

# Hompes Method

## Lesson 29

### - Organic Acids – Part Five

# Detoxification and Organic Acids

- Organic acids can provide an excellent indication of whether your client or patient's detox system is overwhelmed. It provides indicators of acute toxic exposure, nutritional insufficiency, amino acid metabolism and liver/kidney overload. It also provides markers for oxidative stress, inflammation and gut issues. When these are present, it's common to see challenges and overload of the detox pathways.

# Detoxification and Organic Acids

OXIDATIVE DAMAGE AND ANTIOXIDANT MARKERS			
p-Hydroxyphenyllactate	H	Vitamin C to bowel tolerance*	Prooxidant and carcinogen
8-Hydroxy-2'-deoxyguanosine	H	Antioxidants (Vitamins C, E, lipoic acid)	DNA oxidation product
DETOXIFICATION INDICATORS			
2-Methylhippurate	H	Avoidance of xylene; glycine, 2–5 gm/d; B <sub>5</sub> 100 mg TID	Hepatic conjugation
Orotate	H	Arginine, 1–3 gm/day; a-KG, 300 mg TID Aspartic Acid, 500 mg BID; magnesium, 300 mg	Ammonia clearance, Pyrimidine synthesis,
Glucarate	H	Glycine, GSH, NAC, 500–5000 mg/day	Detox. liver enzyme induction
α-Hydroxybutyrate	H	NAC, 1000 mg, glutathione, 300 mg Taurine, 500 mg BID	Hepatic GSH synthesis
Pyroglutamate	H		Renal amino acid recovery
Sulfate	L		Detox & anti-oxidant functions

Metamatrix Interpretive Guide

# Detoxification and Organic Acids

DYSBIOSIS MARKERS (PRODUCTS OF ABNORMAL GUT MICROFLORA)			
Benzoate	H	Glycine, 2–5 gm/d; vitamin B <sub>5</sub> , 100 mg TID	Hepatic Phase II glycine conjugation
Hippurate	H	<p>These compounds may reflect intestinal overgrowth, usually accompanied by microbial hyperpermeability. Take appropriate steps to ensure favorable gut microflora population.</p> <p>Glutamine, 10–20 gm daily, digestive aids (betaine, enzymes, bile) and free-form amino acids help to normalize gut permeability.</p>	Intestinal bacterial overgrowth
Phenylacetate	H		
Phenylpropionate	H		
p-Hydroxybenzoate	H		
p-Hydroxyphenylacetate	H		<p>General bacterial or <i>L. acidophilus</i> overgrowth</p> <p>Clostridial overgrowth</p> <p>Intestinal yeast overgrowth</p>
Tricarballylate	H		
D-Lactate			
3,4-Dihydroxyphenylpropionate	H		
D-Arabinitol	H		

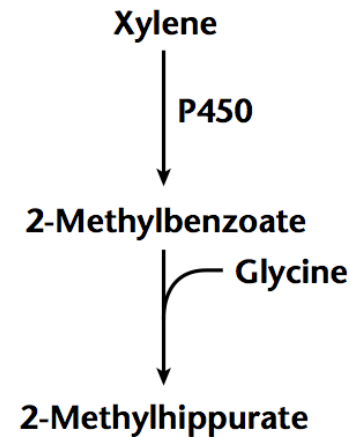
Metamatrix Interpretive Guide

# Detox Markers - 2-Methylhippurate

- Urinary excretion of 2-methylhippurate is a sensitive and specific marker for xylene exposure which increases oxidative stress. Xylene is a common solvent present in household and workplace air, exhaust fumes, etc. It's pretty ubiquitous – new paint, spray paint, new carpet, new cars, dry cleaning fluid, cleaning solvents, paint thinners, building products, fuel and exhaust fumes, etc.

# Detox Markers - 2-Methylhippurate

- Xylene is oxidized in a Phase 1 detoxification reaction to 2-methylbenzoate; then in Phase II (glycine conjugation) it becomes 2-methylhippurate.



**FIGURE 8 – METABOLISM OF XYLENE**

Xylene, a toxic environmental compound, is oxidized to 2-methylbenzoate by P450 enzymes and then conjugated with glycine to form 2-methylhippurate. High levels can indicate xylene exposure.

# Detox Markers - 2-Methylhippurate

- If 2-methylhippurate comes back elevated, you know a person has ongoing exposure to (at least) xylene and probably other chemicals. It may also indicate insufficient glycine levels for detoxifying xylene, etc.

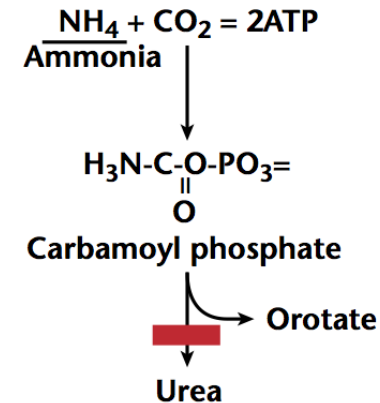
# Detox Markers - Orotate

- Ammonia is a by-product of normal metabolism. It is detoxified through the urea cycle, which takes place in both the liver and kidneys. Excess ammonia is very toxic and can cause significant symptoms. Elevated urine **orotate** indicates ammonia toxicity.



# Detox Markers - Orotate

- Orotate levels increase in the urine when urea cycle capacity is exceeded and is a very sensitive marker to anything that increases ammonia in liver:



**FIGURE 9 – OROTATE AND AMMONIA**

When ammonia, a metabolic by-product of protein, is unable to breakdown to urea to be excreted, it is converted to orotate and excreted. Elevated levels of orotate may be due to elevated ammonia, or a need for magnesium.

# Detox Markers - Orotate

- Possible causes of high orotate:
  - High meat intake
  - Dysbiosis
  - Arginine deficiency (arginine is the key nutrient for detoxification)
  - Possible need for magnesium
  - Long term oral glutamine supplementation above 10 gm/day (rare)

# Detox Markers - Glucarate

- **Glucarate** is an indicator of overall hepatic (liver) detoxification demand – phase I and glucoronidation. High urinary glucarate suggests *above normal exposure* to pesticides, herbicides, fungicides, petrochemicals, alcohol, pharmaceutical compounds, or toxins produced in the gastrointestinal tract.

# Detox Markers - Glucarate

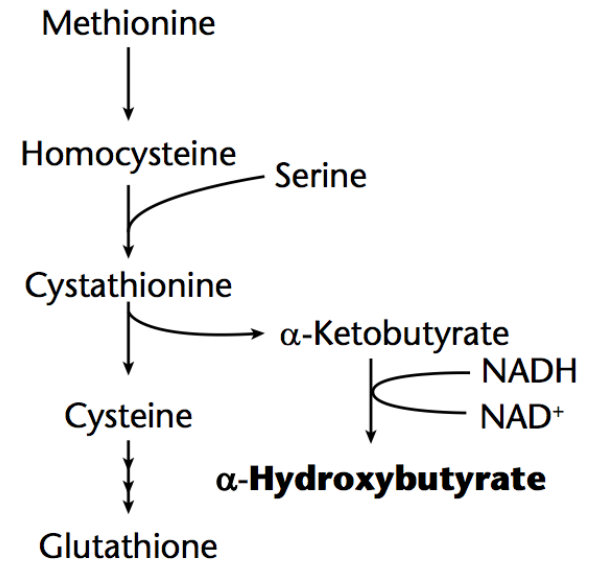
- Elevated glucarate levels can indicate intestinal dysbiosis and exposure to:
  - Fungal toxins
  - Alcohol
  - Food additives
  - Drugs
  - Pesticides, herbicides, fungicides
  - Petrochemicals
  - PAH
  - Nitrosamines

# Detox Markers- $\alpha$ -Hydroxybutyrate (AHB)

- **AHB** is a marker of hepatic glutathione synthesis. GSH is an important antioxidant that helps protect against reactive oxygen species such as free radicals. GSH is constantly used up in the removal of toxic molecules and prevention of oxidative damage. AHB is a by-product from the process in which the body forms more glutathione.

# Detox Markers- $\alpha$ -Hydroxybutyrate (AHB)

- When that process is running at high rates,  $\alpha$ -hydroxybutyrate excretion is increased. If  $\alpha$ -hydroxybutyrate is elevated then glutathione support may be recommended.



**FIGURE 10 – ALPHA-HYDROXYBUTYRATE FORMATION FROM GLUTATHIONE BIOSYNTHESIS**

Alpha-hydroxybutyrate is a by-product of glutathione production. Levels of alpha-hydroxybutyrate in the urine may reflect levels of glutathione production.

# Detox Markers- $\alpha$ -Hydroxybutyrate ( $\alpha$ -HBD)

*“The activity of  $\alpha$ -HBD on the second day after a myocardial infarction is a marker for estimates of infarct size and a measure of reperfusion effectiveness. The intense energy demand of cardiac muscle is likely the reason for such high concentrations of  $\alpha$ -HBD in that tissue, because  $\alpha$ -HB strongly inhibits mitochondrial energy metabolism as measured by  $CO_2$  production.”*

<http://www.metamatrix.com/files/learning-center/leifm/book-Laboratory-Evaluations-in-Molecular-Medicine.pdf>

# Detox Markers- $\alpha$ -Hydroxybutyrate (AHB)

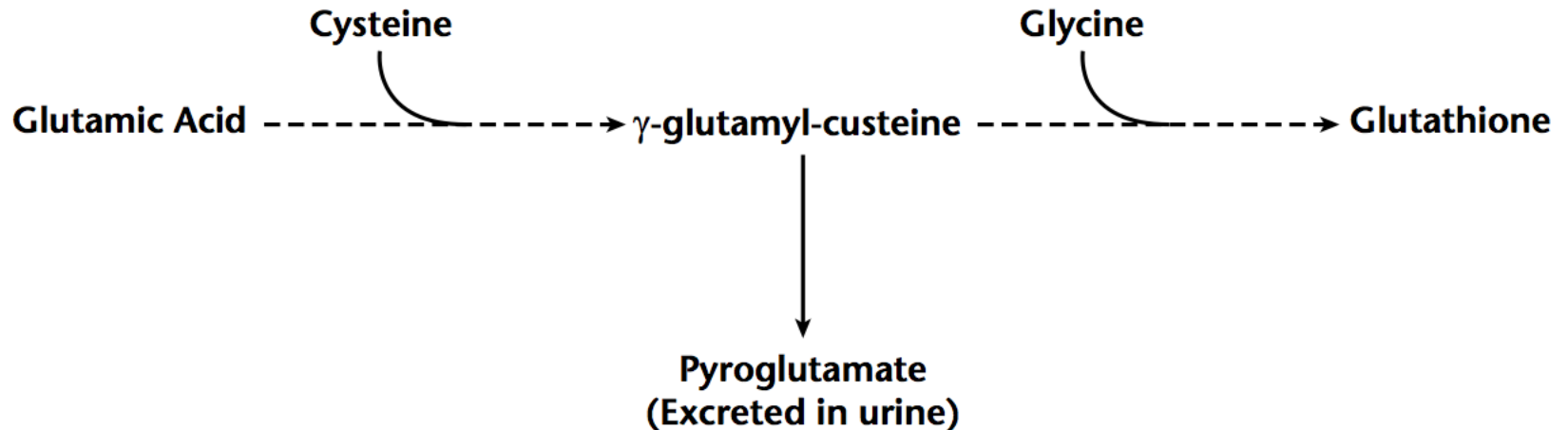
*“Smoking, poor diet, and lack of exercise significantly inhibit the activity of  $\alpha$ -HBD, suggesting that urinary elevation of  $\alpha$ -hydroxy-butyrate may be related to these factors. High  $\alpha$ -hydroxybutyrate is also found during phases of increased lymphocyte destruction in infectious diseases such as measles.”*

<http://www.metamatrix.com/files/learning-center/leifm/book-Laboratory-Evaluations-in-Molecular-Medicine.pdf>



# Detox Markers - Pyroglutamate

Pyroglutamate elevates in urine when glutathione is being used up rapidly or when there is not enough methionine, glycine or cysteine for glutathione production.



# Detox Markers - Pyroglutamate

- Glutathione is constantly used up in the removal of toxic molecules and prevention of oxidative damage. AHB is a by-product from the process in which the body forms more glutathione. When that process is running at high rates, AHB excretion is increased. Elevated levels of the marker pyroglutamate also reveal that glutathione is being lost at a high rate.

# Detox Markers - Sulfate

- Elevated **sulfate** can indicate increased Phase II detoxification or inorganic sulfate intake. Low urinary sulfate is an indication that total body glutathione is low due to chronic demand and sulfur-containing amino acids are needed.

# Detox Markers - Sulfate

- Since both pyroglutamate and sulfate are markers of sulfur compound depletion, explanation of the interpretation of various combinations of abnormalities is needed. Severe depletion of organic sulfur sources will cause simultaneous **high pyroglutamate and low sulfate excretion.**

# Detox Markers - Sulfate

- High pyroglutamate with normal sulfate indicates inadequate organic sulfur sources for production of cysteine required for glutathione synthesis. Only organic sulfur in the form of compounds such as N-acetylcysteine or methionine will restore normal glutathione levels.

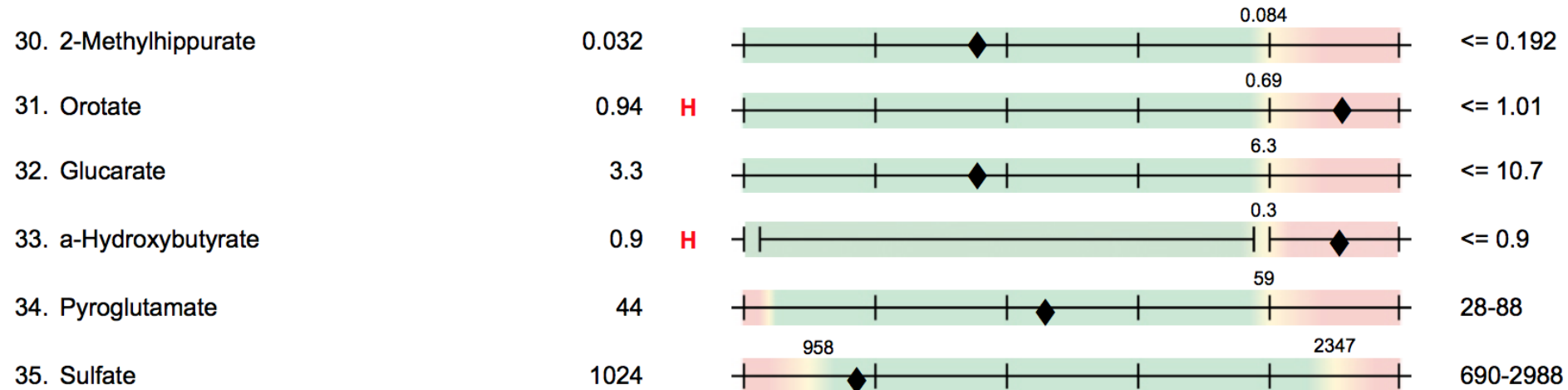
# Detox Markers - Sulfate

- Normal pyroglutamate with low sulfate levels can occur in individuals with impaired sulfate activation. In these cases, rapid replenishment of hepatic sulfate may be accomplished with either sulfur donors like N-acetylcysteine or inorganic sulfate such as sodium sulfate.

# Detoxification Markers - Sample Report 1

## Detoxification Indicators

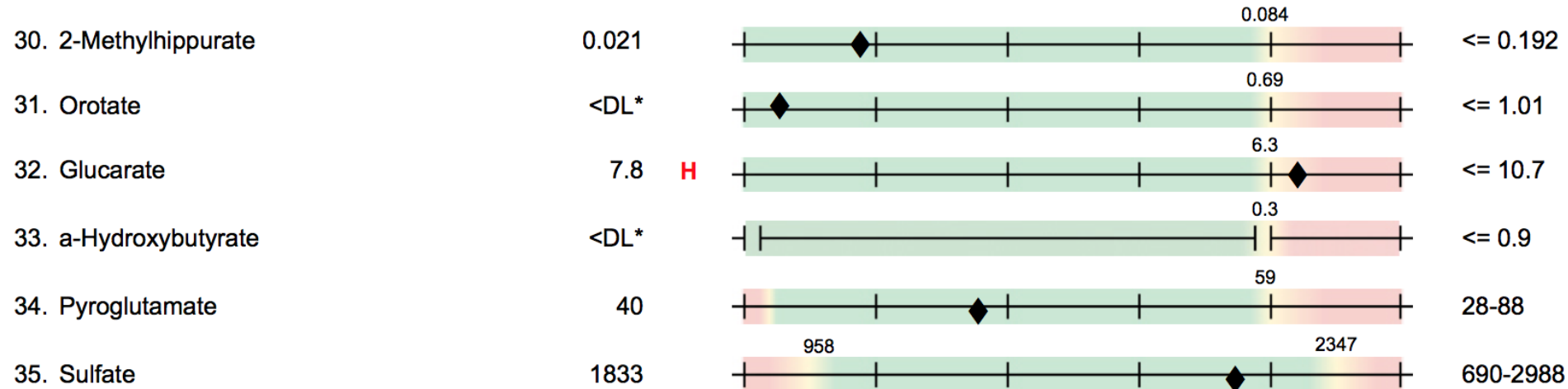
*(Arg, NAC, Met, Mg, antioxidants)*



# Detoxification Markers - Sample Report 2

## Detoxification Indicators

(Arg, NAC, Met, Mg, antioxidants)

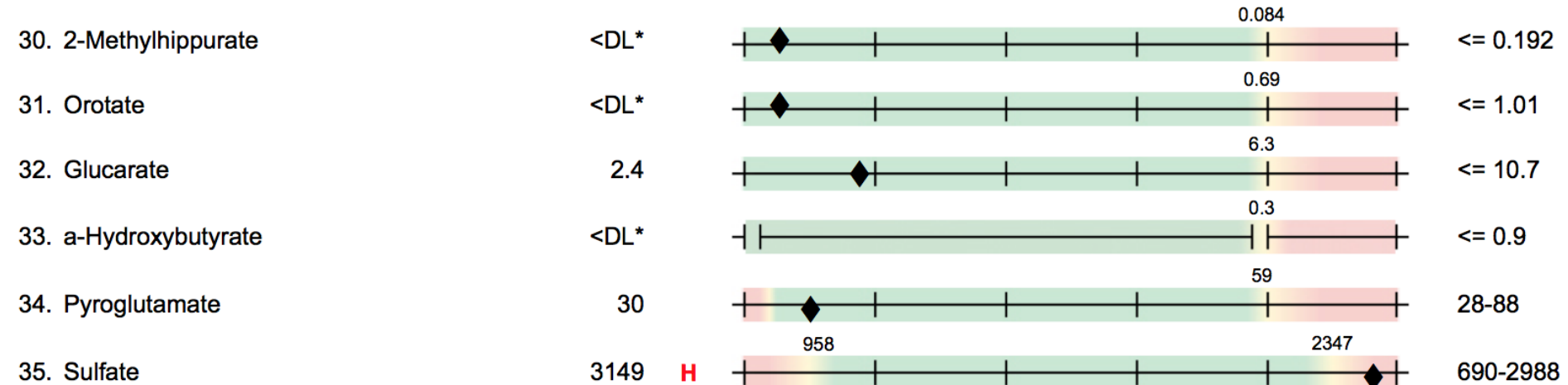




# Detoxification Markers - Sample Report 3

## Detoxification Indicators

(Arg, NAC, Met, Mg, antioxidants)



# Detox Markers - Methylation

- In simple terms, **methylation** is a process in which certain chemicals called 'methyl groups' are added to various constituents of proteins, DNA and other molecules. These are needed to keep them in good 'working' condition.

# Detox Markers - Methylation

- Methylation is a primary method of removing toxins in the phase 2 liver detoxification. With adequate methylation, we can detoxify with greater ease but without it, the body's ability to detoxify is undermined.

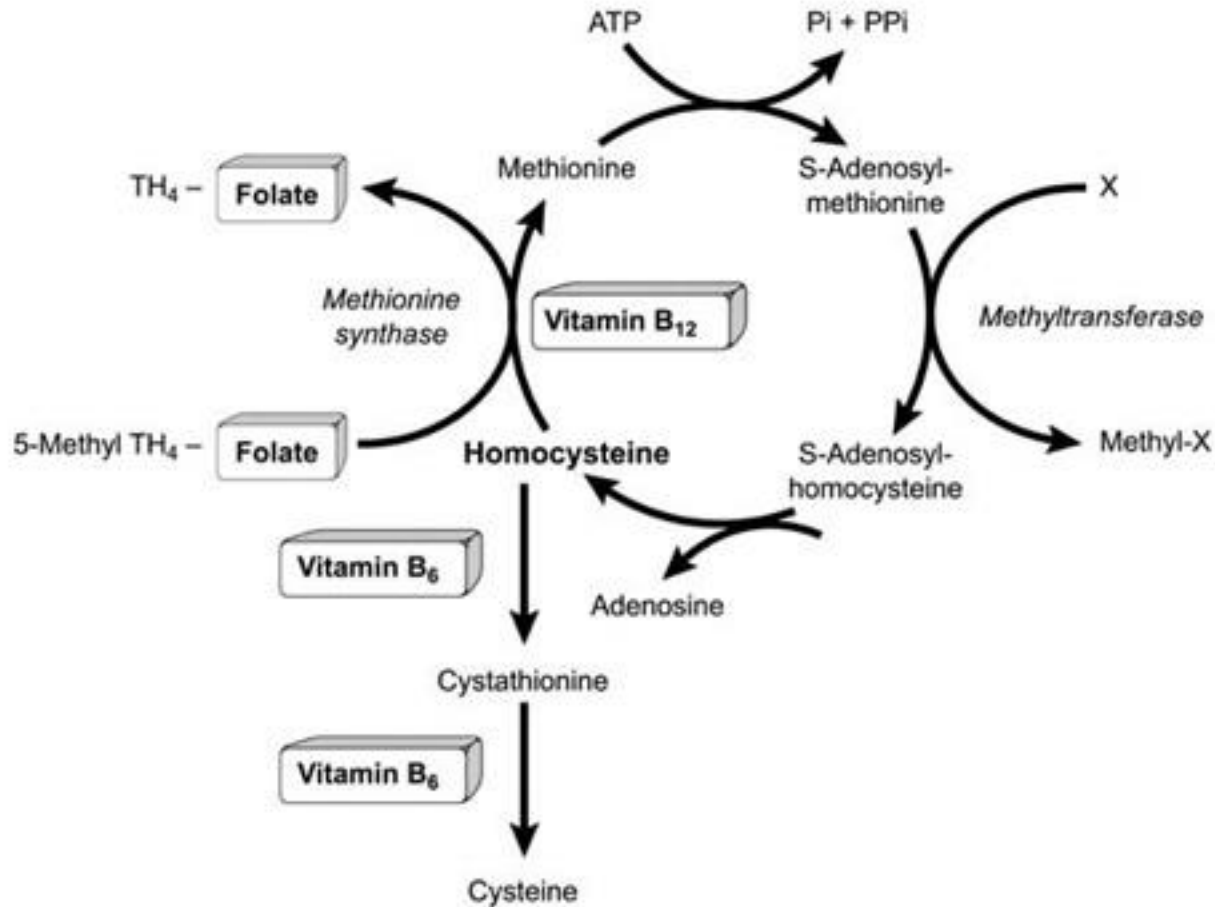
# Detox Markers - Methylation

- An important methylation process is when it is applied to homocysteine, which is what remains when the amino acid methionine is used to methylate protein and DNA. Homocysteine needs to be methylated to convert it back to methionine. If this process does not happen, it's a big problem. As with everything, methylation must be balanced. Too much can be as bad as too little.

# Detox Markers - Methylation

- There are four cornerstones to the methylation cycle and on each cornerstone sit four molecules:
  - Homocysteine
  - Methionine
  - S-adenosylmethionine (SAMe)
  - S-adenosylhomocysteine

# Detox Markers - Methylation



<http://lpi.oregonstate.edu/infocenter/vitamins/fa/fadiag2.html>

# Detox Markers - Methylation

- There are three groups of compounds that are helpful in methylation with varying levels of efficacy. They are:
  - B Vitamins, B<sub>6</sub>, B<sub>12</sub> and folic acid
  - Tri-methyl-glycine TMG
  - S-Ado-Me.

# Detox Markers - Methylation

- Poor methylation, leading to increased levels of homocysteine is implicated in:
  - Heart disease and stroke
  - Higher levels of oxidized LDL cholesterol
  - Dementia and Alzheimer's
  - Liver Disease
  - Depression
  - Aging in general



# Detox Markers - Methylation

- There are two methylation cofactor markers in organic acids testing – methylmalonate ( $B_{12}$ ) and formiminoglutamate (FIGLU – folic acid). When elevated, these markers can indicate insufficiencies in methylation pathways, which can have a dramatic impact on detoxification, amongst other body functions.

# Detox Markers - Methylation

Scenario	FIGLU	Methylmalonate	Xanthurenate	Homocysteine	Vitamin Deficiency Indication
1	↑	N	N	↑, N	Folate - Not methylfolate
2	N	↑	N	↑, N	B12
3	N	N	↑	↑, N	B6
4	N	N	N	↑	Methylfolate or Methyl donors (betaine, etc.)
5	↑	N	N	↑	Folate (and Methyl donors) or Methylfolate
6	N	↑	N	↑	B12
7	↑	↑	↑	↑	Folate, B12, B6, and Methyl donors

# Methylation – Sample Report 1

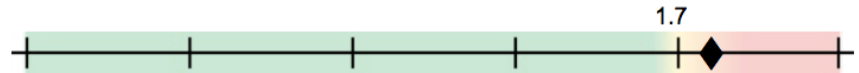
## Methylation Cofactor Markers

*(B12, Folate)*

20. Methylmalonate

2.0

H



$\leq 2.3$

21. Formiminoglutamate

0.4



$\leq 2.2$

# Methylation – Sample Report 2

## Methylation Cofactor Markers

*(B12, Folate)*

20. Methylmalonate

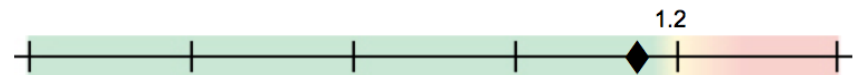
1.4



$\leq 2.3$

21. Formiminoglutamate

1.1



$\leq 2.2$

# Methylation – Sample Report 3

## Methylation Cofactor Markers

*(B12, Folate)*

20. Methylmalonate

1.3



$\leq 2.3$

21. Formiminoglutamate

2.3

H



$\leq 2.2$

# Organic Acids - Dysbiosis

- While stool testing has been the long-established method for identifying dysbiosis, "there is increasing support that the fecal microbiota does not accurately reflect the colonic condition." Stool testing does not reveal the situation in the **small intestine**, however, and there is increasing evidence that the fecal microbiota does not necessarily mirror the colonic situation.

# Organic Acids - Dysbiosis

- The major limitations of stool testing are its high degree of false negatives and the greater potential of missing a significant dysbiotic clinical situation. A client with negative stool specimen can have dysbiosis markers in urine, revealing metabolic by-products of pathogenic microbiota growing in the small intestine.

# Organic Acids - Dysbiosis

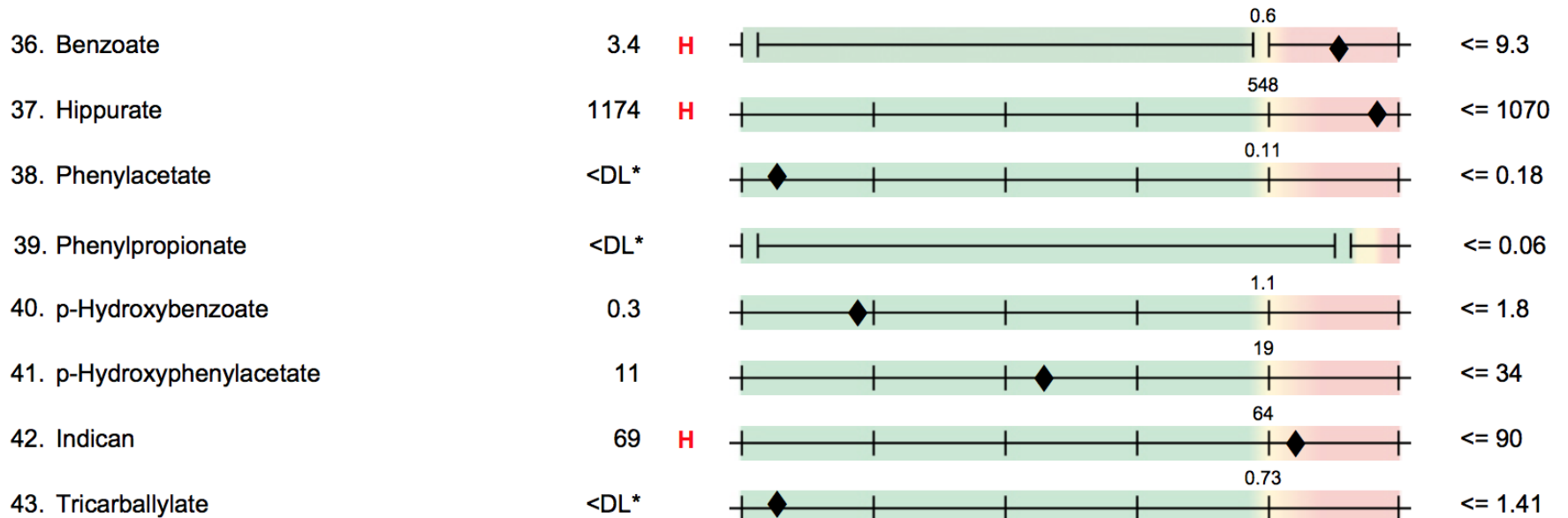
- Microflora create distinct toxins and metabolic products that can be measured in the urine. The compounds in this category normally appear in urine only at low levels. The compounds are absorbed into the blood from the intestines and eventually appear in the urine. Microbial overgrowth can lead to a wide variety of symptoms due to reactions to the toxic products produced by bacteria, parasites, or fungi.



# Sample Report

## Compounds of Bacterial or Yeast/Fungal Origin

### Bacterial - general



### L. acidophilus / general bacterial



### Clostridial species



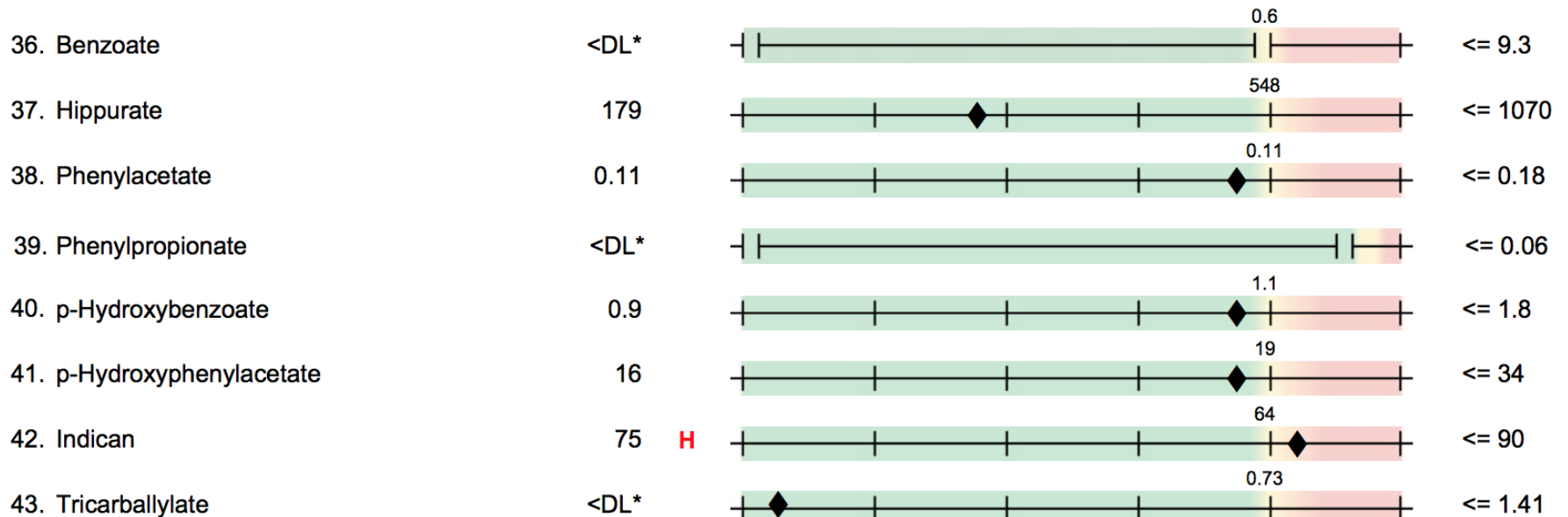
### Yeast / Fungal



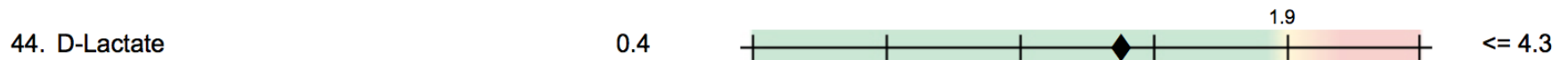
# Sample Report

## Compounds of Bacterial or Yeast/Fungal Origin

### Bacterial - general



### L. acidophilus / general bacterial



### Clostridial species



### Yeast / Fungal



# High Benzoate

- Benzoate is produced by intestinal bacteria.
- Under ideal circumstances, benzoate is metabolized in Phase II glycine conjugation into hippurate.
- Enzymes from certain gut bacteria may reverse this process, producing high benzoate in the urine.
- Bacterial deamination of the amino acid phenylalanine also produces benzoate. This can increase due to malabsorption of phenylalanine as a result of low stomach acid.
- Inadequate conversion to hippurate in the liver can also lead to high benzoate - glycine and B<sub>5</sub> are the rate-limiting factors.
- Benzoate can also accumulate in the urine because of exposure to foods that contain benzoate as a preservative, such as pickles and lunchmeats.

# High Hippurate

- Hippurate is produced from the phase II conjugation of benzoate.
- Gut bacteria can convert certain food compounds (phenols) into hippurate.
- High hippurate may be a marker for bacterial overgrowth.
- It may also indicate poor phenylalanine absorption due to low stomach acid.

# High Phenylacetate (PAA)

- PAA is produced from bacterial degradation of unabsorbed phenylalanine. It can indicate phenylalanine malabsorption (low HCl), and possibly Clostridial overgrowth.

# High p-Hydroxyphenylacetate (HPA)

- Malabsorption of tyrosine and/or phenylalanine due to low stomach acid.
- May indicate dysbiosis (*Proteus vulgaris*, *C. difficile*, *Giardia*, anaerobic bacteria)
- May indicate lactose intolerance.

# High Indican

- The level of urinary indican is an index of the efficiency of protein digestion. High levels can indicate bacterial overgrowth in the small intestine, which act on tryptophan and produce high levels of indican. High indican levels strong indicator of poor protein digestion.

# High Tricarballyate

- Produced by strains of bacteria that may proliferate after antibiotics and acid-blocking drugs are taken. It binds tightly to minerals such as magnesium, calcium and zinc, blocking their absorption, making mineral levels low when this compound is high. I've also seen this marker elevated when folk have yeast and fungal overgrowth.



# High D-Lactate

- *Lactobacillus*, or other D-lactate producing bacterial strains can overgrow and produce toxic amounts of D-lactate. This tends to happen if carbohydrate maldigestion and malabsorption are present. D-lactate is a neurotoxin in large quantities, so dealing with this is a priority.

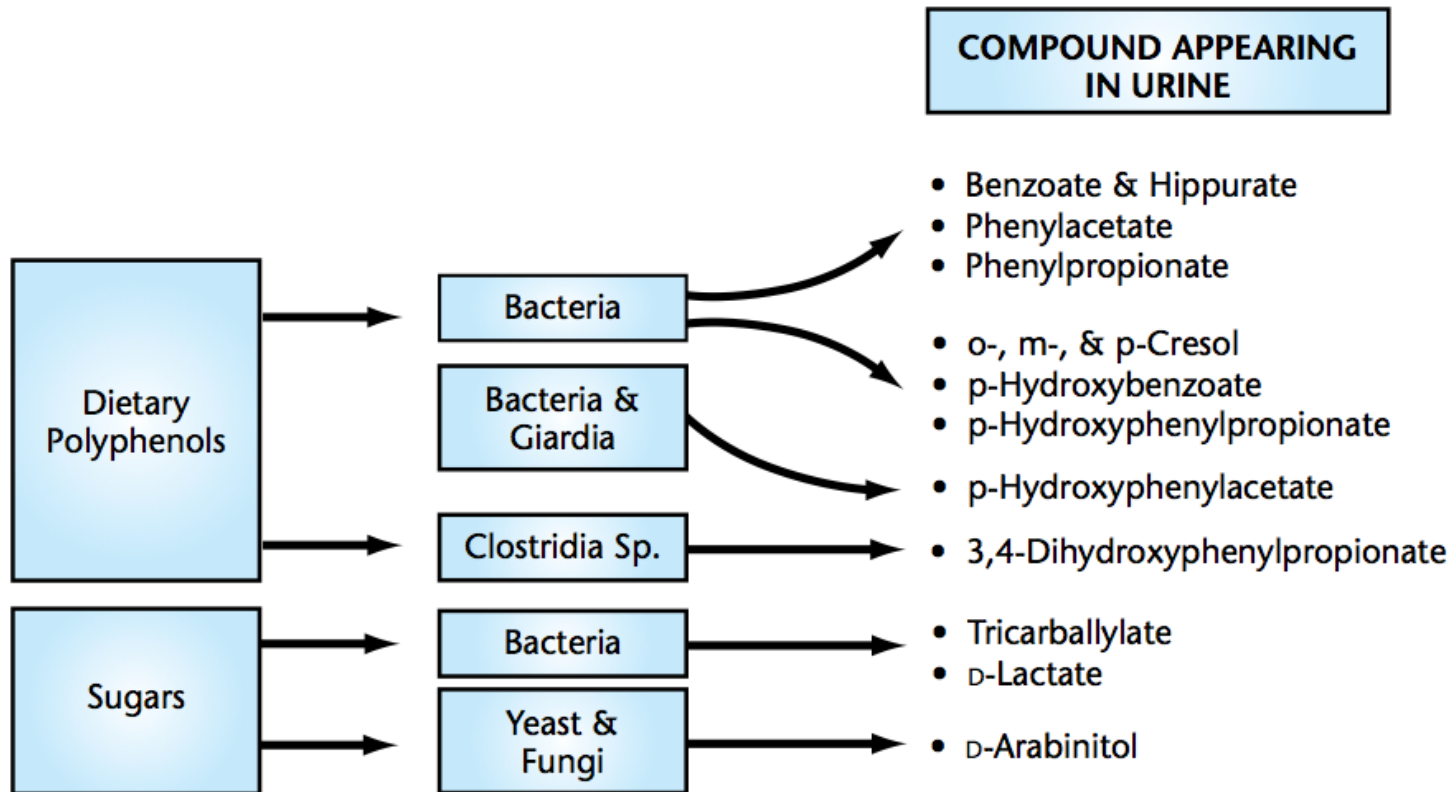
# High 3,4-Dihydroxyphenylacetate

- This compound is produced in larger than normal quantities when Clostridial species overgrow (not necessarily *C. difficile*). As such as it's a marker of gastrointestinal dysbiosis that may not show up in stool testing. High levels may also indicate *Pseudomonas* overgrowth.

# High D-Arabinitol

- D-Arabinitol is a *Candida* by-product. When elevated in the urine it indicates small intestinal *Candida* overgrowth, which may *not* be detected in stool testing.

# Organix – Summary of Abnormal Findings



# Organix – Summary of Abnormal Findings

DYSBIOSIS MARKERS (PRODUCTS OF ABNORMAL GUT MICROFLORA)			
Benzoate	H	Glycine, 2–5 gm/d; vitamin B <sub>5</sub> , 100 mg TID	Hepatic Phase II glycine conjugation
Hippurate	H	<p>These compounds may reflect intestinal overgrowth, usually accompanied by microbial hyperpermeability. Take appropriate steps to ensure favorable gut microflora population.</p> <p>Glutamine, 10–20 gm daily, digestive aids (betaine, enzymes, bile) and free-form amino acids help to normalize gut permeability.</p>	Intestinal bacterial overgrowth
Phenylacetate	H		
Phenylpropionate	H		
p-Hydroxybenzoate	H		
p-Hydroxyphenylacetate	H		General bacterial or <i>L. acidophilus</i> overgrowth
Tricarballoylate	H		Clostridial overgrowth
D-Lactate			Intestinal yeast overgrowth
3,4-Dihydroxyphenylpropionate	H		
D-Arabinitol	H		

# Abnormal Findings - Summary Page



## 0091 Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

### Summary of Abnormal Findings

	<u>Findings</u>	<u>Intervention Options</u>	<u>Common Metabolic Association</u>	
<b>Fatty Acid Metabolism</b>				
	No Abnormality Found			
<b>Carbohydrate Metabolism</b>				
	No Abnormality Found			
<b>Energy Production Markers</b>				
	Citrate	High	Arginine	Renal ammonia loading
<b>B-Complex Vitamin Markers</b>				
	No Abnormality Found			
<b>Methylation Cofactor Markers</b>				
	Methylmalonate	High	B12	Adenosylcobalamin insufficiency
<b>Neurotransmitter Metabolism Markers</b>				
	5-Hydroxyindoleacetate	High	---	Serotonin turnover stimulation
	Kynurenate	High	B6	Receptor antagonist
	Quinolate	High	Magnesium, Immune support	Receptor agonist
<b>Oxidative Damage and Antioxidant Markers</b>				
	p-Hydroxyphenyllactate	High	Vitamin C, Vitamin E	Increased cell turn over
	8-Hydroxy-2-deoxyguanosine	High	Vitamin C, Vitamin E	DNA oxidation product
<b>Detoxification Indicators</b>				
	Orotate	High	Arginine, Magnesium	Urea cycle overload (ammonia toxicity)
	a-Hydroxybutyrate	High	N-acetylcysteine, other sulfur containing amino acids	Glutathione demand
<b>Bacterial - General</b>				
	Indican	High	Probiotics	Intestinal Bacterial Overgrowth

# Abnormal Findings - Summary Page

- There are limitations to the summary page:
  - It doesn't give you the overall picture
  - It doesn't show you all the patterns
  - It doesn't show you borderline markers

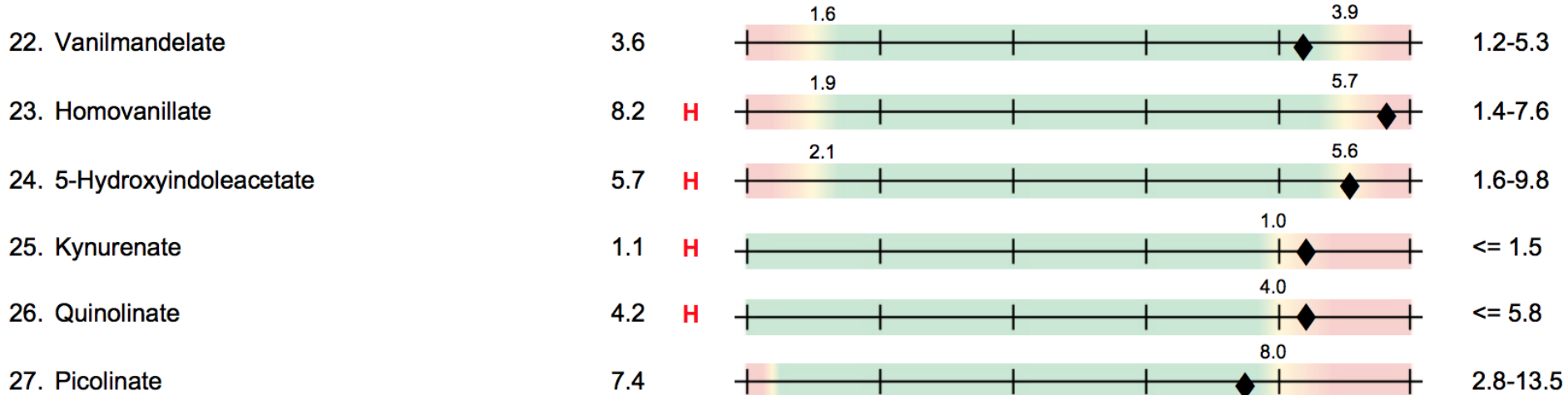
# Abnormal Findings - Summary Page

## Neurotransmitter Metabolism Markers

Homovanillate	Very High	Evaluate stress issues	Dopamine turnover stimulation
5-Hydroxyindoleacetate	High	---	Serotonin turnover stimulation
Kynurenate	High	B6	Receptor antagonist
Quinolinate	High	Magnesium, Immune support	Receptor agonist

## Neurotransmitter Metabolism Markers

*(Tyrosine, Tryptophan, B6, antioxidants)*





# Abnormal Findings - Summary Page

- In my humble opinion, it's very, very important to go through the full test and make additional notes to the obvious stuff you see on the cover sheet. On another day and in another urine sample, markers may well appear on that cover sheet!

# Supplement Recommendations

- At the back of an Organix profile (or Genova and US Biotek) you're presented with a series of supplement recommendations, along with basic lifestyle and nutrition recommendations where applicable (e.g. "reduce stress").

# Supplement Recommendations

*“With knowledge of a patient's full medical history and concerns, the Organix Comprehensive Profile laboratory results may be used to help healthcare professionals create an individually optimized nutritional support program. Based strictly on the results from this test, the summary table below shows estimates of nutrient doses that may help to normalize nutrient-dependent metabolic functions.”*

# Supplement Recommendations

Nutrient	Daily Amounts	
	Base	Units Added
Vitamin A*	2500 IU	
B-Carotene*	5500 IU	
Vitamin C	250 mg	2000 mg
Vitamin D*	400 IU	
Vitamin E	100 IU	400 IU
Vitamin K*	100 mcg	
Thiamin (B1)	5 mg	
Riboflavin (B2)	5 mg	10 mg
Niacin (B3)	25 mg	
Pyridoxine (B6)	15 mg	60 mg
Folic Acid (or 5-Methyl-THF)	400 mcg	
Vitamin B12	50 mcg	
Biotin	100 mcg	
Pantothenic Acid (B5)	25 mg	
Calcium citrate	500 mg	
Iodine*	75 mcg	
Magnesium	250 mg	200 mg
Zinc*	15 mg	
Selenium	100 mcg	200 mcg
Copper	1 mg	
Manganese*	5 mg	
Chromium	200 mcg	
Molybdenum*	25 mcg	
Boron*	1 mg	

\* Nutrients with an asterisk are not modified based on the Organix test results.

MM03

# Supplement Recommendations

## Other Items Indicated for individual supplementation

Various conditionally essential nutrients and other potentially beneficial interventions appear in this section only if relevant abnormalities are present. These ingredients are not included in the customized vitamin formula on the previous page.

<b>Nutrient</b>	<b>Amount</b>
Potential to benefit from probiotics	Low
Coenzyme Q10	60 mg
Glycine	3000 mg
Need for other antioxidants	Moderate
S. Boulardii	As needed

Note: this is not the supplement recommendation list for the example Summary of Abnormal Findings provided earlier.

# Supplement Recommendations

- I highly recommend you get hold of a copy (by hook or by crook!) of the Metamatrix Handbook as it contains a wealth of information to help you with Organix Interpretation (e-book version is available at iTunes)



<https://itunes.apple.com/us/book/metamatrix-handbook/id534350729?mt=11>

# Organic Acids - Summary

- I hope in these five lessons I've been able to demonstrate how powerful the organic acids tests can be. We've covered the Metametrix "Organix" test, but remember Genova and US Biotek also run organic acids.
- We're looking at another UK provider right now.

# Organic Acids - Summary

- I also hope I've shown you that organic acids testing tells you much more about a client or patient's metabolic state than simply vitamin and other nutrient deficiencies.



# Organic Acids - Summary

- Fat and CHO metabolism, energy production, B vitamin status, neurotransmitter metabolism, detoxification and gut function are all part of a bigger picture – STRESS – so I recommend you don't just take your clients' organic acids results on face value.

# Thank You!

- Thanks a million for tuning in. I appreciate your time and I appreciate you choosing me as one of your teachers. In the next lesson we'll move onto this whole concept of “stress” and then onto the final module of the program – **hormones** – which I know a lot of you are looking forward to!