

Pattern Recognition

In Organix Comprehensive

With RupaHealth

Presented by: Garric Vosloo Functional Medicine Fast Track <u>www.fm-ft.com</u>

@ 2020

- Organic acid testing (OAT) has become very popular amongst functional medicine practitioners
- This urine-based test provides a wealth of information about the functioning of various bodily systems and can be used to identify possible nutrient deficiencies, gut dysbiosis, and more.



What Is an Organic Acid?

In humans, organic acids are byproducts or intermediates of chemical reactions that occur within the body (1).

The quantity (and sometimes the type) of organic acids produced are unique to each individual and can be influenced by a variety of factors.

Some factors that can influence organic acid production within the body include (2, 3):

- Diet
- Environmental toxins
- Gut microbes
- Genetics
- Kidney and liver function
- Medications
- Nutrient status
- Oxidative stress



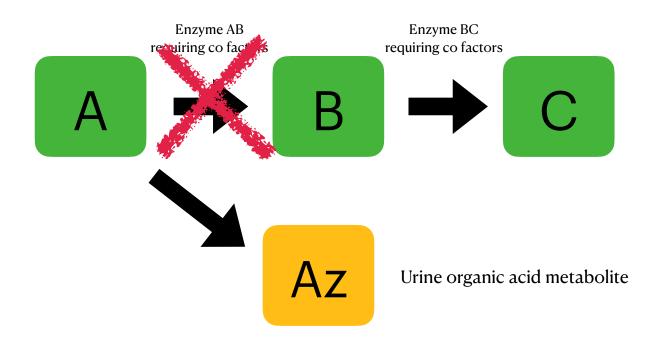
What Is an Organic Acid?

In order for the body to run effectively, it needs proper amounts of vitamins and minerals to act as cofactors for enzymatic reactions.

Without enough of these nutritional cofactors (or if someone has genetic mutations that affect how well their enzymes work), these chemical pathways are unable to proceed at their normal pace.

As a result, organic acids begin to build up and are excreted in the urine:







Reasons for Abnormal OAT Results

When the body isn't functioning optimally, organic acids in the urine can become elevated or depleted, depending on what is occurring.

The main reasons for abnormal urinary organic acid results include:

- 1.Inborn errors of metabolism
- 2.B-vitamin deficiencies
- 3.Gut dysbiosis
- 4.Impaired fatty acid metabolism
- 5.Ketosis or poor carbohydrate metabolism
- 6.Neurotransmitter metabolism
- 7.Mitochondrial dysfunction
- 8.Oxidative stress
- 9. Poor detoxification
- 10.Inflammation

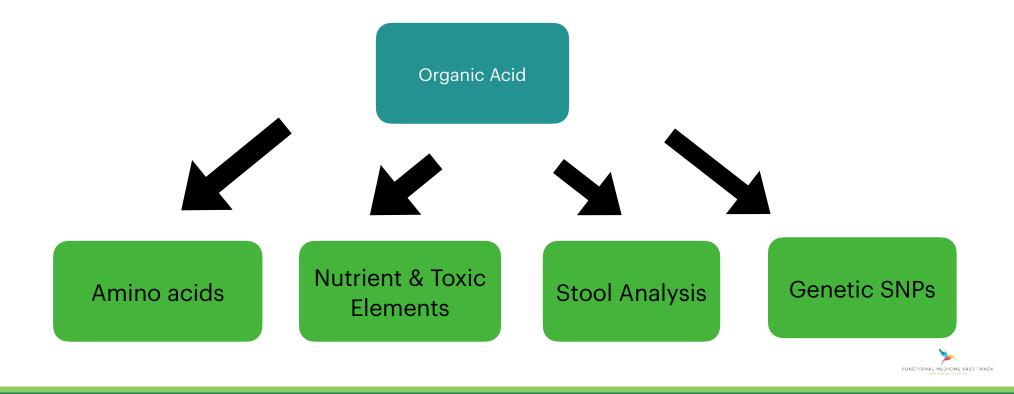


5 Examples of Pattern Recognitions In Organix Comprehensive

- 1. Low patterns
- 2. High patterns
- 3. Glutathione Status patterns
- 4. Kynunerine Patterns
- 5. Lipogenesis patterns



Pattern Recognition In Organix Comprehensive: Confirming with other tests

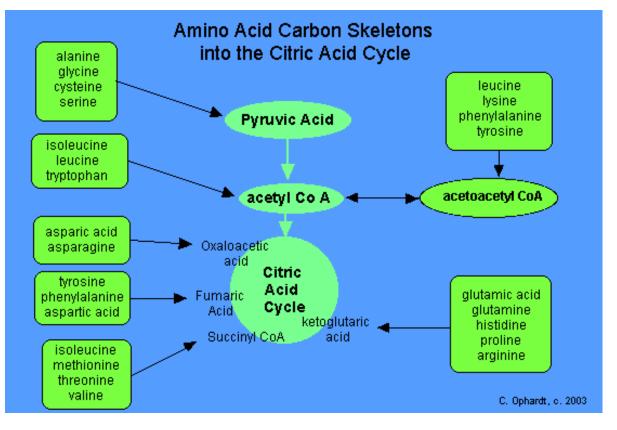


Pattern #1: Dominant LOW Markers

Fatty Acid Metabolism (Carnitine & B2) 6.2 1. Adipate 1.8 <= 11.1 2.1 2. Suberate 0.4 <= 4.6 3.6 3. Ethylmalonate 1.6 <= 6.3 Carbohydrate Metabolism (B1, B3, Cr, Lipoic Acid, CoQ10) 3.9 4. Pyruvate 4.1 <= 6.4 8.5 5. L-Lactate 7.5 0.6 - 16.4 2.1 6. β-Hydroxybutyrate <DL <= 9.9 **Energy Production (Citric Acid Cycle)** (B Comp., CoQ10, Amino Acids, Mg) 601 7. Citrate 208 56 - 987 51 8. Cis-Aconitate 28 18 - 78 98 9. Isocitrate 44 39 - 143 19.0 10. α-Ketoglutarate <= 35.0 11.8 11.6 11. Succinate 3.0 <= 20.9 0.59 12. Fumarate <DL <= 1.35 1.4 13. Malate 0.3 <= 3.1 3.6 2.1 14. Hydroxymethylglutarate <= 5.1



24 yo Female Weight gain Chronic Fatigue Brain Fog IBS Acne





Origins of low adipate, suberate or ethylmalonate

Low ethylmalonate is not directly associated like adipate and suberate with mitochondrial retracted states, but rather with pathways of amino acid catabolism. However, it is quite common to find ethylmalonate low along with low adipate and suberate. The linking factor is cellular free amino acid concentrations that are directly correlated with both amino acid catabolic flux and mitochondriogenesis via mTOR activation.

Excerpt From: Richard S. Lord. "Paths to Health: Organic Acids." Arrowhead Bioscience, 2018. Apple Books. https://books.apple.com/us/book/paths-to-health-organic-acids/id143949298



Low Amino Acid Patterns in Organic Acids

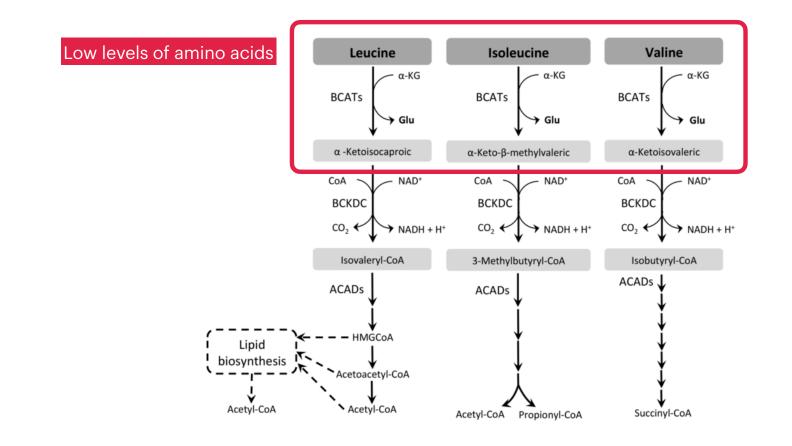
Patient A:

24 yo Female Weight gain Chronic Fatigue Brain Fog IBS Acne

B-Complex Vitamin Markers (B1, B2, B3, B5, B6, Blotin)			0.05
15. α-Ketoisovalerate	<dl< td=""><td></td><td></td></dl<>		
16. α-Ketoisocaproate	<dl< td=""><td></td><td>• • • • • • • • • • • • • • • • • • •</td></dl<>		• • • • • • • • • • • • • • • • • • •
17. α-Keto-β-Methylvalerate	<dl< td=""><td></td><td>0.38</td></dl<>		0.38
18. Xanthurenate	0.94	н	
19. β-Hydroxyisovalerate Methylation Cofactor Markers (B12, Folate)	3.0		7.6
20. Methylmalonate	1.3		
21. Formiminoglutamate	1.1		



Branched Chain Amino Acid Metabolism

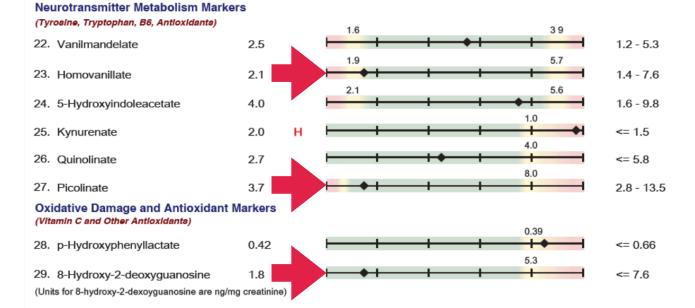


FUNCTIONAL MEDICINE FAST TRACK

Low Amino Acid Patterns in Organic Acids



24 yo Female Weight gain Chronic Fatigue Brain Fog IBS Acne



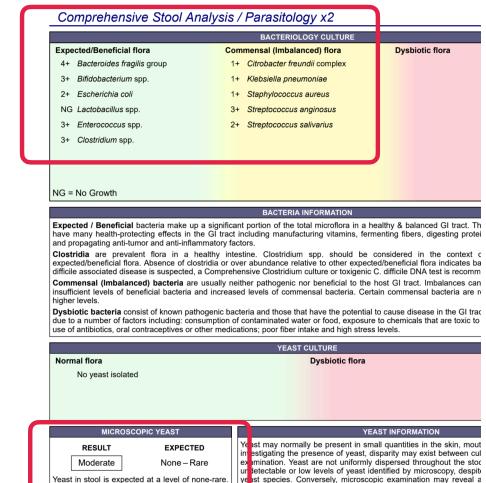


Connecting Organic Acid to Amino Acid

Essential Amino Acids										
Lin	niting Amino Acids				183					
1.	Lysine	70		I → → → →		63 - 220				
2.	Methionine	11			28	10 - 33				
3.	Tryptophan	30			45	24 - 52				
Bra	anched Chain Amino Acids			95	77					
4.	Isoleucine	40		35	77	28 - 96				
5.	Leucine	77			139	59 - 162				
6.	Valine	179			229	105 - 266				
Oth	ner Essential Amino Acids			43	72					
7.	Phenylalanine	19	L	<mark>▶ </mark>		37 - 86				
8.	Histidine	35		31	84	22 - 99				
9.	Threonine	124			143	54 - 169				
Co	nditionally Essential Amino Acids			28	71					
10.	Arginine	40		⊢ 		17 - 91				
11.	Taurine	82	L	145	245	124 - 282				
12.	Glycine	129	L	243	449	207 - 559				
13.	Serine	71	L	95	219	79 - 310				

ges: Ages 13 and over.	Results µmol/L		1st 2nd	UINTILE DISTRI 3rd	4th	5th	95% Reference
	μπονε	F	unctional Categ	iories	1		Range
scular Function				Joneo			
Arginine	40		28	◆ 		71	17 - 91
			145	_		245	
Taurine urotransmitters and Precur	82	L	-				124 - 282
			43			72	
Phenylalanine	19	L	44	- i		85	37 - 86
Tyrosine	27	L.					36 - 99
Tryptophan	30		28			45	24 - 52
Glutamic Acid	122		112			207	97 - 258
Giutamic Acid	122		145			245	97 - 258
Taurine	82	L					124 - 282
lfur Amino Acids (Glutathio	ne - related)		12			28	
Methionine	11				+		10 - 33
Taurine	82	L.	145			245	124 - 282
ea Cycle and Ammonia Dete	oxification						
Arginine	40		28	◆	+	71	17 - 91
-	17		19	_		41	10 51
Citrulline	17		68	1		158	16 - 51
Ornithine	24	L	307		+	520	50 - 210
Glutamine	248		307			520	209 - 573
Asparagine	38	L	49			77	42 - 88
			44			180	
Aspartic Acid	75			- + •			26 - 233
tios							
Phenylalanine/Tyrosine	0.70		0.26			0.51	<= 1.19
Glutamic Acid/Glutamine	0.49				+	•	0.22 - 0.88
Tryptophan/LNAA*	0.088		0.061			0.093	0.050 - 0.105
*Large neutral amino acids (Leu+II	e+Val+Phe+Tyr)						

Connecting Organic Acid connection to CSAP

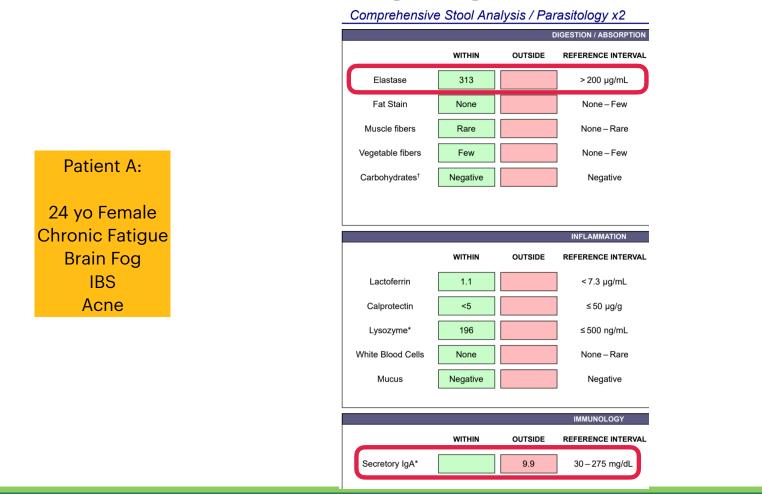




Patient A:

24 yo Female Weight gain Chronic Fatigue Brain Fog IBS Acne

Connecting Organic Acid to CSAP



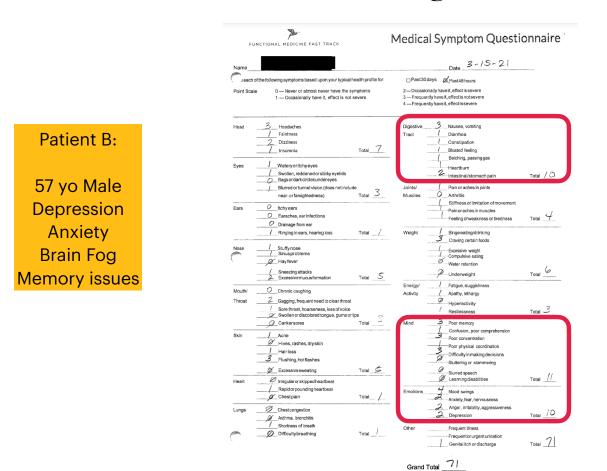


Clinical Application

- 1. Essential Amino Acids
- 2. Improve maldigestion and malabsortption
- 3. Use betaine HCL testing for optimal stomach acidity
- 4. Add digestive enzymes to aid low pancreatic function



Pattern #2: Dominant High Markers





Pattern #2: Dominant High Markers

			Nutrient Markers	
	tty Acid Metabolism rnitine & B2)			
1.	Adipate	2.4		<= 11.1
2.	Suberate	1.7		<= 4.6
3.	Ethylmalonate	3.2		<= 6.3
	rbohydrate Metabolism , B3, Cr, Lipoic Acid, CoQ10)		3.9	
4.	Pyruvate	<dl< td=""><td></td><td><= 6.4</td></dl<>		<= 6.4
5.	L-Lactate	12.2		0.6 - 16.4
6.	β-Hydroxybutyrate	<dl< td=""><td>2.1</td><td><= 9.9</td></dl<>	2.1	<= 9.9
	ergy Production (Citric Acid Cy Comp., CoQ10, Amino Acids, Mg)	/cle)	601	
7.	Citrate	971		56 - 987
8.	Cis-Aconitate	63		18 - 78
9.	Isocitrate	84	98 	39 - 143
10.	α-Ketoglutarate	17.4		<= 35.0
11.	Succinate	2.0		<= 20.9
12.	Fumarate	<dl< td=""><td>0.59</td><td><= 1.35</td></dl<>	0.59	<= 1.35
13.	Malate	1.3		<= 3.1
14.	Hydroxymethylglutarate	3.2		<= 5.1

Patient B:

57 yo Male Depression Anxiety Brain Fog Memory issues



Pattern #2: Dominant High Markers

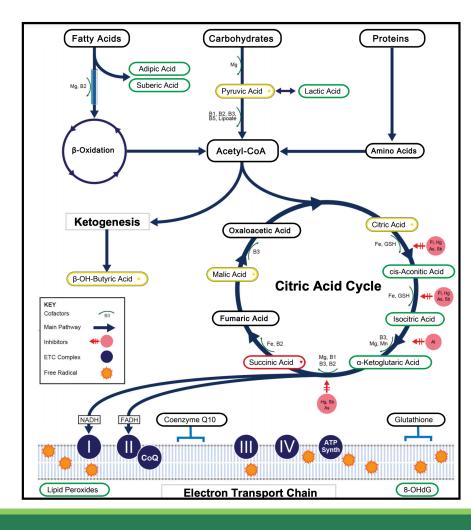
Vitamins B 1,2,3,5 Magnesium Iron Manganese Lipoic acid

Reason #1: Main Co factors:

Reason #2: Main Heavy Metal Inhibitors:

> Fluoride Arsenic Mercury Lead Aluminium Antimony

Reason #3: Genetic SNPs





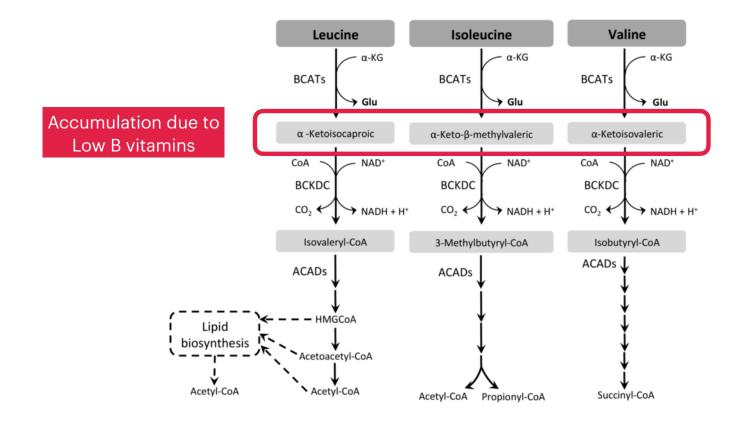
High B Vitamin markers

	Results mcg/mg creat	inine	QUNITE DISTRIBUTION	5th	95% Reference Range
			Nutrient Markers		
B-Complex Vitamin Markers (B1, B2, B3, B5, B6, Biotin)				0.25	
15. α-Ketoisovalerate	0.70	н	⊩	0.34	<= 0.49
16. α-Ketoisocaproate	1.06	н		0.34	<= 0.52
17. α-Keto-β-Methylvalerate	<dl< td=""><td></td><td>F</td><td>0.34</td><td><= 1.10</td></dl<>		F	0.34	<= 1.10
18. Xanthurenate	0.95	н	⊢ । । ।	7.6	<= 0.46
19. β-Hydroxyisovalerate Methylation Cofactor Markers (B12, Folate)	8.2			^{7.0}	<= 11.5
20. Methylmalonate	1.8		· · · · · · · · · · · · · · · · · · · 	1.7 1.4 1.2	<= 2.3
21. Formiminoglutamate	2.3	н	· · · · ·		<= 2.2

57 yo Male Depression Anxiety Brain Fog Memory issues

Patient B:

Branched Chain Amino Acid Metabolism



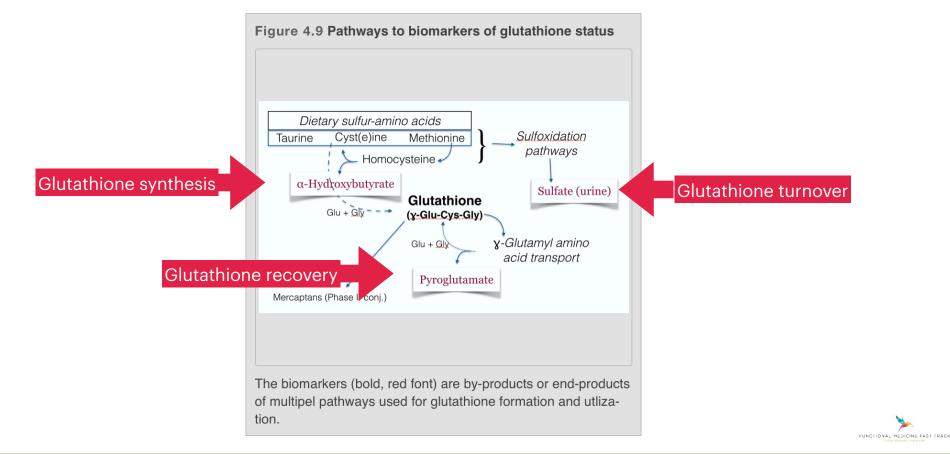


Clinical Application

- 1. B Vitamin Complex
- 2. Optimize gut health
- 3. Use 5R program
- 4. Multimineral
- 5. Possibly additional magnesium and iron



Pattern Recognition #3: Glutathione Status



Pattern Recognition #3: Glutathione Status

able 5.1 Stages of Glutathione Capacity Erosion										
<u>Stage</u> AHB PYRO SO₄ 8-OHdG ^{Plasma} Met, Tau, H										
Early	> 4th Quintile	Variable	> 3rd Quintile	Normal	Normal					
Middle	> 95th %ile.	High	< 3rd Quintile	> 4th Quintile	Low normal					
Late	< DL	Low	Low	> 95th %ile	Low					



Mid Stage Glutathione Depletion

	Т	oxic	ants and Detoxificatior	n	
Detoxification Indicators (Arg, NAC, Met, Mg, Antioxidants)				0.084	
30. 2-Methylhippurate	0.052		⊢ + +	0.69	<= 0.192
31. Orotate	0.57			6.3	<= 1.01
32 Glucarate	3.5		├─── ├ ●		<u>-</u> 10 7
33. α-Hydroxybutyrate	1.7	н	ŀ	0.3	<= 0.9
34. Pyroglutamate	52		958	2,347	28 - 88
35. Sulfate	3,053	н			690 - 2,98

Patient B:

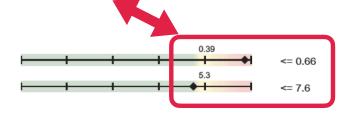
57 yo Male Depression Anxiety Brain Fog Memory issues

Oxidative Damage and Antioxidant Markers (Vitamin C and Other Antioxidants)

28. p-Hydroxyphenyllactate 0.72

29. 8-Hydroxy-2-deoxyguanosine 4.1

(Units for 8-hydroxy-2-dexoyguanosine are ng/mg creatinine)





End Stage Glutathione Depletion

	m	cg/mg creatinine							Range			
	Toxicants and Detoxification											
	ification Indicators AC, Met, Mg, Antioxidants)						0.084					
30. 2-	Methylhippurate	0.028	—				0.69		<= 0.192			
31. O	rotate	<dl< td=""><td>+</td><td></td><td>-</td><td></td><td>6.3</td><td></td><td><= 1.01</td></dl<>	+		-		6.3		<= 1.01			
32. G	lucarate	6.3	-				+		<= 10.7			
33. α-	Hydroxybutyrate	<dl< td=""><td>-</td><td></td><td></td><td></td><td>59</td><td></td><td><= 0.9</td></dl<>	-				59		<= 0.9			
34. Py	yroglutamate	32	⊢•						28 - 88			
35. Si	ulfate	1,183	-	958	+			347	690 - 2,988			
	Oxidative Damage and Antioxidant Markers (Vitamin C and Other Antioxidante)											
28.	. p-Hydroxyphenyllactate	0.71 H	F				5.3	+	<= 0.66			
	. 8-Hydroxy-2-deoxyguanosine hits for 8-hydroxy-2-dexoyguanosine are n	4.5 g/mg creatinine)	F		-	→t	◆	-	<= 7.6			



Glutathione response insufficiency confirmatory tests:

1. *LOW AMINO ACID* markers:

- Amino acids, plasma Sulfur-containing amino acids Met, Tau, HCys
- GSH precursor amino acids: Gly, Ser,

2. Markers of **OXIDATIVE STRESS** protection will be **HIGH**

- DNA oxidative damage 8-OHdG High
- Membrane PUFA damage Lipid peroxides High



Hypometabolic Compensatory States (HCS)

Compensatory responses, broadly defined, include hormonal secretions and cytokine responses that act to slow or reverse deviations from median or normal physiologic states. (Garcia-Fontana et al. 2016)



Hypometabolic State Pattern Recognition

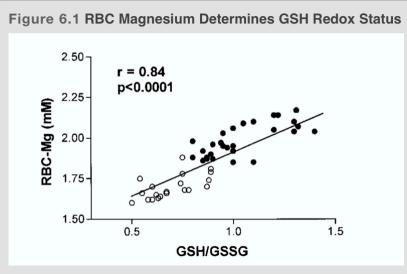
"The Glutathione - Magnesium Dyad"

Because assimilation of magnesium produces immediate stimulation of mitochondrial ROS production, it is resisted by inadequate capacity for glutathione generation to offset the oxidative stress"

Excerpt From: Richard S. Lord. "Paths to Health:

Organic Acids." Arrowhead Bioscience, 2018. Apple Books. https://books.apple.com/us/book/paths-tohealth-organic-acids/id1439492989

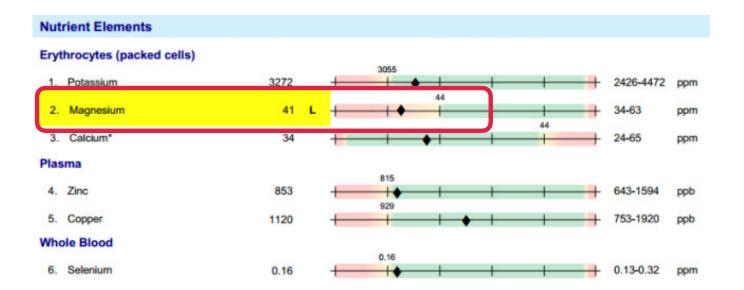




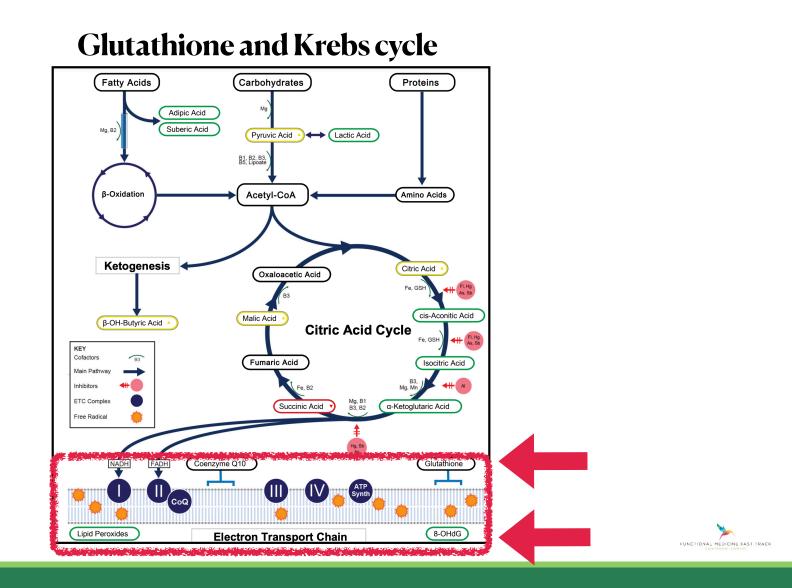
Hypertensive (open circles) and normotensive (closed circles) humans fall on a continuum of GSH redox status that varies directly with RBC magnesium. A common clinical outcome is that oral Mg therapy fails to correct low RBC Mg for individuals with poor GSH status. And, when GSH status is normalized, Mg levels may correct without added oral Mg.



Glutathione corrosion pattern associated with low magnesium





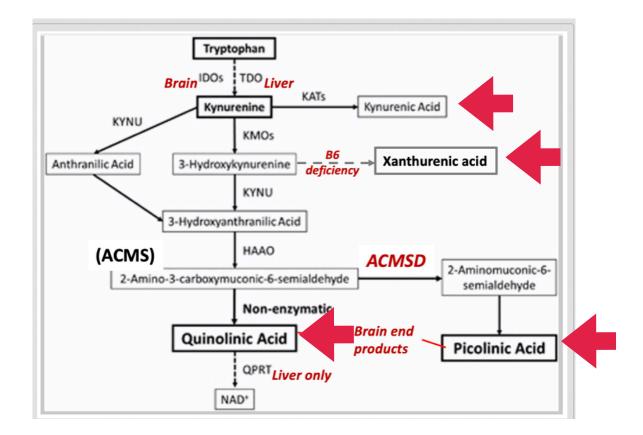


Clinical Application for Glutathione Depletion with Low Magnesium

NAC 600mg-1200mg
 Glutathione
 Methylation support
 Magnesium glycinate
 Amino acid



Pattern Recognition #4: Kynurenate and Xanthurenate





Pattern Recognition #4 : B6 vs INFg

Table 5.2 Interpretations of patterns found for xanthurenate, kynurenate, quinolinate and picolinate in urine.



Pattern	Interpretation
High Xanthurenate	Vitamin B6 deficiency metabolic effects on the hepatic conversion of
AND	Tryptophan to NAD. Finding this this pattern means that Kynurenate
High Kynurenate	elevation is from hepatic, not brain kynurenin pathway.
High Xanthurenate AND Not High Kynurenate	A milder form of B6 deficiency
Not High Xanthurenate	Normal B6 status with brain-specific kynurenin pathway stimulation
AND	due to immune activation (INF-g). Quinolinate agonizes
High Kynurenate &	glutamatergic neurons, producing increased pain and sensitivities to
Quinolinate	light and sound.



Pattern Recognition of B6 Deficient Status: Kynurenate and Xanthurenate

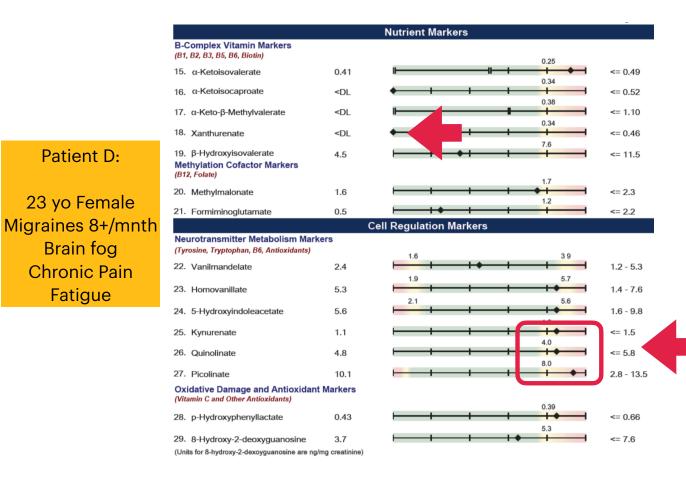
Patient C:

58 yo Female Weight gain Fatigue Lethargy Apathy Anxiety MSQ: 79





Pattern Recognition of Immune Activation: Kynurenate and Xanthurenate





Pattern Recognition #5: BMI / Lipogeneisis

Lipogenesis

Lipogenesis is the metabolic process through which acetyl-CoA is converted to triglyceride for storage in fat. The triglycerides in fat are packaged within cytoplasmic lipid droplets. The process begins with acetyl-CoA, which is an organic compound used to transfer energy from metabolism of carbohydrates, fatty acids, and ethanol.

Figure 6.2 Regulation of Acetyl-CoA formation and mitochondrial activity Pyruvate, CoA Acetyl-CoA, CO₂ PDC Active 1 NADH/NAD ↓ NADH/NAD AcetylCoA/CoA ↓ AcetylCoA/CoA PDC kinase PDC phosphatas Hypoxia (HIF1a) Ø Ca² Mg²⁺ PDC

Hypoxia, coenzyme A, and magnesium determine the moment-bymoment activity of the pyruvate dehydrogenase complex (PDC) signalling long term mitochondrial plasticity.



"CoA-restriction Adaptive Hypometabolic Responses The rate of lipogenesis falls when mitochondrial CoA is diverted to hippurate formation from benzoate"

"the available CoA in a given cell determines rates of metabolic activity. Surges in a given pathway tend to "soak up" available CoA, causing transient slowing of multiple other CoA-dependent processes."

Excerpt From: Richard S. Lord. "Paths to Health: Organic Acids." Arrowhead Bioscience, 2018. Apple Books. https://books.apple.com/us/book/paths-to-health-organic-acids/ id1439492989



"benzoate is the only one identified to date that can deplete available mitochondrial Coenzyme A to such an extent that slowing is demonstrable in the flux of energetic substrates and lipogenesis. Interrupted lipogenesis leads to slower rates of adipose fat deposition and lower BMI. In other words, people with sufficient intake of dietary polyphenols to produce post-prandial surges of benzoate have lower BMI than those with low urinary benzoate and hippurate."

Excerpt From: Richard S. Lord. "Paths to Health: Organic Acids." Arrowhead Bioscience, 2018. Apple Books. https://books.apple.com/us/book/paths-to-health-organicacids/id1439492989



"The principal metabolite pattern in people with higher BMI included low hippurate, citrate and succinate in addition to other compounds that are not organic acids. This is an example of a beneficial hypometabolic state transiently produced during postprandial intervals in healthy individuals"

Excerpt From: Richard S. Lord. "Paths to Health: id1439492989

Organic Acids." Arrowhead Bioscience, 2018. Apple Books. https://books.apple.com/us/book/paths-to-health-organic-acids/



Pattern Recognition High BMI

Energy Production (Citric Acid Cycle) (B Comp., CoQ10, Amino Acids, Mg) 601 7. Citrate 56 - 987 51 18 - 78 8. Cis-Aconitate 28 98 9. Isocitrate 44 39 - 143 19.0 10. α-Ketoglutarate 11.8 <= 35.0 11.6 <= 20.9 11. Succinate 0.59 12. Fumarate <DL <= 1.35 1.4 13. Malate 0.3 <= 3.1 3.6 14. Hydroxymethylglutarate <= 5.1 2.1

Patient A:

24 yo Female Weight gain Chronic Fatigue Brain Fog IBS Acne



Pattern Recognition High BMI

Co	ompour	nds o	of Bacterial or Yeast/Fun	gal Origin
Bacterial - General				0.6
36. Benzoate	<dl< td=""><td></td><td></td><td>548</td></dl<>			548
37. Hippurate	146			+ + +
38. Phenylacetate	<dl< td=""><td></td><td>♦ </td><td>0.11</td></dl<>		♦ 	0.11
39. Phenylpropionate	<dl< td=""><td></td><td>ŀ</td><td></td></dl<>		ŀ	
40. p-Hydroxybenzoate	0.3		↓ ◆ ↓ ↓	1.1
41. p-Hydroxyphenylacetate	8			19
				64
42. Indican	34		i i♥	0.73
43. Tricarballylate	0.67			+ + +
L. acidophilus / General Bacterial				2.0
44. D-Lactate	0.8			
Clostridial Species				
45. 3,4-Dihydroxyphenylpropionate	0.49	н	 	
Yeast / Fungal				36
46. D-Arabinitol	18			
0				



Weight gain Chronic Fatigue Brain Fog IBS Acne

Patient A:



Pattern Recognition: Low BMI and High Hippurate / Benzoate

	Compounds of Bacterial or Yeast/Fungal Origin						
	Bacterial - General 36. Benzoate	98.3	н	0.6			
	37. Hippurate	1,279	н				
				0.11			
Patient D:	38. Phenylacetate	0.11		<= 0.18			
	39. Phenylpropionate	<dl< td=""><td></td><td>1.1 <= 0.06</td></dl<>		1.1 <= 0.06			
42 yo Male	40. p-Hydroxybenzoate	2.4	н	1 1 1 1 1 1 1 1 1 1			
Ex pro cyclist	41. p-Hydroxyphenylacetate	6		I ← I I I − I = 34			
BMI 21	42. Indican	50		□			
Seasonal allergies	43. Tricarballylate	0.64		<pre></pre>			
	L. acidophilus / General Bacterial			2.0			
	44. D-Lactate	1.0		├ 			
	Clostridial Species						
	45. 3,4-Dihydroxyphenylpropionate	<dl< td=""><td></td><td>I−−−− <= 0.05</td></dl<>		I−−−− <= 0.05			
	Yeast / Fungal			36			
	46. D-Arabinitol	NR		<mark>├── ┼── ┼── ┼</mark> ── <=			
	Creatinine = 199 mg/dL						



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Pattern Recognition: Low BMI and High Hippurate / Benzoate

	Compounds of Bacterial or Yeast/Fungal Origin				
	Bacterial - General		0.6		
	36. Benzoate	<dl< td=""><td>548</td></dl<>	548		
	37. Hippurate	413			
	38. Phenylacetate	0.08	i i i i i i <= 0.18		
Patient E: 63 yo Male Age group athlete BMI 22	39. Phenylpropionate	<dl< td=""><td>1.1 <= 0.06</td></dl<>	1.1 <= 0.06		
	40. p-Hydroxybenzoate	0.6	19 <= 1.8		
	41. p-Hydroxyphenylacetate	10	→ 		
	42. Indican	48	0.73		
	43. Tricarballylate	0.95	← + + + + + ← <= 1.41		
	L. acidophilus / General Bacterial		2.0		
	44. D-Lactate	3.1	I I I I I I I I I I I I I I I I I I I 		
	Clostridial Species				
	45. 3,4-Dihydroxyphenylpropionate	<dl< td=""><td>I→ <= 0.05</td></dl<>	I → <= 0.05		
	Yeast / Fungal		36		
	46. D-Arabinitol	15	+ + + + + + + + + + + + + + + + + + + 		

Creatinine = 118 mg/dl



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"That subject was thoroughly reviewed by Jeremy Nicholson and coworkers (Lees et al. 2013) prior to their landmark metabolomic study revealing that human BMI is inversely related to urinary hippurate."



- 1. Low patterns amino acids
- 2. High patterns cofactors, inhibitors, genetics
- 3. Glutathione Status patterns NAC, GSH, amino acids, magnesium
- 4. Kynunerine Patterns B6 or immune support
- 5. Lipogenesis patterns microbiome and polyphenols



The End - Thank you

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