MethylGenetic Nutrition Reference Guide

The "Good Guys" & the "Bad Guys"

The Good Guys (Boost)

- Nutrient filled food-based nutrition
- Superoxide Dismutase
- Catalase
- Glutathione
- SAMe
- NADH
- Nitric oxide
- BH4
- Folate
- Choline
- Nrf2
- Balanced Neurotransmitters

The Bad Guys (Reduce)

- Excess glutamate
- Ammonia
- Sulfites
- Sulfates
- Superoxide Free radical
- NOS Uncoupling
- Peroxynitrite
- Homocysteine
- Zonulin
- Histamine

Urine Organic Acids

Reference Guide

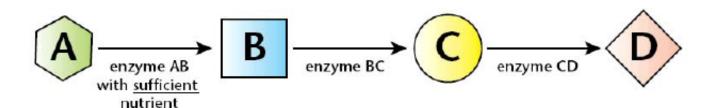
ORGANIC ACIDS BASICS

- The organic acid profile is like an emission test performed on your car in which the exhaust is examined to see how well your engine is burning fuel. Similarly, certain compounds called organic acids in your urine reveal how well your body is performing its metabolic activities.
- Many organic acids result from the metabolic pathways or chemical reactions your body uses to transform food into energy, and to repair, grow and maintain body tissues.

Organic Acids Basics

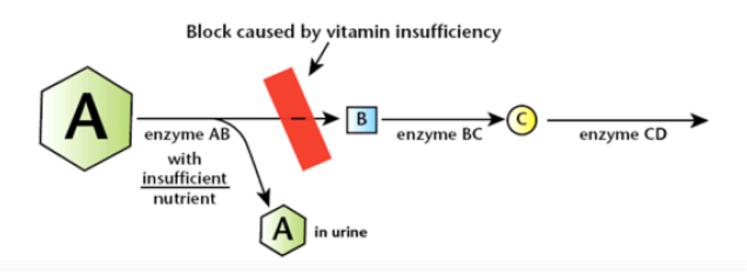
Well Functioning pathway

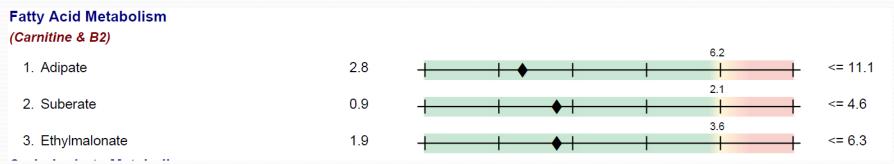
The figure below illustrates a well-functioning metabolic pathway. Molecule A is converted to Molecule B by the enzyme AB. Molecule B is converted to Molecule C by the enzyme BC and so on all the way down the metabolic pathway. Many enzymes require nutrients such as specific vitamins and minerals in order to perform their functions in converting one molecule to another.



Organic Acids Basics

If specific nutrients are not available in adequate amounts, important reactions cannot occur as well as they should. The illustration below shows what happens when the nutrient is not present in adequate amounts so that enzyme AB functions inefficiently. A small amount of Molecule A is converted to Molecule B and the remainder builds up and spills into the urine. Notice that Molecules B through D downstream are also affected.





- Carnitine is needed to move fatty acids into the mitochondria where they are converted to energy using vitamin B2.
- When inadequate levels of carnitine or vitamin B slow down this process, fatty acids are converted by other biochemical pathways to make adipate and suberate.
- A similar block in another pathway causes high ethylmalonate.
- Since most of the body's energy is produced from the oxidation of fatty acids, your muscles and brain suffer when this energy pathway is blocked.

(Carnitine & B2)

- Adipate
 - by-product of long-chain fatty acid breakdown **outside** of the mitochondria
 - Indicates inadequate amounts of carnitine
 - *Carnitine*, made in small amounts by the body, helps your body use fatty acids.
 - If minimum requirements are not met, carnitine dependent functions fail to proceed normally
 - Long-chain fatty acids go through beta-oxidation *in* the mitochondria, *carnitine dependent
 - Low levels may indicate a need for Lysine

(Carnitine & B2)

Suberate

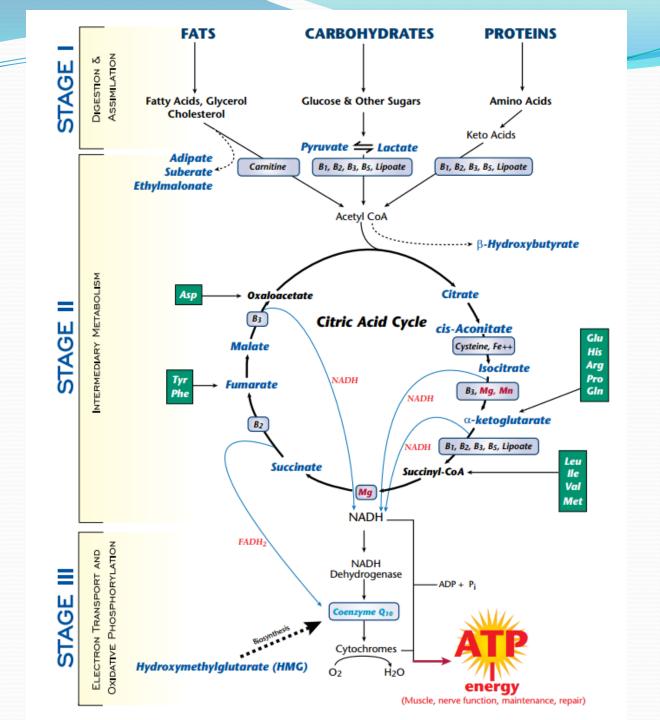
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(Carnitine & B2)

- Ethylmalonate
 - comes from the breakdown of butyrate
 - has a carnitine-dependent pathway
 - can accumulate with an insufficient amount of carnitine
 - Dietary fat, carbohydrate, and protein are all broken down to produce energy using pathways that require vitamin B2 (riboflavin). If you do not have sufficient riboflavin, compounds such as adipate, suberate, and ethylmalonate may increase in urine.

Carbohydrate Metabolism

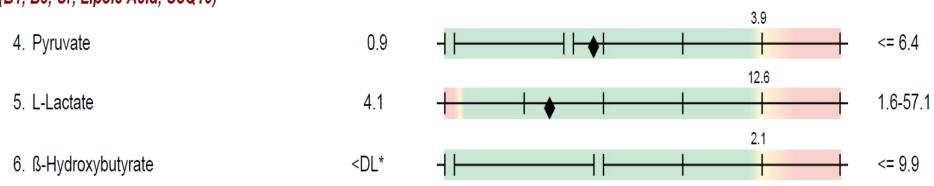
Creating Acteyl-CoA from carbs



Organic Acid Carbohydrate Metabolism Markers

Carbohydrate Metabolism

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



Carbohydrate Metabolism

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

Pyruvate

- Pyruvate is another major player in anaerobic energy production and gluconeogenesis.
- Enters the Krebs cycle via a dehydrogenase enzyme
- Dehydrogenase enzymes require, B1 (thiamin), B2, B3 (niacin), B5 (pantothenic acid), and lipoic acid to function correctly.
- If these nutrients are not available then pyruvate may build up and become elevated
- Elevated levels can indicate a need for lipoic acid

L-Lactate

- Lactate is the main product of glucose metabolism in skeletal muscle and is a major player in anaerobic energy production and gluconeogenesis.
- Gluconeogenesis is a metabolic pathway that produces glucose from non-carbohydrate carbon substrates such as pyruvate, lactate, glycerol, and glucogenic amino acids.

L-Lactate

- requires B1, B2, B3, B5, and lipoic acid
- builds up when the Krebs cycle is not working efficiently
- Elevated levels can indicate a need for lipoic acid and Coenzyme Q10

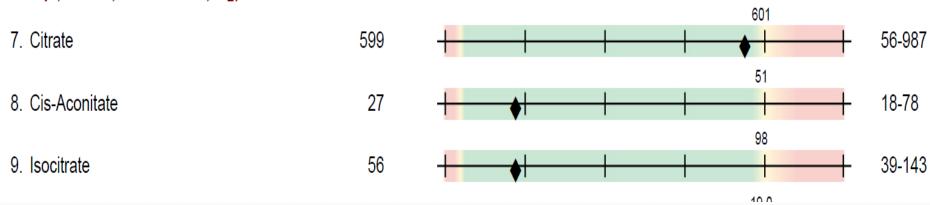
- β-Hydrobutyrate
 - Beta-hydroxy butyrate is a metabolic marker of blood sugar utilization and insulin function.
 - It is also a byproduct of ketosis. Ketosis occurs when cells are burning fat instead of dietary carbohydrate. If your diet is low in carbohydrates or if your insulin is not working then you may have metabolic ketosis.

- β-Hydrobutyrate
 - Builds up in urine when someone is on a low carbohydrate diet or fasting
 - Will also build up in someone with impaired insulin functions.
 - Chromium and vanadium have been shown to help regulate insulin functions and may be helpful.
 - The major function of chromium and vanadium is to help insulin act on your cells to regulate blood sugar.

Energy Production

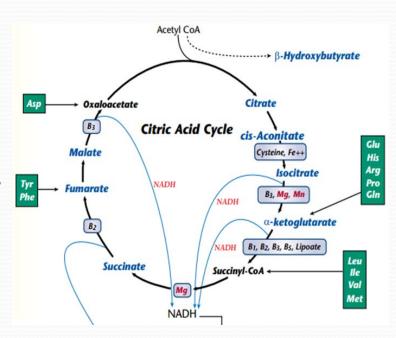
Energy Production (Citric Acid Cycle)

(B comp., CoQ10, Amino acids, Mg)

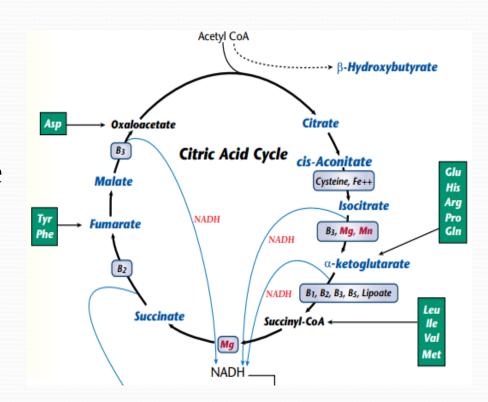


For now, no DNA, but will be added as soon as possible. So just using Organic Acids for assessment at this time.

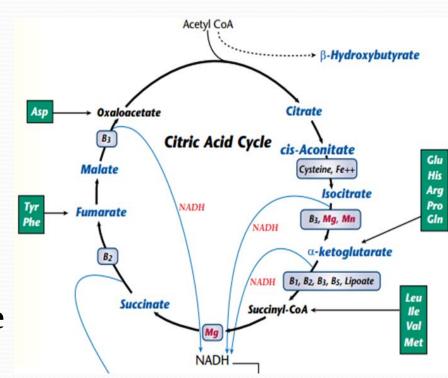
- Citrate
 - Citric Acid Cycle Intermediate
 - Renal ammonia clearance
- When high, indicates a need for Arginine
- When low, indicates a need for Aspartic acid and magnesium citrate



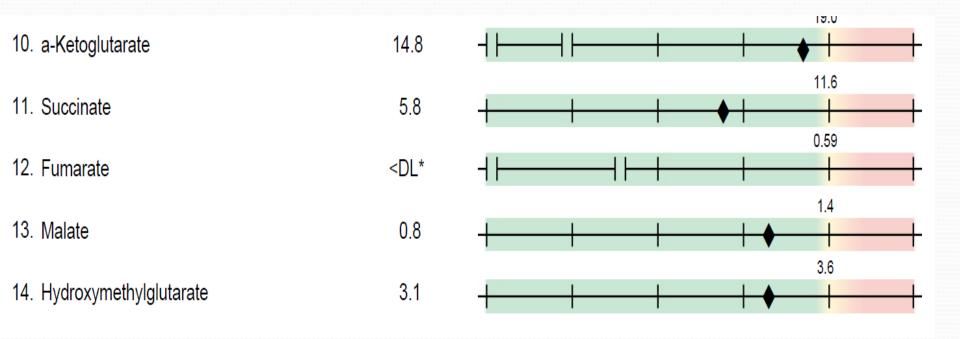
- Cis-Aconitrate
 - Citric Acid Cycle
 Intermediate
 - Renal ammonia clearance
 - May indicate a need for cysteine
 - Check for iron deficiency when elevated



- Isocitrate
 - Citric Acid Cycle
 Intermediate
 - Renal ammonia clearance
- When elevated, indicates a need for Lipoic acid, magnesium, and manganese



Energy Production (Citric Acid Cycle)



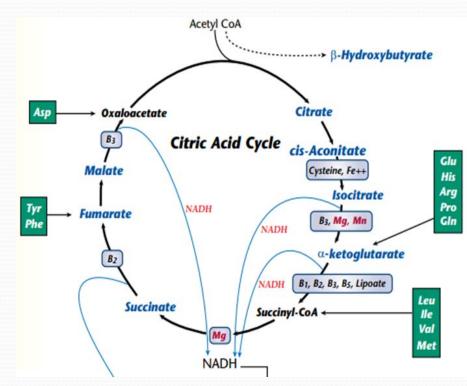
Common symptoms stemming from high levels of succinate, fumarate, and Malate may include fatigue, weakness, myocardial degeneration, and neurological degeneration.

- a-Ketoglutarate
 - Requires a dehydrogenase enzyme which requires vitamin B1, B2, B3, B5, and lipoic acid to function properly
 - An elevation of α -ketoglutarate can indicate a need for one or more of these B vitamins.
 - Indicates whether your body is able to produce energy efficiently by utilizing CoQ10.
 - A need for CoQ10 may also be identified when α-ketoglutarate, succinate, fumurate, and malate are all elevated and strong need may also raise citrate, cis-aconitate, and isocitrate

- Succinate
 - Magnesium is required for conversion of succinate
 - Entire central energy pathway is dependent on iron and manganese
 - Indicates whether your body is able to produce energy efficiently by utilizing CoQ10.
 - A need for CoQ10 may also be identified when α-ketoglutarate, succinate, fumurate, and malate are all elevated and strong need may also raise citrate, cis-aconitate, and isocitrate

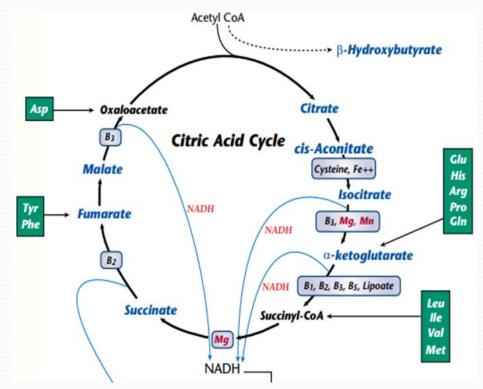
Fumarate

- Indicates whether your body is able to produce energy efficiently by utilizing CoQ10.
 - A need for CoQ10 may also be identified when α-ketoglutarate, succinate, fumurate, and malate are all elevated and strong need may also raise citrate, cisaconitate, and isocitrate

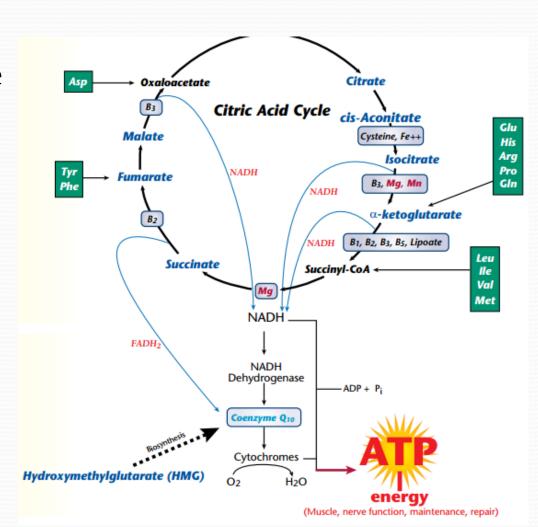


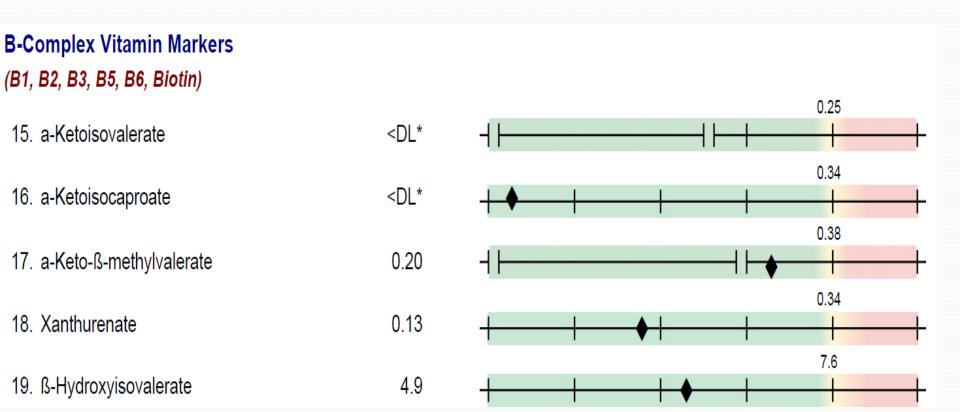
Malate

- Indicates whether your body is able to produce energy efficiently by utilizing CoQ10.
 - A need for CoQ10 may also be identified when αketoglutarate, succinate, fumurate, and malate are all elevated and strong need may also raise citrate, cis-aconitate, and isocitrate

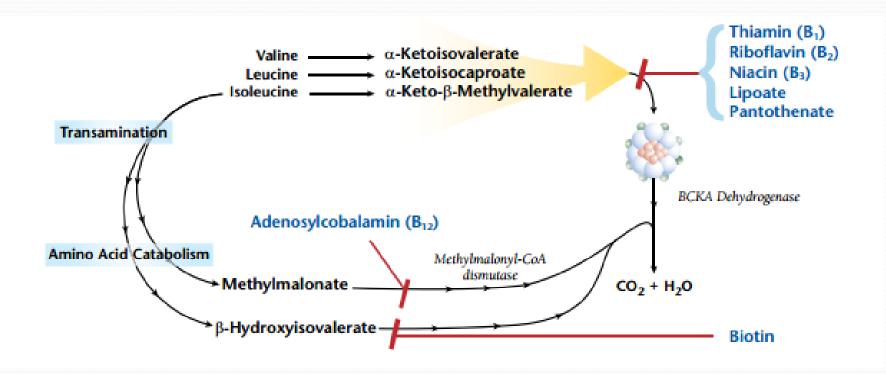


- Hydroxymethylglutarate (HMG)
 - Precursor to Coenzyme
 Q10 (CoQ10) production
 - When it is elevated it may indicate that the body is trying to increase its production of CoQ10.
 - Elevation of HMG can reveal a block in your body's synthesis of CoQ10





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



B-Complex Vitamin Markers (B1, B2, B3, B5, B6, Biotin)

- a-Ketoisovalerate
 - A dehydrogensase enzyme is needed for the breakdown of branched-chain amino acids.
 - Vitamins B1, B2, B3, B5, and lipoic acid are needed for this dehydrogenase to function properly.
 - If these nutrients are insufficient, the keto acids may build up in the urine.
 - If pyruvate and α -ketoglutarate are also both elevated, then there may be a strong need for these specific nutrients since all of them utilize a dehydrogenase enzyme

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

- a-Ketoisocaproate
 - The branched-chain amino acids are broken down to form α -ketoisovalerate, α -ketoisocaproate, and α -keto- β methylvalerate.
 - A dehydrogensase enzyme is needed for this step.
 - Vitamins B1, B2, B3, B5, and lipoic acid are needed for this dehydrogenase to function properly.
 - If these nutrients are insufficient, the keto acids may build up in the urine.

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

- a-Keto-β-methylvalerate
 - The branched-chain amino acids are broken down to form α -ketoisovalerate, α -ketoisocaproate, and α -keto- β methylvalerate.
 - A dehydrogensase enzyme is needed for this step.
 - Vitamins B1, B2, B3, B5, and lipoic acid are needed for this dehydrogenase to function properly.
 - If these nutrients are insufficient, the keto acids may build up in the urine.

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

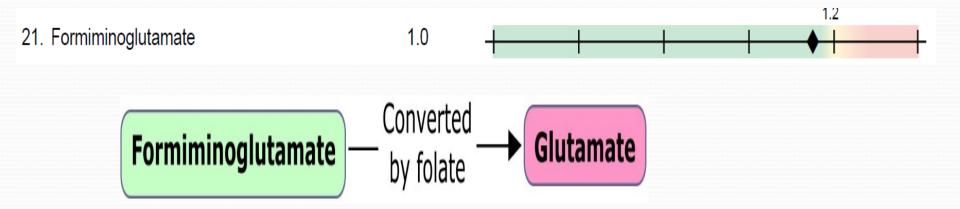
Xanthurenate

- by-product of tryptophan catabolism (hepatic)
- body needs vitamin B6 (pyridoxine) to utilize amino acids derived from dietary protein
 - Inadequate vitamin B6 is one factor that leads to increased concentrations of xanthurenate and kynurenate in urine

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

- β-Hydroxyisovalerate
 - biotin dependent catabolic product from isoleucine
 - An elevated β -hydroxyisovalerate indicates a need for biotin.
 - β-Hydroxyisovalerate is a *specific and sensitive* metabolic marker for functional biotin deficiency

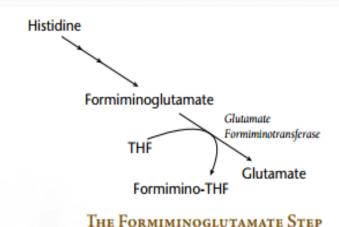
Urine Organic Acids Folate Levels



FIGLU is converted into glutamate by folate. Hi FIGLU in the urine indicates a functional need for more folate. There is a blood test for folate, but at times it comes back normal despite a functional need for more folate. In these cases the FIGLU marker serves as a functional assessment where the blood folate test does not.

Methylation Cofactor Markers (Folate)

Formiminoglutamate



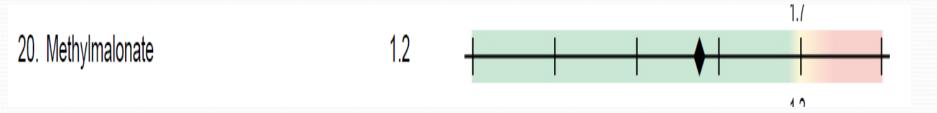
IN THE CATABOLISM OF HISTIDINE

The essential amino acid histidine breaks down to glutamate.

The enzyme glutamate formiminotransferase needs adequate folate to function properly. An elevation of formiminoglutamate could be due to a lack of folate.

- a compound made from the amino acid histidine
- The essential amino acid histidine breaks down to formiminoglutamate, which breaks down to glutamate.
- The enzyme glutamate formiminotransferase needs adequate folate to function properly.
- An elevation of formiminoglutamate in urine could be due to a lack of folate.
 - Folic acid is especially critical for prenatal and childhood development and in sufficient amounts is associated with lower risks of cardiovascular disease and cancer

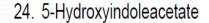
Urine Organic B12 Marker

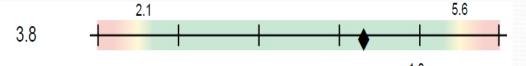


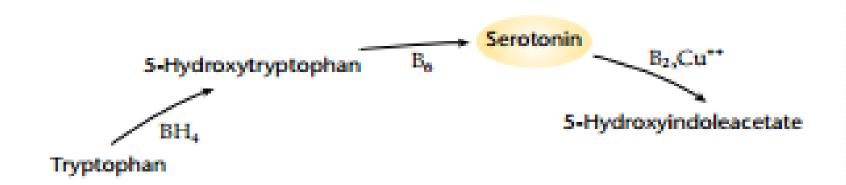
Methylmalonate

- A sensitive, functional marker for vitamin B₁₂
- High levels of methylmalonate in serum or urine can indicate a need for vitamin B₁₂
- Dietary deficiency of vitamin B12 and folic acid are associated with increased risk of many diseases, including anemia, cardiovascular disease, and chronic fatigue.
- Increased alcohol consumption, dysbiosis, aging and HIV infection will all have a detrimental impact on B12 absorption.

Organic Acid







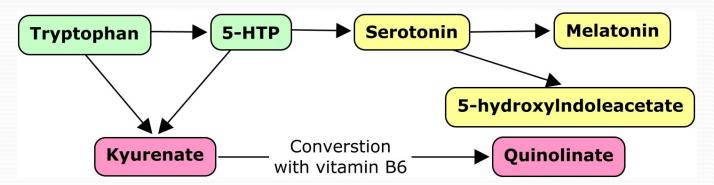
FORMATION AND CLEARANCE OF SEROTONIN

The essential amino acid tryptophan is processed into the neurotransmitter serotonin. Serotonin is broken down and excreted as 5-hydroxyindolacetate. A high level of 5-hydroxyindolacetate may indicate a high turnover of serotonin, and a low level may identify low serotonin production.

5-Hyrdoxyindoleacetate (5-HIA)

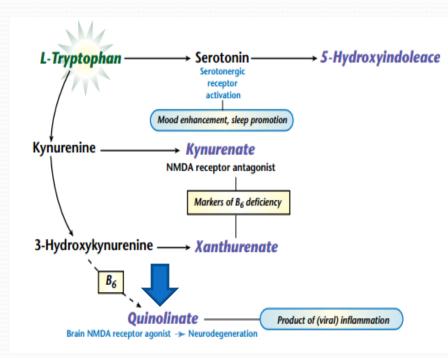
- The breakdown product of *serotonin*
- Acting as a neurotransmitter, serotonin controls functions relating to mood, behavior, appetite, sleep, and bowel contractions.
- The compound 5-HIA is measured as a marker of serotonin metabolism.
- When 5-HIA is elevated, it indicates higher than normal turnover of serotonin with potential depletion of tryptophan or a high turnover due to antidepressants such as serotonin reuptake inhibitors (Prozac, Zoloft, etc.).
- 5-Hydroxytryptophan (5-HTP) is an intermediate in the production of serotonin
- 5-HTP can be used for individuals who are depressed, have sleep problems, or chronic pain such as fibromyalgia. Supplementation may increase production of serotonin and excretion of 5-HIA

- Kynurenate
 - Abnormal levels of kynurenate (KYN) can have a direct effect on brain function
 - shows a need for vitamin B6
 - breakdown product of tryprophan catabolism



Quinolinate

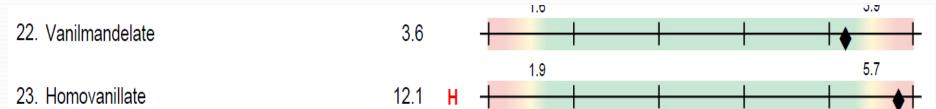
- produced from tryptophan via interferongamma (IFN-γ) stimulated astroglial cells and macrophages, a Th1-driven response.
- associated with increased oxidative stress, virus, parasitic, fungal or bacterial infection, gastrointestinal overgrowth, autoimmune disorder or irritable bowel disease (IBD).
- If elevated, avoid tryptophan supplementation.
- In inflammatory disease a high QUIN / KYN ratio increases the risk of neurotoxicity.
- QUIN levels can be increased with tryptophan supplementation

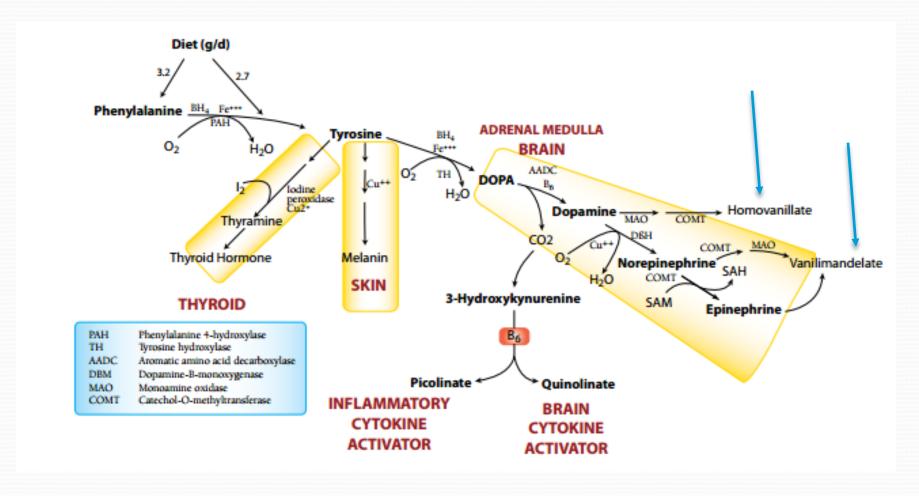


Picolinate

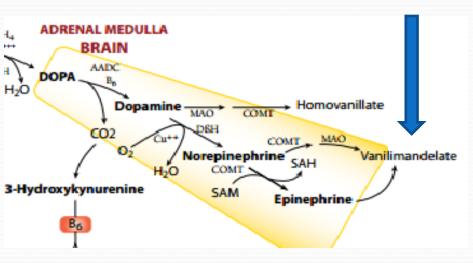
- a hepatic kynurenine pathway metabolite of tryptophan
- activator of Th-1 associated inflammatory cytokines
- High protein intake is speculated to stimulate production
- PUFAs, as in fish oil, may decrease production

Urine Organic Acids



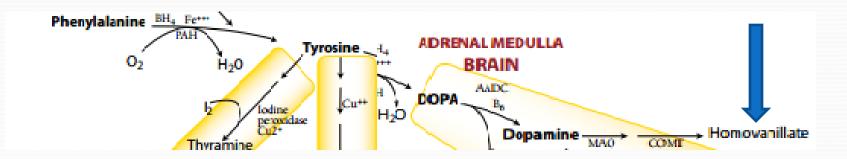


Vanilmandelate (VMA)



- the breakdown product of both epinephrine and norepinephrine
- Elevated levels indicate a high turnover of these fight or flight neurotransmitters.
- Phenylalanine and tyrosine are the amino acid precursors; supplementing with these may increase production
- Reducing stress and/or supplementing with calming herbs or compounds may help.
- If levels are low it may indicate that these products are no longer being made due to adrenal exhaustion. Supplementing with needed amino acids and co-factors may help to increase levels.
 - Checking cortisol levels can help determine treatment.

- Homovanillate (HVA)
 - the breakdown product of *dopamine*
 - amino acid precursors are phenylalanine and trysosine; supplementing these and co-factors may help to increase levels.
 - If levels are low it may indicate that these products are no longer being made due to adrenal exhaustion.
 - Elevated levels indicate a high turnover.
 - Reducing stress and/ or supplementing with calming herbs or compounds (such as GABA, magnesium, and lemon balm) may help to reduce levels.
 - If VMA is elevated and HVA is low it may indicate a need for copper.



Urine Organic Oxidative Stress Markers



Oxidative Damage and Antioxidant Markers (Vitamin C and other antioxidants)

- p-Hydroxyphenyllactate
 - Marker of cell turnover
 - Metabolite in tyrosine degradation
 - May be useful for studying disorders of tyrosine metabolism, including inborn errors of metabolism, and liver disease.
 - High levels of p-hydroxyphenyllactate may respond to high intakes of vitamin C, which aids in restoration of normal metabolism and cell control

Oxidative Damage and Antioxidant Markers (Vitamin C and other antioxidants)

- β-Hyrdoxy-2-deoxyguanosine
 - marker of oxidative damage to the gaunine of DNA.
 - Antioxidants protect your cells from damage.
 - Conditions that increase oxidative metabolism tend to raise your requirements for antioxidant nutrients, such as vitamins C and E, and lipoic acid.
 - Supplementing with individual nutrients or increasing your intake of foods high in concentrated sources of antioxidants (fruits, berries, tomato paste, green tea, curcumin) can increase antioxidant status.
 - High levels of p-hydroxyphenyllactate and β -hydroxy-2-deoxyguanosine are associated with increased oxidative stress, and may indicate a strong need for other antioxidants.

Organic Acids for Glutathione



Detoxification Indicators

(Arg, NAC, Met, Mg, antioxidants)

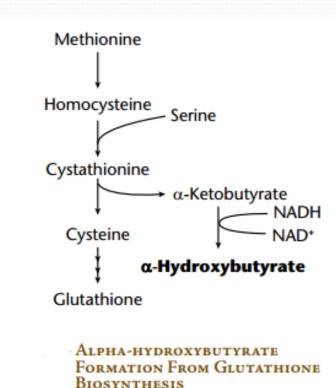
- Glucarate
 - Serves as a biomarker for exposure to a wide array of potentially toxic chemicals, including many drugs.
 - High urinary glucarate suggests above normal exposure to pesticides, herbicides, fungicides, petrochemicals, alcohol, pharmaceutical compounds, or toxins produced in the gastrointestinal tract.
 - General detoxification treatment may be advised.
 - Need for Glutathione: Use Glutathione Accelerator, NRf2 Accelerator, GSH Assist

Detoxification Indicators

(Arg, NAC, Met, Mg, antioxidants)

a-Hydroxybutyrate

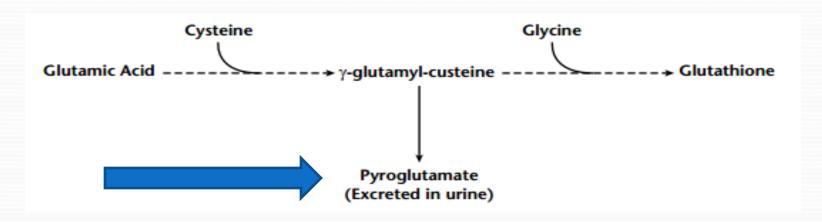
- marker of hepatic glutathione synthesis.
 - Glutathione is an important antioxidant that helps protect against reactive oxygen species such as free radicals. Glutathione is constantly used up in the removal of toxic molecules and prevention of oxidative damage.
- α-Hydroxybutyrate is a by-product from the process in which the body forms more glutathione. When that process is running at high rates, α-hydroxybutyrate excretion is increased.
- If α-hydroxybutyrate is elevated then glutathione support may be recommended.



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

Detox Indicator - Pyroglutamate

- Levels reflect glutathione wasting and a possible need for glycine.
 - Low pyroglutamate excretion can identify a need for glycine
- Treatments are similar to those utilized in elevated α -hydroxybutyrate.
- Under normal conditions, only a small fraction of pyroglutamate, a product of glutathione metabolism is excreted
- during times of increased glutathione synthesis urinary excretion of pyroglutamate increases.
- Pyroglutamate excretion also increases when glycine is limited.
- Use GSH Assist, Glutathione Accelerator and NRf2 Accelerator



Detox Indicator - Sulfate

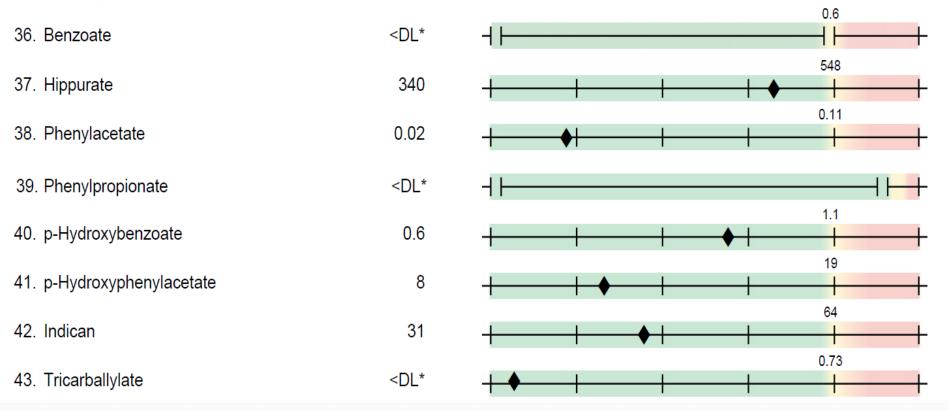
Sulfate

- Hepatic sulfation is used in Phase II detoxification.
- Elevated levels of sulfate can indicate increased Phase II detoxification or inorganic sulfate intake.
- Low sulfate levels may identify chronic glutathione demand on Phase II detoxification.
 - Treatments are similar to those utilized with elevated α -hydroxybutyrate.
- Dietary intake of sulfur-containing amino acids like cysteine is required to maintain levels of glutathione.
- The amino acid N-Acetyl-Cysteine (NAC) is effective for raising both glutathione and sulfate levels. **Use Glutathione Accelerator**
- Lipoic acid, may also be considered when there is evidence of detoxification stress on the liver.

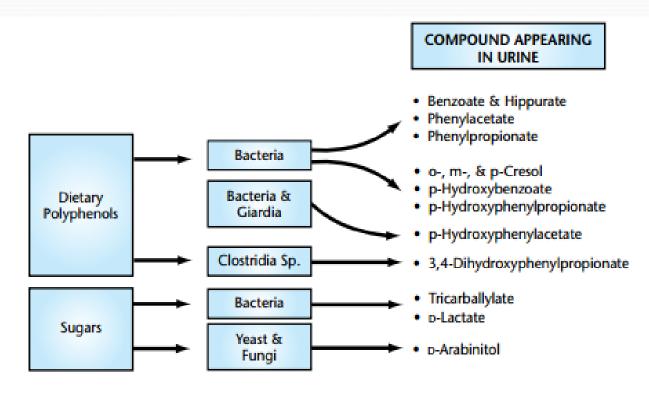
Urine Organic Dysbiosis

Compounds of Bacterial or Yeast/Fungal Origin

Bacterial - general



Intestinal Microbial Balance Markers



ORIGINS OF URINARY DYSBIOSIS MARKERS

Bacteria and yeasts in the intestines produce by-products that are excreted in the urine. An elevated level of these by-products may identify an overgrowth of one or more bacteria or yeast in the intestine.

Bacterial- general

Benzoate

- Metabolic pathway indicates hepatic phase II glycine conjugation
- Elevated levels indicate a need for both glycine and B5

Bacterial-general

 Hippurate, Phenylacetate, Phenylpropinate, p-Hydroxybenzoate

- Bacteria and yeasts in the intestines produce by-products that are excreted in the urine.
- An elevated level of these by-products may identify an overgrowth of one or more bacteria or yeast in the intestine
- usually accompanied by microbial hyperpermeability.
- Take appropriate steps to ensure favorable gut microflora population
- Glutamine, digestive aids (betaine, enzymes, bile) and freeform amino acids may help to normalize gut permeability

Bacterial- general

- p-Hydroxyphenylacetate
 - Treatment for dysbiosis can include diet changes, preand probiotics, mucosal support, and possibly further testing such as a stool test or immune reactions from food
 - An elevated level of this by-product may identify an overgrowth of one or more *bacteria* or *Giardia* in the intestine

Bacterial- general

- Indican
 - Ff there is intestinal dysbiosis due to poor diet, inadequate digestion, or leaky gut due to an immune reaction, there may be an overgrowth of unfavorable microflora.
 - Treatment for dysbiosis can include diet changes, preand probiotics, mucosal support, and possibly further testing such as a stool test or immune reactions from food

Bacterial- General

Tricarballylate

- An elevated level of this by-product may identify an overgrowth of one or more bacteria or yeast in the intestine
- usually accompanied by microbial hyperpermeability.
- Take appropriate steps to ensure favorable gut microflora population

Urine Organic Acids



L. Acidophillus / general bacteria

D-Lactate

- D-Lactate elevation is *an exception to the rule* for probiotic potential just described.
- Lactobacillus acidophilus is widely considered a favorable bacterium to colonize the human gut. It has beneficial effects in many individuals. However, if you have any tendency for carbohydrate malabsorption, even favorable organisms (e.g., L. acidophilus) can grow and lead to increased highly acidic conditions that favor formation of D-Lactate. This condition is revealed by high D-Lactate in urine.
- Special forms of probiotic organisms that do not form D-Lactate may be used.

Clostridial species

- 3,4-Dihydroxyphenylpropionate
 - A compound that can be produced by Clostridia, though other bacteria may also produce it.
 - Frequently the cause of Traveler's diarrhea, but its byproducts may produce other symptoms.
 - Species of Clostridia are particularly susceptible to displacement by the favorable organism called *Saccharomyces boulardii* readily available in capsule form.

Yeast / Fungal

D-Arabinitol

- Yeast is another class of microbes that can chronically grow in the intestinal tract and cause adverse health effects through the release of toxic metabolites.
- Because of the multiple, non-specific symptoms that they can produce, doctors have searched for ways to analyze when yeast overgrowth is a problem.
- D-Arabinitol is uniquely produced by intestinal yeast, and the degree of elevation is a useful marker of their growth.
- Favorable organisms (Saccharomyces boulardii) and herbal or pharmaceutical antifungal agents or changes in diet can suppress intestinal yeast.