ug/mgCR
22. beta-Hydroxyisovaleric Acid	4.42	0.00 - 11.50 ug/mgCR



METHYLATION COFACTORS

(B12, Folate)

23. Methylmalonic Acid.	0.84	0.00 - 2.30 ug/mgCR
24. Formiminoglutamic Acid **	0.8	0.0 - 2.2 ug/mgCR

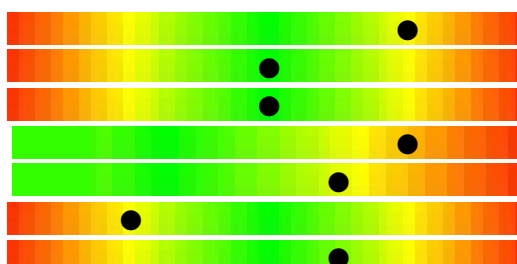


Cell Regulation Markers

NEUROTRANSMITTER METABOLISM

(Tyrosine, Tryptophan, B6, Antioxidants)

25. Homovanillic Acid (HVA)	8.48 *H	1.40 - 7.60 ug/mgCR
26. Vanillylmandelic Acid (VMA)	3.55	1.20 - 5.30 ug/mgCR
27. 5-Hydroxyindoleacetic Acid (5HIAA)	6.82	1.60 - 9.80 ug/mgCR
28. Kynurenic Acid.	1.66 *H	0.0 - 1.5 ug/mgCR
29. Quinolinic Acid (OA)	5.25	0.00 - 5.80 ug/mgCR
30. Picolinic Acid	4.4	2.8 - 13.5 ug/mgCR
31. Cortisol (OA)	451	166 - 507 nmol/L



Oxidative Damage/AntiOxidant Markers

(Vitamin C and Other Antioxidants)

32.	ParaHydroxyphenyllactate	0.41	0.00 - 0.66 ug/mgCR	
33.	8 OH-deoxyguanosine	5.0	0.0 - 7.6 ug/mgCR	

Toxicants and Detoxification

DETOXIFICATION INDICATORS

(Arg, NAC, Met, Mg, Antioxidants)

34.	2-Methylhippuric Acid	<dl	0.00 - 0.19 ug/mgCR	
35.	Orotic Acid.	1.50 *H	0.00 - 1.01 ug/mgCR	
36.	Glucaric Acid.	8.80	0.00 - 10.70 ug/mgCR	
37.	a-OH-Butyric Acid	0.46	0.10 - 0.90 ug/mgCR	
38.	Pyroglutamic Acid.	63.0	28.0 - 88.0 ug/mgCR	

Compounds of Bacterial or Yeast/Fungal Origin

BACTERIAL DYSBIOSIS MARKERS.

39.	Benzoate (OA)	2.88	0.00 - 9.30 ug/mgCR	
40.	Hippurate (OA)	937	0.0 - 1070 ug/mgCR	
41.	Phenylacetate	<dl	0.0 - 0.2 ug/mgCR	
42.	Phenylpropionate	<dl	0.0 - 0.1 ug/mgCR	
43.	ParaHydroxyBenzoate	1.4	0.0 - 1.8 ug/mgCR	
44.	p-HydroxyPhenylacetate	0.5	0.0 - 34.0 ug/mgCR	
45.	Indoleacetic Acid	30.7	0.00 - 90.00 ug/mgCR	
46.	Tricarballic acid	0.70	0.00 - 1.41 ug/mgCR	

L. acidophilus/General Bacteria

47.	D-Lactate	2.0	0.0 - 4.1 ug/mgCR	
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CLOSTRIDIAL SPECIES

48.	Dihydroxyphenylpropionic Acid	<dl	0.00 - 0.05 ug/mgCR	
49.	4-Cresol	1.0	0.0 - 75.0 ug/mgCR	
50.	3-OH-Propionic Acid	27.3	0.0 - 208.0 ug/mgCR	

YEAST/FUNGAL DYSBIOSIS MARKERS.

51.	Arabinitol	50.3	0.0 - 73.0 ug/mgCR	
52.	Citramalic Acid	2.7	0.0 - 3.6 ug/mgCR	
53.	Tartaric Acid.	4.9	0.0 - 7.0 ug/mgCR	

Oxalate Metabolites

54.	Oxalic Acid	5.64	0.77 - 7.00 ug/mgCR	
55.	Glyceric Acid	22.3	16.0 - 117.0 ug/mgCR	
56.	Glycolic Acid	27.8	6.8 - 101.0 ug/mgCR	

Nutritional Markers

57.	Pyridoxic Acid (Vit B6)	8.8	5.0 - 34.0 ug/mgCR	
58.	Pantothenic Acid (Vit B5)	2.6	2.0 - 10.0 ug/mgCR	
59.	Glutaric Acid (Vit B2) **	0.3	0.0 - 0.4 ug/mgCR	
60.	Ascorbic Acid (Vit C)	111	10.0 - 200 ug/mgCR	
61.	CoEnzyme-Q10 (CoQ10) **	0.86	0.17 - 39.00 ug/mgCR	
62.	N-Acetylcysteine (NAC)	0.10	0.10 - 0.28 ug/mgCR	
63.	Biotin (Vit H)	1.93	0.19 - 2.70 ug/mgCR	

Creatinine, Urine Spot.	11.4	5.0 - 13.0 mmol/L	
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Results reported as <dl = Less than detectable limit ** A high value for this marker may indicate a deficiency of this vitamin



Nutritional Guide

Nutrient	Adult Dose Range	Units	Clinician Notes
Vitamin-C	1000.0	mg	
Vitamin-E	500.0	IU	
Vitamin-B1	15.0	mg	
Vitamin-B2	40.0	mg	
Vitamin-B3	150.0	mg	
Vitamin-B5	85.0	mg	
Vitamin-B6	150.0	mg	
Folinic Acid.	500.0	ug	
Magnesium .	600.0	mg	
Coenzyme Q10.	300.0	mg	
alpha Lipoic Acid.	125.0	mg	
Calcium-D-glucurate.	600.0	mg	
Acetyl-L-Carnitine.	600.0	mg	
N-Acetylcysteine.	125.0	mg	
Glutathione.	125.0	mg	
5-hydroxyTryptophan (5-HTP).	60.0	mg	
Aspartic Acid.	1000.0	mg	
L-Arginine.	2000.0	mg	
Glycine .	1000.0	mg	
Methionine.	250.0	mg	
Tryptophan.	375.0	mg	
Lactobacillus	5.0	billion CFU	
Probiotics (Multistain)	15.0	billion CFU	

Disclaimer:

Supplement recommendations are based on the Organic Acid test results. The prescribing health practitioner must take into consideration the age, weight, sex, and pregnancy or lactation state. In addition, consider clinical state, medication regime, associated drug-nutrient depletion and allergies. The doses listed above are considered optimal, based on lab results and do not apply to specific disease conditions where doses may need to be altered. The vitamins, minerals or amino acids listed are elemental quantities. Use clinical discretion when choosing the right salt with the guidance of your compounding health professional. For example, Magnesium may be prescribed as a glycinate for its calming effect or threonate may be used for a Magnesium that crosses the blood-brain-barrier.

References:

Laboratory Evaluations for Integrative and Functional Medicine by Richard Lord.
J.Alexander Bralley; Textbook of Nutritional Medicine by Alan Gaby.



Laboratory Comments

Ketone/FA Metabolites Comment

Organic acids provide functional markers for the metabolic effects of micronutrient adequacy, toxic exposure, neuroendocrine activity, intestinal bacterial and fungal overgrowth. Organic acid testing indicates the need for nutrients, diet modification, detoxification, antioxidant protection or further testing.

In a healthy state, organic acids are excreted in the urine at low concentrations. Low range results may be associated with hypometabolic compensatory states. Compensatory responses include hormonal secretions and cytokine responses that can slow or reverse deviations from median or normal physiologic states.

The Krebs cycle is a process of conversion of fats, carbohydrates and protein to mitochondrial energy, ATP.

Metabolic blocks in the Krebs cycle due to insufficient enzymes or cofactors will result in the elevation of organic acids that accumulate and spill into urine.

FATTY ACID METABOLISM:

Adipate, suberate, pimelate, Ethylmalonate and 2-methylsuccinate are organic compounds from fatty acid metabolism. Long chain fatty acids (LCFAs) undergo beta-oxidation in the mitochondria which is carnitine dependant. Dietary fat is broken down to produce free fatty acids, energy substrates using pathways that require carnitine and vitamin B2 (Riboflavin).

Low levels of Ethylmalonate with high adipate and suberate may be associated with carnitine deficient hypometabolic states where multiple amino acid catabolic pathways are restricted due to mitochondrial retraction.

Carbohydrate Metabolism Comment

CARBOHYDRATE METABOLISM/GLYCOLYSIS:

Dietary carbohydrates are broken down into Glucose and other sugars where carbohydrate breakdown products, pyruvate and lactate are formed. Pyruvate enters the Krebs cycle via dehydrogenase enzymes which require vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B3 (niacin), vitamin B5 (pantothenic acid), and lipoic Acid to function correctly. Review Vitamin B Levels in conjunction with Pyruvate and Lactate levels.

In the absence of these nutrients, lactate builds up leading to lactic acidosis. Elevated pyruvate and lactate can indicate a need for lipoic acid.

Cit Acid Cycle Metabs Comment

The Citric Acid Cycle is the pathway for energy released from food components and the source of anabolic molecules to support organ maintenance and neurological function. Therefore, the citric acid cycle serves both anabolic and catabolic functions representing the crossroads of food conversion and utilisation.

B-Vitamins/Amino Acids Comment

B-COMPLEX VITAMIN MARKERS:

B-Complex Vitamin Markers are metabolic intermediates in the degradation of amino acids. When hepatic enzymes remove branched-chain amino acids, they form keto acids.

B-complex vitamins are essential for many in metabolic functions in the body used to extract energy from cellular health, remove toxins, and maintain the immune system.

B-Complex vitamin deficiencies produce symptoms associated with homocysteinemia effects or mitochondriopathy-associated symptoms which include periodic weakness, nausea, fatigue, attention deficit or Reye syndrome.

XANTHURENATE ELEVATED:

Xanthurenate is a by-product of tryptophan catabolism in the liver, arising from conversion of tryptophan to nicotinic acid which is Vitamin B6 dependent. Vitamin B6 deficiency leads to elevated excretion of the



xanthurenate and kynurenate because of pyridoxal-5-phosphate-dependent step in this metabolic pathway called kynurenine pathway.

Elevations in Xanthurenate and Kynurenate are markers for Vitamin B6 (pyridoxal) deficiency. Assess blood Vitamin B6 levels.

Supplementation Recommendations:
Vitamin B6.

Neurotransmitter Metabolism Comment

HOMOVANILLIC ACID (HVA) ELEVATED:

Homovanillate is the main metabolite of Dopamine.

Elevated levels of homovanillate may be due to amino acid deficiencies, the use of L-Dopa as a treatment for Parkinson's disease, copper deficiency (especially if Vit A is low), cocaine or amphetamine use or chronic depletion of Tyrosine.

Elevations reflect the increased rate of synthesis and degradation in normal tissues.

Drugs that may have an adverse effect to the result: Aspirin.

Symptoms and Conditions: Agitation, delirium, psychosis.

Supplementation Recommendations:

Supplement with Tyrosine 2x daily 500mg, Vitamin C, Folate, Broad spectrum essential amino acids. Stop related drug use.

Tyrosine is essential to the synthesis of protein, catecholamines, melanin and thyroid hormones. Vitamin C and Folate are essential to its metabolism. The formation of thyroid hormone is dependent upon the absorption and sequestering of iodine which then attaches to tyrosine to form thyroxine.

5HIAA IS WITHIN RANGE:

5HIAA is the major metabolite of Serotonin.

KYNURENATE ELEVATED:

Elevations of this Tryptophan metabolite is consistent with vitamin B6 deficiency, possible inflammatory processes from chronic infections, interferon-gamma stimulated macrophages or excessive tryptophan supplementation (not 5HTP). Abnormally high levels can cause an increase in pain sensations and may, in multiple sclerosis (MS) patients, be a marker for an exacerbation period.

Kynurenate antagonises glutamate receptors and has a preferential affinity for NMDA receptor that governs synaptic plasticity learning and memory. Studies suggest that elevated Kynurenate represent conditions that are seen in schizophrenia, mediated by vitamin B6.

Kynurenate is a biochemical precursor to Quinolinic acid and found to be simultaneously elevated in inflammatory responses. Because Quinolinic acid is a powerful agonist of NMDA receptors and Kynurenate antagonises this effect, the relative amount of the two metabolites should relate to neuronal degradation.

Supplementation Recommendations:

Vitamin B6, Mg can help support metabolism of kynurenate.

Detoxification/Toxicants Comment

OXIDATIVE DAMAGE AND ANTIOXIDANT MARKERS:

The assessment of protection from oxidant and ammonia challenge should be of priority when detoxification requirement is suspected. Oxidative stress has been associated with a variety of diseases like diabetes, cancer, neurodegenerative disorders and aging.

DETOXIFICATION INDICATORS:

The organic acids of this group serve as biomarkers of detoxification status or biotransformation capacities, distinct parts of the detoxification system, providing insight about both exogenous toxin accumulation and endogenous detoxification responses.

Elevations in toxicant and detoxification markers reveal aspects of xenobiotic exposure, endogenous toxins and detoxification functions.

OROTIC ACID ELEVATED:

Elevations are a sensitive marker of ammonia build-up or arginine deficiency or excessive lysine intake or an



intracellular magnesium deficiency.

Most of the symptoms of arginine deprivation can be accounted for by decreased efficiency of ammonia detoxification or intestinal bacteria metabolism of amino acids.

Supplementation Recommendations:

Arginine, aspartic acid, alpha-ketoglutarate, B complex (B3, B6), magnesium, Citrulline and glutamic acid. Also consider a Microbiome assessment to determine microbial overgrowth.

Nutritional Markers Comment

N-ACETYLCYSTEINE (NAC) LOW:

Cysteine, a sulphur-containing amino acid are found at many catalytic sites of many enzymes and turnover of glutathione. Cysteine rich protein, keratin is found in hair. NAC helps to replenish glutathione levels in the body, assists in detoxification in liver and kidney, relieves respiratory disorders, and improves mood. It also aids in regulating glutamate. NAC supplementation is associated side effects of dry mouth, nausea, vomiting, and diarrhoea.

Supplementation Recommendations:

Adult Repletion: 200-600mg