Organix
Urine Organic Acids

Interpretive Guide

NutriPATH

GENOVA DIAGNOSTICS®

How Your Doctor Can Use This Test

To be healthy your body must process food through a complex metabolic system that produces energy and restores healthy tissues such as skin and muscle. If you have specific requirements for any of the few dozen essential nutrients or if you are simply failing to eat and assimilate them, then those healing processes can fail. A further reason for special requirement is your exposure to toxic chemicals.

Metabolism is the process in which your body converts the food you eat into energy and new structures. The study of human metabolism has revealed how vitamins and minerals are used to perform those hundreds of necessary chemical reactions. This is a test that shows your doctor weaknesses in your metabolism. Many of the weaknesses can be overcome by increasing your intake of a vitamin or other essential nutrient. Some of the measurements show nerve or detoxification functions. The final set of compounds shows disturbances in the balance of bacteria that may grow from food residues in your digestive system.

By correcting problems shown in your Organix test results, your doctor is improving your body's ability to heal and stay healthy. This approach has been shown to improve treatments for conditions ranging from childhood autism to adult chronic fatigue syndrome. It also can help people reduce their risk of heart disease, obesity, fatigue, or many other conditions. When your main imbalances are corrected, you may be able to make simple diet changes to achieve the balance that lets you sustain health as you age.

Your Organix profile report contains:

- Laboratory results with individualized integrative comments
- A Supplement Recommendation Summary
- This Organix Patient Guide booklet

Your Laboratory Results

The compounds that were measured in your urine specimen are reported on the laboratory results pages. The chemical names are organized into categories according to their biochemical role. The compounds on the first page are signals or markers of specific vitamin-dependent processes. The nutrients that are usually given to help correct abnormalities are listed in the parentheses under the category headings. On the second page, categories of cell regulators and toxicants are found with their associated urinary marker compounds.

In addition to the data from your measurements, the report shows an "H" or "L" next to each result that is abnormal. The graphs show where your values fall relative to a reference population. If your result is where the average person tends to fall, then a mark will appear at the 50th percentile or in the third quintile. If a mark appears in the fifth quintile, then that result is higher than 80% of the population. The 95% Reference Interval is even broader. It represents the range that includes 95% of people.

The analytes are color-coded based on the profile your practitioner chose for you.

- Comprehensive Profile
- Basic Profile
- Dysbiosis Profile

Your Supplement Recommendations

The Supplement Recommendation Summary has two sections. The first page contains nutrients usually found in multivitamin-mineral products that are often the cornerstone of a nutritional treatment protocol. The amounts under "Units Added" vary according to the number of pertinent abnormalities found in your results. If no abnormalities are found, no extra amounts are added to the base. Any dose printed in the right-hand column tells you that some related abnormality was found in the Organix results. Your healthcare practitioner can build a custom program using combinations of dietary recommendations and supplements of multiple or individual vitamins.

The second page of recommendations contains nutrient entries only if an abnormality is present. The nutrients included in this section are generally used as separate products as needed. The recommended dose ranges are considered safe and effective in meeting your needs based on this test alone. All amounts are adult doses and should be reduced for children according to body weight. Your healthcare practitioner may modify these recommendations according to your clinical needs.

Your Organix Patient Guide

Your healthcare practitioner, with full knowledge of your medical history and concerns, can use your laboratory results to provide you with an individually optimized nutritional support program. For many of the organic acids that are measured, abnormally high levels in urine may indicate low levels of a vitamin needed to break down that compound. This booklet translates abnormalities of organic acids into information about areas where you may need extra nutrients, or a change in diet. A summary table listing Organix compounds, or markers, and the associated nutrients is found on the next page (Table 1). The center section is divided into major nutrient categories and individual nutrient subcategories. The paragraphs that follow explain the importance of each measured compound in your biochemistry and health, the way each compound reveals your areas of internal strengths and weaknesses, and the indications of need for specific nutrients. Biochemical pathway charts throughout the booklet further illustrate the relationships between the compounds measured in the Organix profile and the way your body uses essential nutrients in metabolism.

Table 1 – Summary of Abnormalities for Organic Acids in Urine

Name		Potential Intervention	Metabolic Pathway	
Fatty Acid Oxidation				
Adipate	H	L-Carnitine, 500–1000 mg TID; L-Lysine (if low), 500 mg TID; B2, 100mg BID See text for other interventions in genetic disorders	Fatty acid oxidation	
Suberate	H			
Ethylmalonate	H			
Carbohydrate Metabolism				
Pyruvate	H	B_1, up to 100mg TID with B complex support; For concurrent H Lactate: lipoic acid, 500mg TID	Aerobic/anaerobic energy production	
Lactate	H	Coenzyme Q_{10}, 50 mg TID		
β-Hydroxybutyrate	H	Chromium picolinate, 200 µg BID	Balance of fat and CHO metabolism	
Energy Production (Citric Acid Cycle)				
Citrate	H	Arginine, 1–3 gm/day	Citric Acid Cycle Intermediates	Renal ammonia clearance
	L	Aspartic acid, 500 mg; magnesium citrate, 500 mg		
Cis-aconitate	H	Cysteine, 1000 mg BID; Check for iron deficiency		
Isocitrate	H	Lipoic acid, 25 mg/kg/day Magnesium, 400 mg; manganese, 20 mg		
α-Ketoglutarate	H	B-complex, 1 TID; lipoic acid 100 mg		
Succinate	H	CoQ_{10}, 50 mg TID, magnesium, 500 mg		
Fumarate	H	CoQ_{10}, 50 mg TID, magnesium, 500 mg		
Malate	H	CoQ_{10}, 50 mg TID, B_3, 100 mg TID		
Hydroxymethylglutarate	L,H	CoQ_{10}, 50 mg TID	(L) Substrate-limited CoQ_{10} synthesis (H) HMG-CoA reductase inhibition	
B-Complex Vitamin Markers				
α-Ketoisovalerate	H	B-complex, 1 TID; lipoic acid 100 mg	Valine catabolism	
α-Ketoisocaproate	H		Leucine catabolism	
α-Keto-β-methylvalerate	H		Isoleucine catabolism	
Xanthurenate	H	Vitamin B_6, 100 mg/d	Tryptophan catabolism (hepatic)	
β-Hydroxyisovalerate	H	Biotin, 5 mg/day; magnesium, 100 mg BID	Isoleucine catabolism	
Methylmalonate or Propionate	H	B_{12}, 1000 µg TID	Valine or odd-chain fatty acid catabolism	
Formiminoglutamate	H	Folic acid, 400 µg/d	Histidine catabolism	
Neurotransmitter Metabolism				
Vanilmandelate	L,H	Tyrosine, 1000 mg BID-TID, between meals and phenylalanine hydroxylase cofactors as needed Contraindicated for patients taking MAO inhibitors	(L) Tyrosine-limited or (H) Tyrosine-depleting epinephrine & norepinephrine catabolism	
Homovanillate	L,H		(L) Tyrosine-limited or (H) Tyrosine-depleting DOPA catabolism	
5-Hydroxyindolacetate	L,H	5-Hydroxytryptophan, 50–100 mg TID; magnesium, 300 mg; vitamin B_6, 100 mg (5-HTP may be contraindicated with SSRI's)	(L) Tryptophan-limited or (H) Tryptophan-depleting Serotonin catabolism	

Table 1 – Summary of Abnormalities for Organic Acids in Urine

Name		Potential Intervention	Metabolic Pathway
Kynurenate	H	B_6, 100 mg; magnesium, 300 mg	Inflammation-stimulated macrophage and astrocyte kynurenine pathway activity
Quinolinate	H	Magnesium, 300 mg	
Picolinate	H	decrease protein; add fish oil	
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_5 100 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
Dysbiosis Markers (Products of Abnormal Gut Microflora)			
Benzoate	H	Glycine, 2–5 gm/d; vitamin B_5, 100 mg TID	Hepatic Phase II glycine conjugation
Hippurate	H	These compounds may reflect intestinal overgrowth, usually accompanied by microbial hyperpermeability. Take appropriate steps to ensure favorable gut microflora population. Glutamine, 10–20 gm daily, digestive aids (betaine, enzymes, bile) and free-form amino acids help to normalize gut permeability.	Intestinal bacterial overgrowth
Phenylacetate	H		
Phenylpropionate	H		
p-Hydroxybenzoate	H		
p-Hydroxyphenylacetate	H		
Tricarballylate	H		
D-Lactate			General bacterial or *L. acidophilus* overgrowth
3,4-Dihydroxyphenylpropionate	H		Clostridial overgrowth
D-Arabinitol	H		Intestinal yeast overgrowth

** Bowel tolerance is usually up to 100 mg/kg, as determined by 500 mg dosing repeated every 30 minutes.*

Organic Acids

Organic acids provide a view into several metabolic processes. Identifying metabolic blocks that can be treated nutritionally allows individual tailoring of interventions in order to maximize patient's responses and lead to improved patient outcomes.

Fatty Acid Metabolism

- 1. Adipate
- 2. Suberate
- 3. Ethylmalonate

Adipate, Suberate and Ethylmalonate

These compounds give information about your ability to process fatty acids. Carnitine helps your body use fatty acids. The body makes small amounts of carnitine. However, if minimum requirements are not met, carnitine dependent functions fail to proceed normally. Long-chain fatty acids go through beta-oxidation in the mitochondria, which is a carnitine dependent step (Figure 1). If there are inadequate amounts of carnitine, the long-chain fatty acids will get processed outside of the mitochondria; **Adipate** and **suberate** are by-products of long-chain fatty acid breakdown outside of the mitochondria.

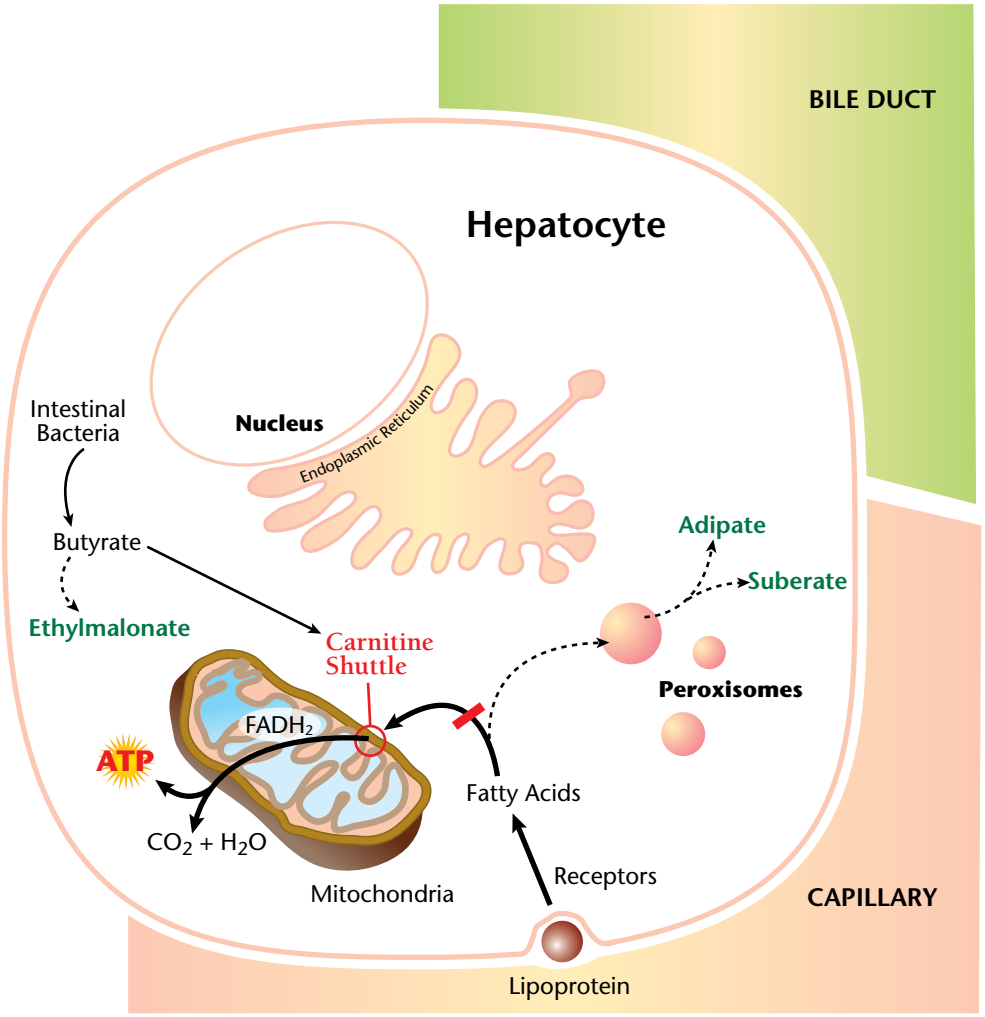


Figure 1 – Mitochondrial Fatty Acid Metabolism Markers

Fatty acids, including butyrate, go into the mitochondria via a carnitine dependent shuttle to be metabolized. If carnitine is in inadequate amounts, the fatty acids cannot get into the mitochondria and get metabolized in the peroxisomes outside the mitochondria. The by-products of this process are ethylmalonate, adipate, and suberate.

Ethylmalonate, which comes from the breakdown of butyrate, also has a carnitine-dependent pathway and 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 B_2 (riboflavin). If you do not have sufficient riboflavin, compounds such as adipate, suberate, and ethylmalonate may increase in urine.

Carbohydrate Metabolism

- 4. Pyruvate
- 5. Lactate
- 6. β-Hydroxybutyrate

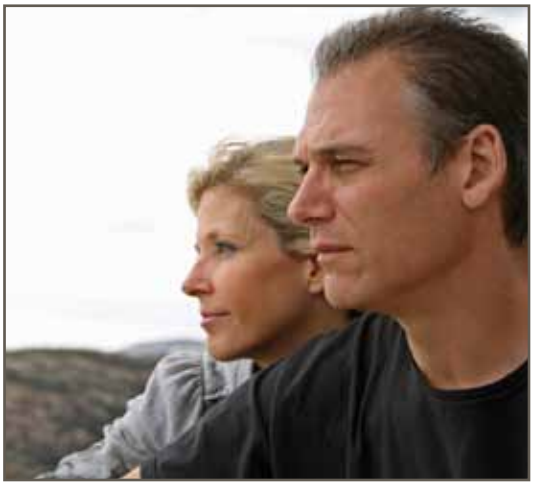
As food is broken down, specific compounds are formed at steps that require B vitamin assistance. Such steps occur in carbohydrate breakdown where **pyruvate** and **lactate** are formed. Pyruvate enters the Krebs cycle via a dehydrogenase enzyme. Dehydrogenase enzymes require, B_1 (thiamin), B_2, B_3 (niacin), B_5 (pantothenic acid), and lipoic acid to function correctly. If these nutrients are not available then pyruvate may build up and become elevated. Lactate also requires these same B vitamins. Lactate builds up when the Krebes cycle is not working efficiently. Elevated pyruvate and lactate can indicate a need for lipoic acid. **β-Hydroxybutyrate** is a primary ketone body. It builds up in urine when someone is on a low carbohydrate diet or fasting. It 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 (Citric Acid Cycle)

- 7. Citrate
- 8. cis-Aconitate
- 9. Isocitrate
- 10. α-Ketoglutarate
- 11. Succinate
- 12. Fumarate
- 13. Malate
- 14. Hydroxymethylglutarate

α-Ketoglutarate, like pyruvate, requires a dehydrogenase enzyme which also requires vitamin B_1, B_2, B_3, B_5, and lipoic acid to function properly. An elevation of α-ketoglutarate can indicate a need for one or more of these B vitamins. The mineral elements magnesium, iron, and manganese are additional factors that are frequently needed in the Krebs cycle pathways. Magnesium is required for conversion of **succinate**. In addition, the entire central energy pathway is dependent on iron and manganese.

Hydroxymethylglutarate (HMG) is the precursor to Coenzyme Q10 (CoQ10) production, and 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. Other functional markers such as lactate, succinate, **fumarate**, and **malate** indicate 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** **(Figure 2)**.



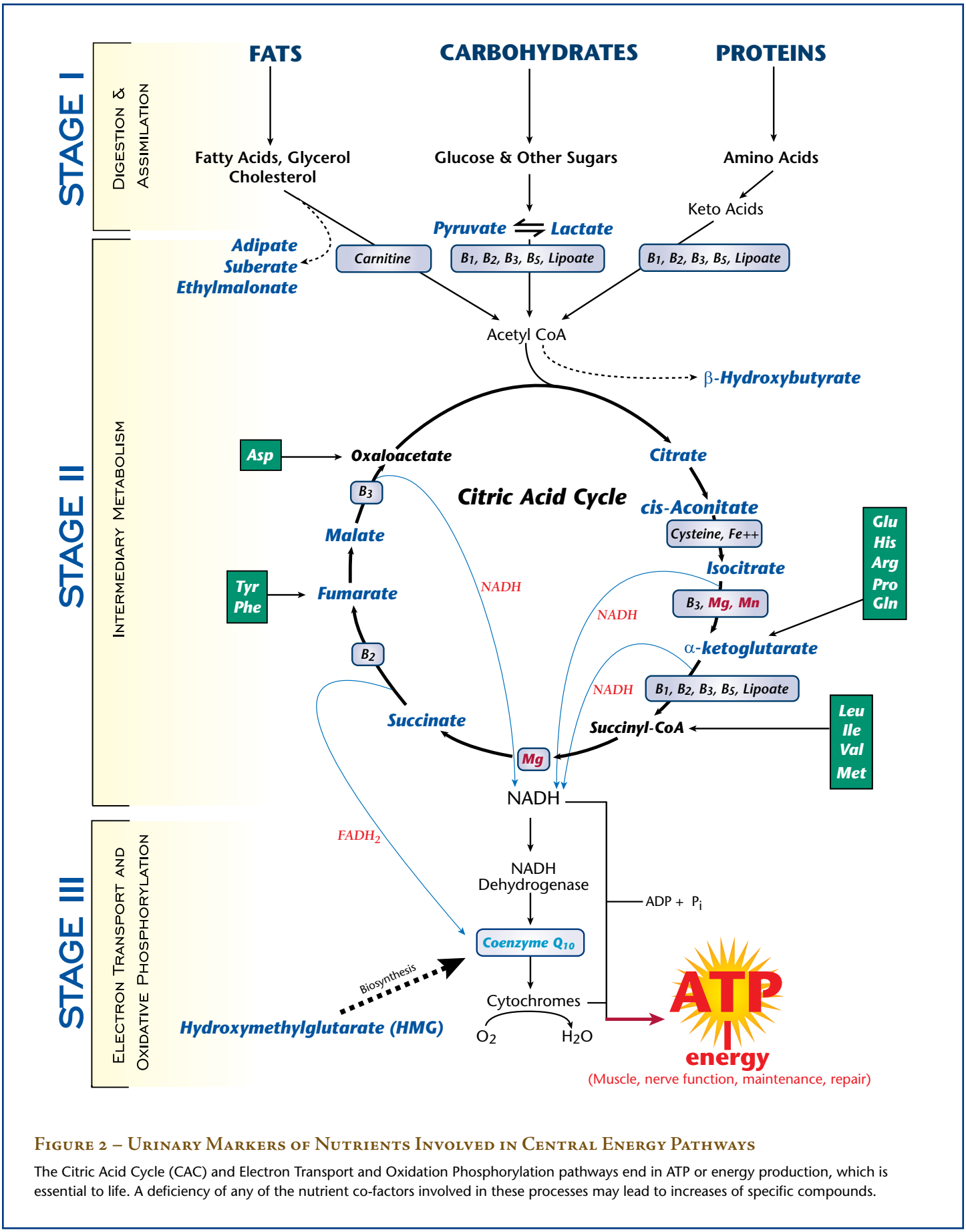


Figure 2 – Urinary Markers of Nutrients Involved in Central Energy Pathways

The Citric Acid Cycle (CAC) and Electron Transport and Oxidation Phosphorylation pathways end in ATP or energy production, which is essential to life. A deficiency of any of the nutrient co-factors involved in these processes may lead to increases of specific compounds.

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

- 15. α-Ketoisovalerate
- 16. α-Ketoisocaproate
- 17. α-Keto-β-methylvalerate
- 18. Xanthurenate
- 19. β-Hydroxyisovalerate

Vitamins are compounds that your body needs to be healthy. Vitamins are "essential" for proper function, which means that they are not made inside your body and must be consumed in the diet. The B-complex vitamins are necessary for many enzymes in your body to function properly. Your body uses enzymes to extract energy from food, to build new tissue, to remove toxins, and to maintain the immune system.

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 B_1, B_2, B_3, B_5, 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 (Figure 3).

Xanthurenate is a by-product of tryptophan catabolism (hepatic). Your body needs vitamin B_6 (pyridoxine) to utilize amino acids derived from dietary protein. Inadequate vitamin B_6 is one factor that leads to increased concentrations of xanthurenate and kynurenate in urine.

β-Hydroxyisovalerate is a 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.

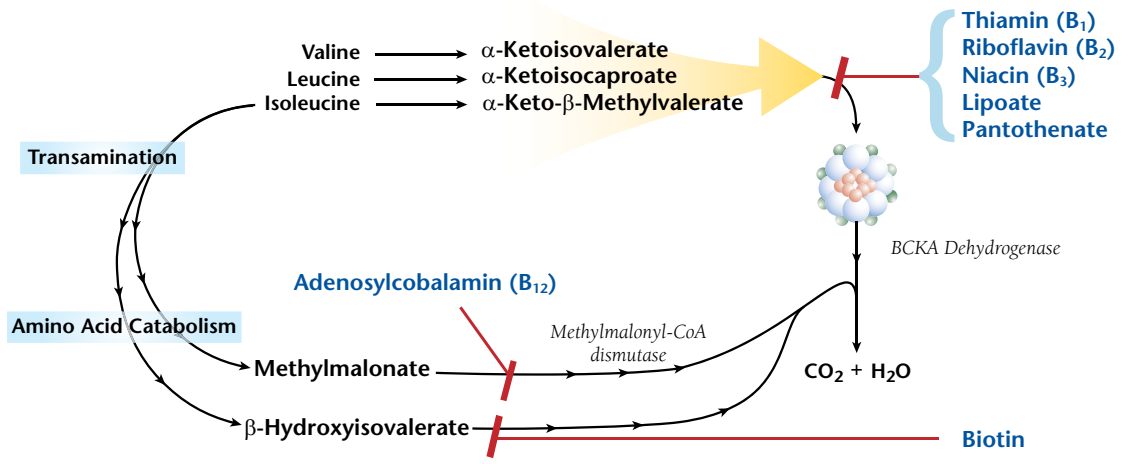


Figure 3 – Biochemical Markers For Vitamins B_1, B_2, B_3, B_5, Lipoic Acid, Vitamin B_{12} and Biotin

Many B vitamins are used as co-factors in the breakdown of amino acids. A deficiency of any of these B vitamins may lead to a block in one of more of these pathways resulting in elevations of the markers.

Methylation Cofactor Markers (B12, Folate)

- 20. Methylmalonate
- 21. Formiminoglutamate

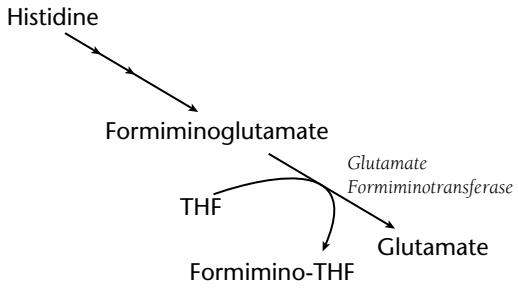


Figure 4 – The Formiminoglutamate Step in the Catabolism of Histidine

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.

Vitamin B12 and Folic Acid

Dietary deficiency of vitamin B_{12} and folic acid are associated with increased risk of many diseases, including anemia, cardiovascular disease (CVD), and chronic fatigue. **Methylmalonate** is a sensitive, functional marker for vitamin B_{12}; high levels of methylmalonate in serum or urine can indicate a need for vitamin B_{12} (Figure 3). **Formiminoglutamate** (FIGLU) is a compound made from the amino acid histidine. Insufficiency of folic acid can lead to high urinary FIGLU. Folic acid is especially critical for prenatal and childhood development and in sufficient amounts is associated with lower risks of cardiovascular disease and cancer (Figure 4).

Neurotransmitter Metabolism

- 22. Vanilmandelate
- 23. Homovanillate
- 24. 5-Hydroxyindoleacetate

Vanilmandelate (VMA) is 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 (Figure 6). Reducing stress and/or supplementing with calming herbs or compounds may help. Supplementing with tyrosine or phenylalanine may increase production. 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. Co-factors include iron, tetrahydrobiopterin (BH4), vitamin B_6, magnesium, and copper. Checking cortisol levels can help determine treatment.

Homovanillate (HVA) is the breakdown product of dopamine. Its amino acid precursors are phenylalanine and trysosine. 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 levels are low it may indicate that these products are no longer being made due to adrenal exhaustion. Supplementing tyrosine or phenylalanine and co-factors may help to increase levels. If VMA is elevated and HVA is low it may indicate a need for copper.

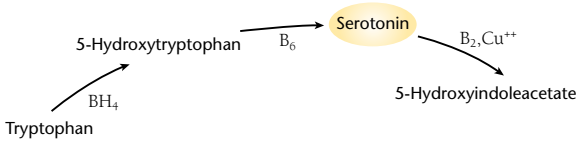


Figure 5 – Formation and Clearance of Serotonin

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-Hydroxyindoleacetate (5-HIA) is the breakdown product of the neurotransmitter serotonin. 5-Hydroxytryptophan (5-HTP) is an intermediate in the production of serotonin (Figure 5). 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. Many drugs, primarily antidepressants, may act in such a way that essential amino acids are lost due to increased metabolic activity to produce neurotransmitters. 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 re-uptake inhibitors (Prozac, Zoloft, etc.). 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 (Table 2).

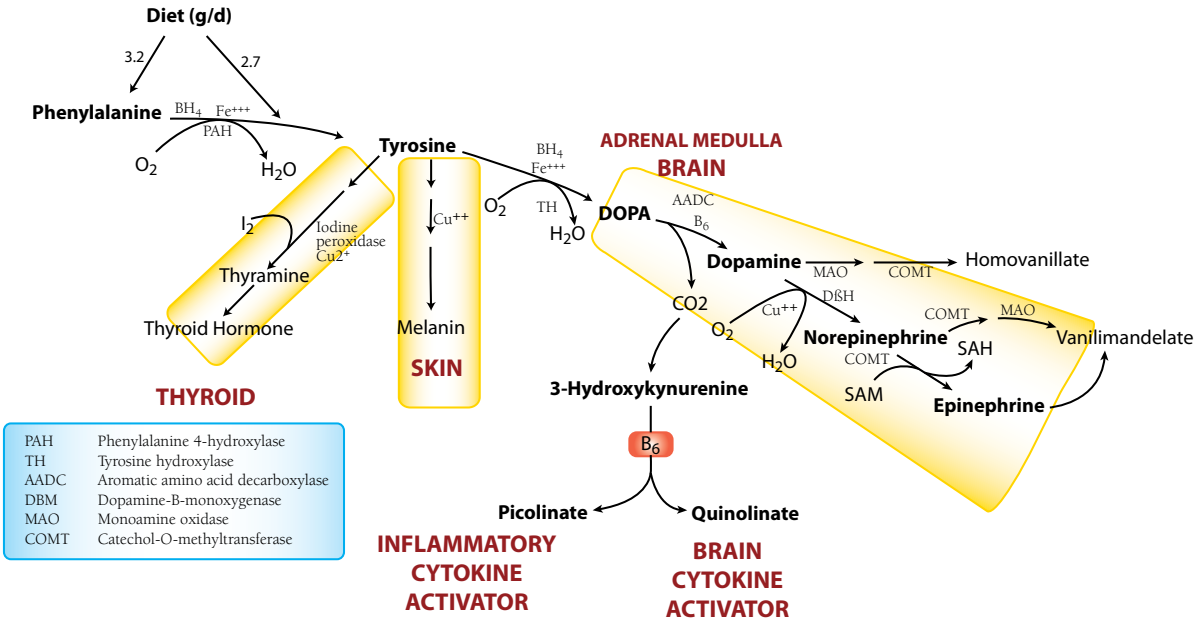


FIGURE 6 – NEUROTRANSMITTERS AND HORMONES FROM PHENYLALANINE AND TYROSINE

The essential amino acid phenylalanine breaks down to tyrosine. Tyrosine is used in the production of thyroid hormones, melatonin in skin, and the neurotransmitters, dopamine, norepinephrine, and epinephrine. These neurotransmitters are further broken down and excreted. Dopamine is excreted as homovanillate, and norepinephrine and epinephrine are excreted jointly as vanilmandelate. High levels of these breakdown products in the urine identify a high turnover; low levels may indicate inadequate production.

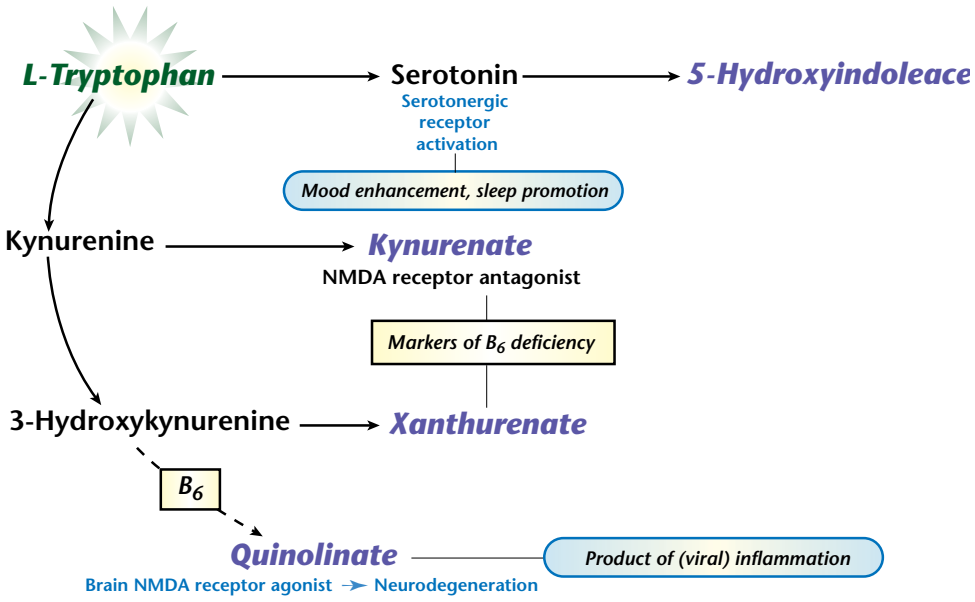


FIGURE 7 - QUINOLINATE PRODUCTION

While tryptophan makes serotonin, it can also go down another pathway to quinolinate and picolinate. These steps are B6 dependent, xanthurenate has been used as a marker of need for B6. Quinolinate is a product of inflammation and is seen with oxidative stress, infections, or autoimmune disorders.

Table 2 – Serotonin Content of Selected Foods

Food	Serotonin mg/100 g
Butternuts	398
Black Walnuts	304
English Walnuts	87
Plantain	30
Pecans	29
Pineapple	17
Banana	15
Kiwi fruit	5.8
Plums	4.7
Tomatos	3.2
Haas Avacado	1.6
Dates	1.3
Grapefruit	0.9

NMDA Modulaators

- 25. Kynurenate
- 26. Quinolinate
- 27. Picolinate

Abnormal levels of **kynurenate** (KYN) can have a direct effect on brain function in addition to showing a need for vitamin B_6. KYN is a breakdown product of tryprophan catabolism (Figure 7).

Quinolinate (QUIN) is produced from tryptophan via interferon-gamma (IFN-γ) stimulated astroglial cells and macrophages, a Th1-driven response. It is 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 (Figure 7).

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

Oxidative Damage (Antioxidant Status) Markers

- 28. p-Hydroxyphenyllactate
- 29. 8-Hydroxy-2'-deoxyguanosine

P-Hydroxyphenyllactate is a marker of cell turnover. It is also a metabolite in tyrosine degradation and 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.

8-Hydroxy-2'-deoxyguanosine (8-OHdG) is a 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 8-hydroxy-2'-deoxyguanosine are associated with increased oxidative stress, and may indicate a strong need for other antioxidants as well.

Toxicant and Detoxification

- 30. 2-Methylhippurate
- 31. Orotate
- 32. Glucarate
- 33. α-hydroxybutyrate
- 34. Pyroglutamate
- 35. Sulfate

Produced from coal tar or crude oil, xylene is used as a solvent for paints and paint thinners, and its vapors are released from many building and decorating materials such as varnishes and new carpets. Excretion of **2-methylhippurate** is a sensitive and specific marker for xylene exposure which increases oxidative stress. Xylene is oxidized in a Phase 1 detoxification reaction to 2-methylbenzoate; then in Phase II (glycine conjugation) it becomes 2-methylhippurate (Figure 8). Glycine supplementation can aid in xylene excretion.

Urea cycle overloads cause increased orotate synthesis and spillage as a secondary ammonia detoxification pathway (Figure 9). **Orotate** is sensitive to anything that increases ammonia, including a high protein diet, intestinal dysbiosis, or arginine deficiency. This leads to increased orotate urinary values. If orotate is elevated due to ammonia, generally citrate, cis-aconitase, and/or isocitrate will also be elevated. Elevated orotate may also identify a need for magnesium.

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 (Table 3). General detoxification treatment may be advised.

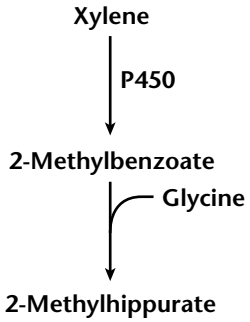


Figure 8 – Metabolism of Xylene

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.

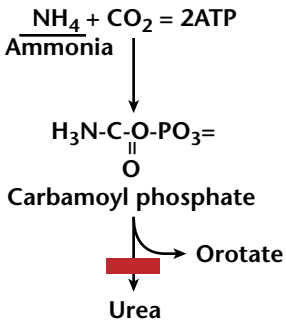


Figure 9 – Orotate and Ammonia

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.

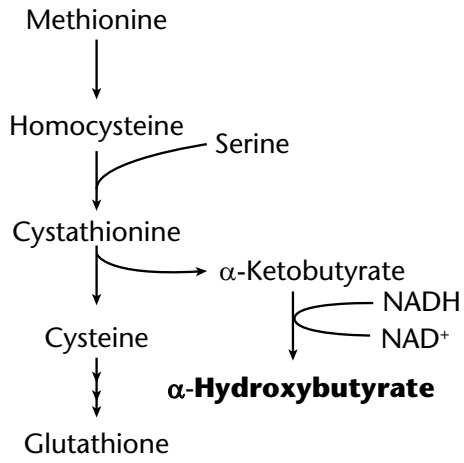


Figure 10 – Alpha-hydroxybutyrate Formation From Glutathione Biosynthesis

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

Table 3 – Classes of Compounds Cleared by Glucuronidation[401]

Class	Examples
Polycyclic aromatic hydrocarbons	Benzo(a)pyrene, benzanthracene, naphthalene
Various nitrosamines	Cured meats, tobacco products, rubber products, pesticides
Fungal toxins	Aflatoxin
Steroid hormones	Estrogen, testosterone
Heterocyclic amines	Well-done, fried, or barbequed meats
Pharmaceutical drugs	Aspirin, lorazepam, digoxin, morphine
Vitamins	Vitamins A, D, E and K

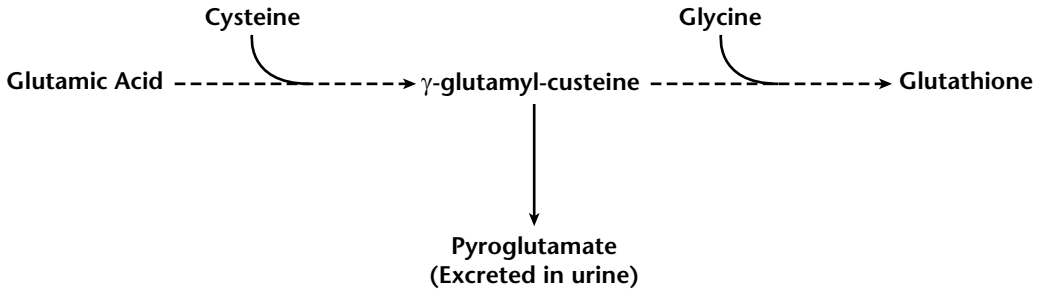


Figure 11 – Pyroglutamate Excretion

Low pyroglutamate excretion can identify a need for glycine. Glycine is needed in the final steps of glutathione production. If glycine is not available, glutathione production slows and pyroglutamate gets excreted in the urine.

α-Hydroxybutyrate is a 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 (Figure 10). If α-hydroxybutyrate is elevated then glutathione support may be recommended.

Pyroglutamate levels reflect glutathione wasting and a possible 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 (Figure 11), is excreted, but during times of increased glutathione synthesis urinary excretion of pyroglutamate increases. Pyroglutamate excretion also increases when glycine is limited.

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. Another sulfur-containing nutrient, lipoic acid, may also be considered when there is evidence of detoxification stress on the liver.

Intestinal Microbial Balance Markers

- 36. Benzoate
- 37. Hippurate
- 38. Phenylacetate
- 39. Phenylpropionate
- 40. p-Hydroxybenzoate
- 41. p-Hydroxyphenylacetate
- 42. Indican
- 43. Tricarballylate
- 44. D-Lactate
- 45. 3,4-Dihydroxyphenylpropionate
- 46. D-Arabinitol

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. With the exception of hippurate, the compounds are not normally produced in the cells of your body. 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.

Probiotics and Antibiotics

In health, beneficial intestinal bacteria produce some vitamins and provide stimulus for proper immune function. However, if 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.

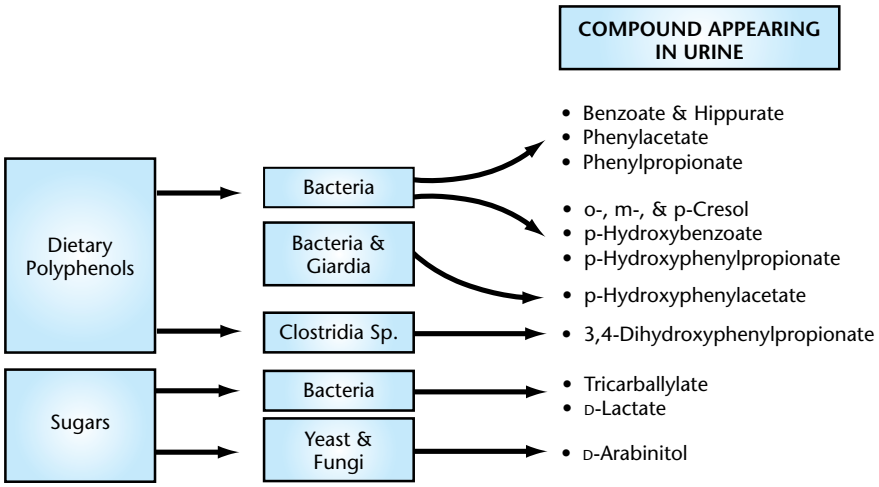


Figure 12 – Origins of Urinary Dysbiosis Markers

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.

The products produced include: **benzoate**, **hippurate**, **phenylacetate**, **phenylpropionate**, **p-hydroxybenzoate**, **p-hydroxyphenylacetate**, **indican**, and **tricarballylate** **(Figure 12)**. Treatment for dysbiosis can include diet changes, pre- and probiotics, mucosal support, and possibly further testing such as a stool test or immune reactions from food.

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.

3,4-Dihydroxyphenylpropionate is a compound that can be produced by Clostridia, though other bacteria may also produce it. This organism is frequently the cause of Traveler's diarrhea, but its by-products 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 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.

For Further Information:

The Organix Profile and other laboratory tests for functional nutrient insufficiency are discussed in-depth in *Laboratory Evaluations in Integrative and Functional Medicine*, which can be ordered at www.gdx.net.

For further information about this test and other services offered visit www.gdx.net.

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