Diagnostic Solutions laboratory

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INTERPRETIVE GUIDE

OAP - Organic Acids Profile™

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner

OAP™

ORGANIC ACIDS PROFILE

OAP™
ORGANIC ACIDS PROFILE

FIRST OF ALL

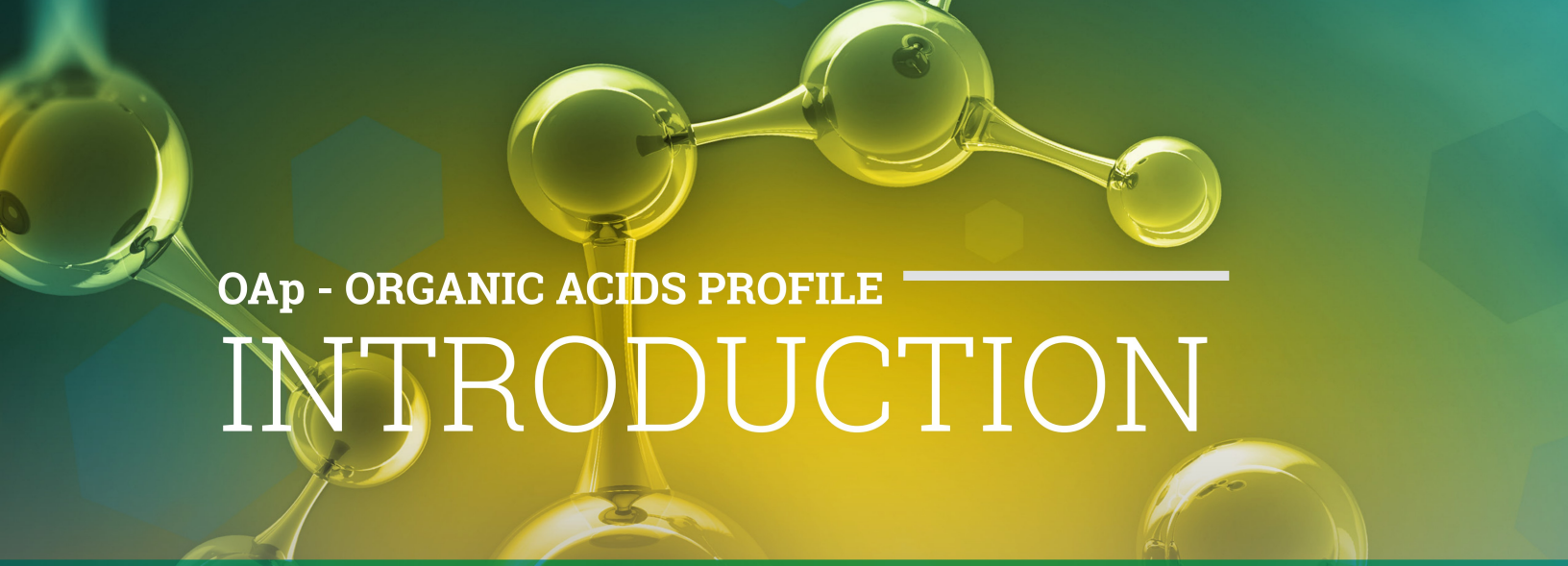
THANK YOU

FOR CONSIDERING US!

"At Diagnostic Solutions Laboratory, we're not content with the range of clinical testing currently available to practitioners. We believe that every patient should achieve optimal health, and we're driven to give clinicians the tools to do so. Our mission, therefore, is to use our resources to bring the most advanced, innovative, and clinically relevant testing to healthcare providers worldwide."

Tony Hoffman
CEO

CONTENT



OAp - ORGANIC ACIDS PROFILE

INTRODUCTION

WHAT ARE ORGANIC ACIDS AND WHY TEST ORGANIC ACIDS?

Organic acids are small molecules produced as byproducts of normal metabolic reactions. These metabolic reactions are involved in energy metabolism, detoxification processes, amino acid catabolism, neurotransmitter synthesis, microbial activity, and environmental exposures, just to name a few.

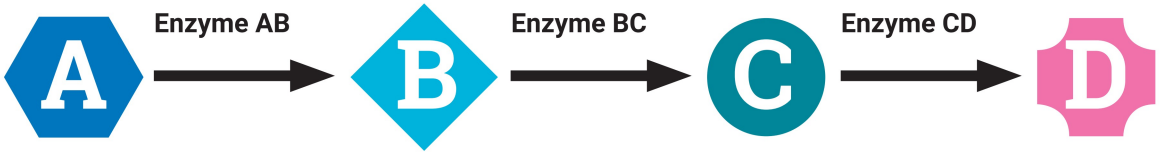
Under conditions of well-functioning metabolic pathways, metabolic intermediates flow smoothly through pathways and will not accumulate in urine. On the other hand, when enzymes are impaired, nutrient cofactors are insufficient, or enzyme inhibitors are present, pathways become blocked. This results in abnormal levels of organic acids in urine.

Testing organic acids offers insights into energy metabolism, mitochondrial function, fat metabolism, nutrient deficiencies, glutathione status, toxic exposure, oxidative stress, neurotransmitter metabolism, microbial overgrowth, and inborn errors of metabolism. Repeat testing can serve as a tool to monitor the effectiveness of treatment therapies and supplementation.

It is standard laboratory procedure to normalize organic acids to creatinine.

Normal Metabolic Pathway

Optimal enzyme function with no inhibition and sufficient nutrient cofactors.



Obstructed Metabolic Pathway

Reduced or blocked enzyme function due to environmental exposures, individual genetics, lifestyle factors, or nutrient co-factor availability can lead to organic acid breakdown products spilling into the urine.

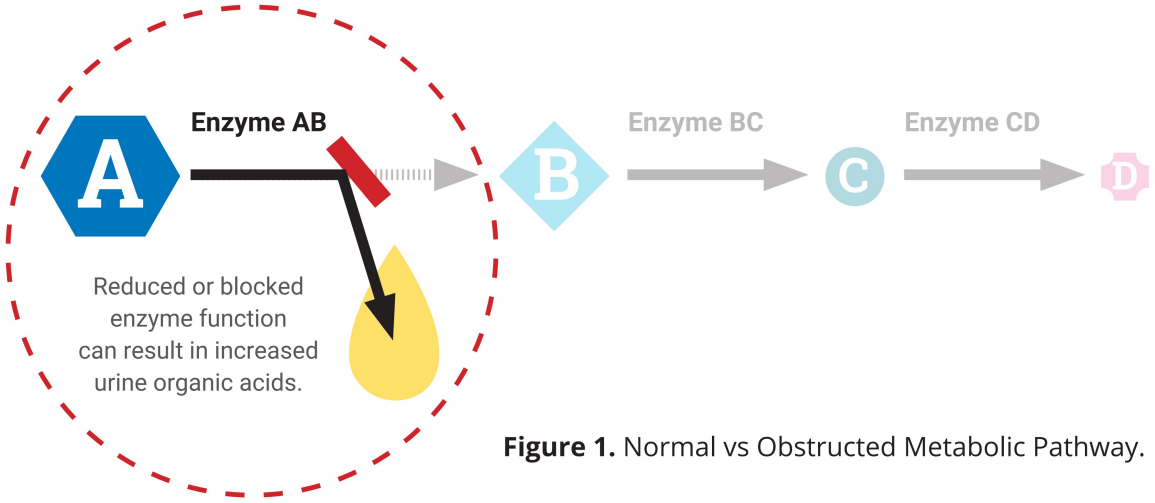


Figure 1. Normal vs Obstructed Metabolic Pathway.

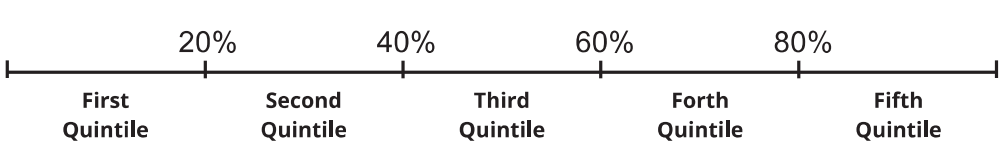
NOTE: The OAp - Organic Acids Profile test should be performed in first morning urine. For optimal results, collect the urine sample upon awakening after an overnight fast. Results may be impacted if samples were not following an overnight night fast or collected later in the day. Avoid consuming fruits, jams, and jellies for 48 hours prior to collecting your sample.

HOW TO READ THE REPORT

DEFINITION OF PERCENTILES AND QUINTILES

OAp reports results as actual values and shows quintile position on a bar graph.

A percentile is a statistical value that ranks results from smallest to largest and divides all results into 20% sections, from 0% to 100%, making five total sections—or quintiles.



- First quintile includes results that fall in 1% to 20%
- Second quintile are results that fall in 21% to 40%
- Third quintile are results that fall in 41% to 60%
- Fourth quintile are results that fall in 61% to 80%
- Fifth quintile are results that fall in 81% to 100%

Figure 1. Percentiles can tell us where a specific result falls in comparison to all other population results.

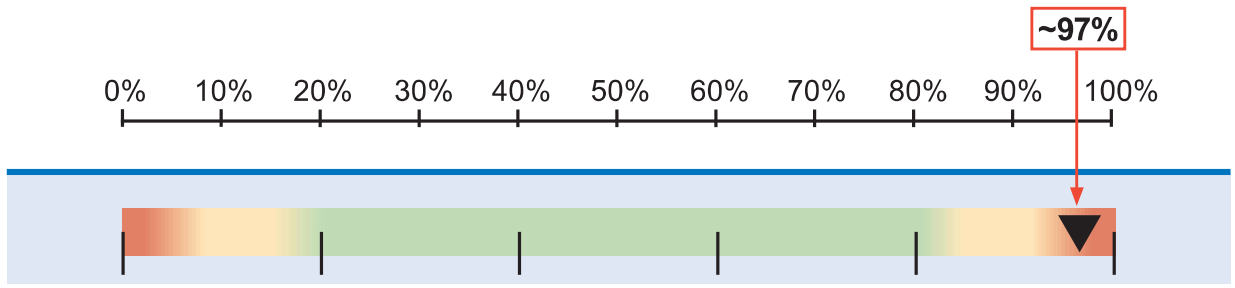


Figure 2. This example shows a result in the top quintile and above 90%. The result is higher than 97% of people in the reference population, putting this value in the top 3% of results.

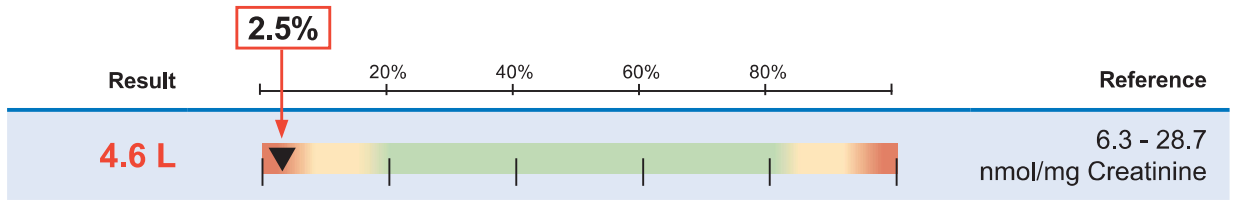


Figure 3. This example shows a result in the bottom 2.5%. This means the result is significantly lower than the reference population, with 97.5% of people testing higher.

One-Tailed Test vs. Two-Tailed Test

Analytes with values at both the high and low ends of the quintile bar are called a two-tailed test. This means high and low results are both significant.

Some analytes are only significant when they are high or low and are called a one-tailed test.

A Note on Nomenclature

Organic acids can end in "-ic acid" or "ate." Using "pyruvic acid" as an example, it is also interchangeably referred to as "pyruvate." Pyruvate is the conjugate base of pyruvic acid, meaning that pyruvate has the potential to gain or absorb a proton in a chemical reaction. Therefore, the main difference between the acid and the conjuage base is that pyruvate is an anion with a negative charge, whereas pyruvic acid is a neutral molecule. Other examples include, succinic acid and succinate, adipic adic and adipate, or methylmalonic acid or methylmalonate (MMA).

Alternate nomenclature is included below some analytes in the quick reference guide. The Human Metabolome Database is the definitive source for metabolomics nomenclature and can be found at hmdb.ca.

THE OAp - ORGANIC ACIDS PROFILE IS DIVIDED INTO THE FOLLOWING SECTIONS

I. ENERGY & MITOCHONDRIAL PROCESSING

II. NUTRITION

III. STRESS & MOOD

IV. TOXIC IMPACTS

V. MICROBIAL METABOLITES

ENERGY & MITOCHONDRIAL PROCESSING

Mitochondrial energy processing involves the conversion of dietary macronutrients into ATP through the processes of cellular respiration. This involves glycolysis, Krebs cycle (citric acid cycle) and oxidative phosphorylation occurs in the mitochondria of cells.

GLYCOLYSIS: B1, B2, B3, B5, Lipoic Acid (LA), Magnesium, and CoQ10 are primary cofactors.

Aerobic Settings: Carbohydrates → glucose → pyruvic acid → acetyl-CoA.

Anaerobic Settings: Carbohydrates → glucose → pyruvic acid → lactic acid.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Glucose	• Glucose identifies overall processing of dietary carbohydrates. • Small amounts of glucose may be found in the urine of healthy individuals.	• Elevated urinary glucose levels should be investigated further. Check microalbumin and creatinine for kidney function and HbA1c in the OMX™ Organic Metabolomics Profile. • Monitor diet/increase exercise/decrease weight. • Consider magnesium supplementation – magnesium aids insulin secretion and glucose utilization.	• Low is the expected finding. • Low urine value does not exclude elevated blood glucose.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Pyruvic Acid (Pyruvate)	• Pyruvic acid feeds into the Krebs cycle and converts to acetyl-CoA in aerobic settings. • In anaerobic conditions, pyruvic acid converts to lactic acid.	• High pyruvic acid is associated with increased glucose uptake, insulin resistance, obesity, and type 2 diabetes mellitus. » If glucose is also elevated, check HbA1c. • Elevated levels are strongly associated with B1 (thiamin) deficiency. • Consider support with B-complex vitamin cofactors, B1, B2, B3, B5, lipoic acid (LA), and magnesium.	• Low is the expected finding.
Lactic Acid (Lactate)	• Lactic acid is produced endogenously under anaerobic conditions. • The main route of lactic acid disposal is conversion to pyruvic acid or excretion via urine.	• High lactic acid is associated with diabetes, fasting glucose, HOMA-IR, inflammatory bowel disease (IBD), and chronic kidney disease. • Associated nutrient deficiencies: vitamin B1, CoQ10, and/or lipoic acid (LA).	• Low is the expected finding. • Consider checking T4.
D-Lactic Acid	• D-lactic acid is a harmful compound. • Methylglyoxal (MGO) is a by-product of glucose metabolism. D-lactic acid levels reflect cumulative MGO exposure. • MGO is a precursor of advanced glycation end products (AGEs), which are associated with inflammation and oxidative stress.	• D-lactic acid levels are associated with increased glucose levels (check glycolysis markers), bowel surgery and dysbiosis (check microbial markers), and foods with propylene glycol (dairy products, salad dressings, and fermented foods).	• Low is the expected finding.

KREBS CYCLE: B1, B2, B3, B5, B6, Lipoic Acid, Magnesium, CoQ10, and Amino Acids are primary cofactors

Carbohydrates (from glycolysis), fats (from beta-oxidation), and protein (via amino acids) all enter the Krebs cycle as acetyl-CoA to generate energy (ATP). Protein intake and breakdown can impact the overall flow of the Krebs cycle. Very high protein intake may increase Krebs cycle markers, while a low protein intake may decrease Krebs cycle markers.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Citric Acid (Citrate)	• Citric acid is a metabolite of acetyl-CoA and a precursor of aconitic and isocitric acid.	• Diet has a significant impact on citric acid levels: » Plant-based diets increase citric acid. » Citrus or pectin foods, alkaline minerals or coconut water, fruits and vegetables, or citrate supplements (such as magnesium citrate) increase citric acid levels. » Urinary citric acid is increased in metabolic alkalosis as well as by increased estrogen, parathyroid hormone and growth hormone, and excess vitamin D. • High citric acid levels can block pyruvate dehydrogenase (PDH) and succinic acid dehydrogenase (SDH) enzymes.	• Low urine citric acid levels are associated with acidosis including dietary or metabolic, hypokalemia, kidney disease, insulin resistance, and immune-mediated inflammatory diseases. » High animal-based proteins or severe carbohydrate restriction can increase acid load. • Low citric acid levels are considered a risk factor for kidney stones. • Low citric acid is also seen with starvation, chronic diarrhea, increased testosterone, strenuous exercise, angiotensin-converting enzyme (ACE) inhibitors, and hypoparathyroidism. • Consider potassium or magnesium citrate supplementation or changes in diet to improve acid-base balance.
cis-Aconitic Acid	• Isocitric acid is formed from citric acid via aconitase enzyme. • Isocitrate dehydrogenase converts isocitric acid to a-ketoglutaric acid (AKG).	• May be elevated in inflammation or impaired metabolism due to a lack of cofactors (B3, magnesium, and manganese). • Consider antioxidant support. • Aluminum may inhibit aconitase activity.	• Reduced in chronic kidney disease. • May be impacted by low citric acid.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Isocitric Acid	• Isocitric acid is formed from citric acid via aconitase enzyme. • Isocitrate dehydrogenase converts isocitric acid to α-ketoglutaric acid (AKG).	• May be elevated in inflammation or impaired metabolism due to a lack of cofactors (B3, magnesium, and manganese). • Consider antioxidant support. • Aluminum may inhibit aconitase activity.	• Reduced in chronic kidney disease. • May be impacted by low citric acid
α-Ketoglutaric Acid (Alpha-ketoglutarate or AKG)	• Metabolite of isocitric acid and glutamic acid; precursor of succinic acid.	• Consider support with B-complex vitamin cofactors, B1, B2, B3, B5, lipoic acid (LA), and magnesium (needed for B1 activity). » Elevated levels strongly associated with B1 (thiamin) deficiency in inborn errors. • On OMX, evaluate levels of amino acids that enter the Krebs cycle at AKG: arginine, histidine, and glutamine.	• Reduced in chronic kidney disease. • On OMX, evaluate levels of amino acids that enter the Krebs cycle at AKG: arginine, histidine, and glutamine. Support if low.
Succinic Acid (Succinate)	• Metabolite of AKG and end product of some amino acids. • Strong indicator of mitochondrial function.	• Consider support with B2, B6, CoQ10, magnesium, and antioxidants. » Succinate is an iron-sulfur cluster dependent enzyme. Iron deficiency decreases function. • On OMX, check amino acids that flow into the Krebs cycle at succinyl CoA: valine, isoleucine, methionine, and threonine.	• Lower in ulcerative colitis and Crohn's disease patients – consider GI-MAP™ stool test. • Reduced in chronic kidney disease. • On OMX, check amino acids that flow into the Krebs cycle at succinyl CoA: valine, isoleucine, methionine, and threonine. Support if low.
Fumaric Acid (Fumarate)	• Metabolite of succinic acid and precursor to malic acid. • End product of tyrosine via homogentisic acid.	• On OMX, check amino acids that flow into the Krebs cycle at fumaric acid: tyrosine and phenylalanine. • Evaluate B-complex status, most notably B2 and B5. Support if low. • May predict disease progression in chronic kidney disease and type 2 diabetes.	• Low is the expected finding. • On OMX, check amino acids that flow into the Krebs cycle at fumaric acid: tyrosine and phenylalanine. Support if low.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Malic Acid (Malate)	• Metabolite of fumaric acid and precursor of oxaloacetate.	• Malic acid is abundant in apricots, black and blueberries, cherries, grapes, peaches, pears, plums, and wine. Dietary intake may increase levels. • Evaluate B-complex status, notably B3. Support if low. • May predict disease progression in chronic kidney disease and type 2 diabetes.	• May be secondary to low fumaric acid or other Krebs cycle intermediates.

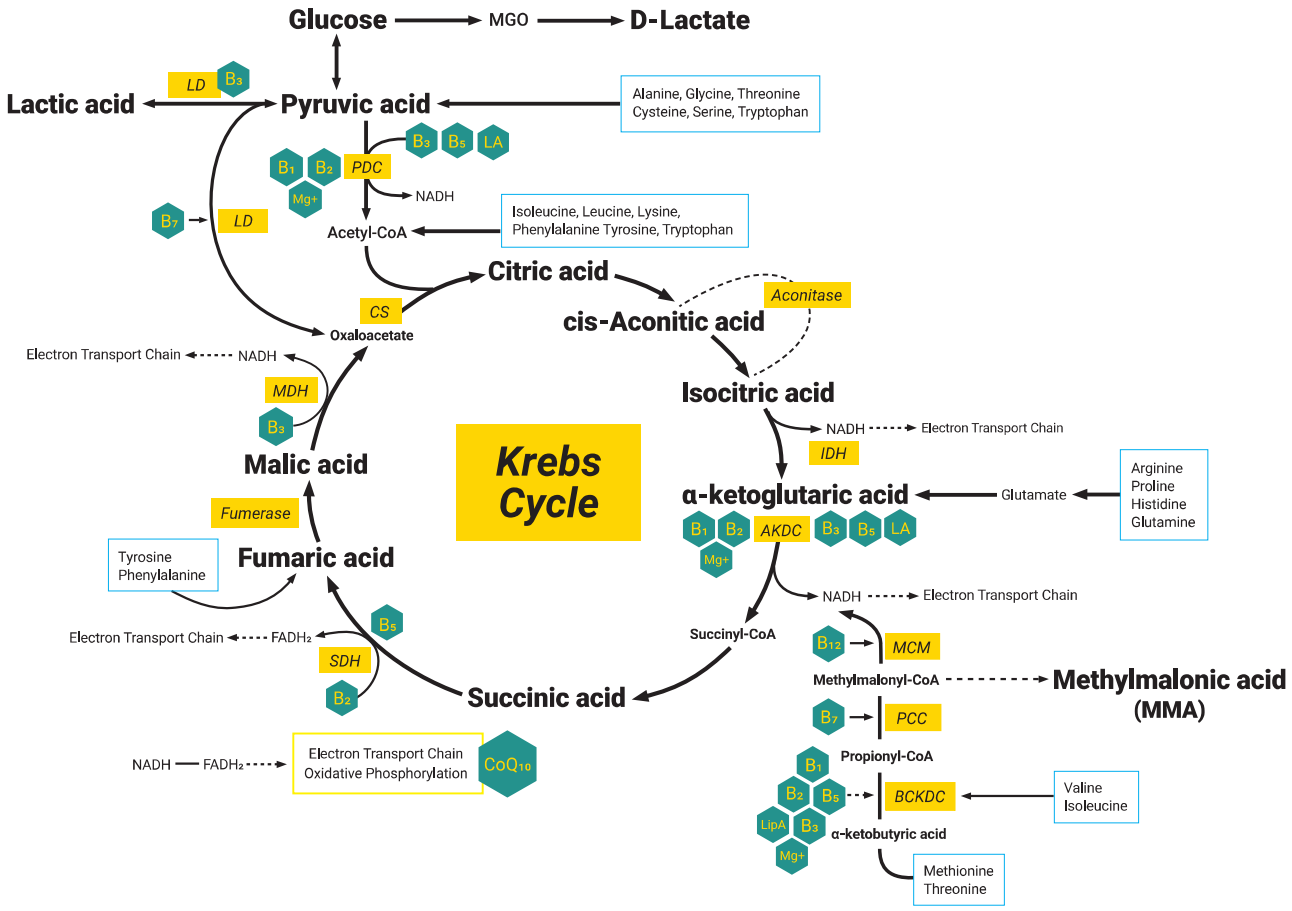


Figure 4. Glycolysis – Krebs Cycle. The tricarboxylic acid cycle (TCA, also known as the citric acid cycle or the Krebs cycle).

FATTY ACIDS OXIDATION: B2, B3, and carnitine are primary cofactors.

Fatty acids undergo beta-oxidation to enter the Krebs cycle to be used as energy.
Via beta-oxidation: Fats → fatty acids → acetyl-CoA.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Branched-Chain, Dicarboxylic Acids: • Ethylmalonic Acid (C5) • 2-Methylsuccinic Acid (C5)	• A deficiency of short-chain acyl-CoA dehydrogenase (SCAD) can result in significantly increased excretion of ethylmalonic acid and methylsuccinic acid. • SCAD deficiency is often asymptomatic, except in times of stress	• Consider supplementation of B2, as well as B6, magnesium, and carnitine. » B2 (riboflavin) has been shown to be effective for decreasing ethylmalonic acid. • Ethylmalonic acid and methylsuccinic acid are increased in SCAD deficiency. Treatment includes a diet high in carbohydrates and low in fat (primarily low in medium-chain triglycerides) and carnitine. » High levels of ethylmalonic acid can induce acidosis. Check urine pH. » Women with the highest ethylmalonic acid excretion had >10-fold increased risk of gestational diabetes. » Increased ethylmalonic acid may be from increased methionine intake or levels.	• Low is the expected finding.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Dicarboxylic Acids: • Adipic Acid (C6) • Pimelic Acid (C7) • Suberic Acid (C8) • Sebacic Acid (C10)	• Dicarboxylic acids are formed from impaired fatty acid oxidation and thus can be used to identify impaired beta-oxidation.	• Dicarboxylic acid levels may be elevated with B2 and carnitine deficiency. » A diet low in methionine or lysine, a vitamin C deficiency, liver disease, or kidney dialysis can lead to carnitine deficiency. • Levels can increase in ketosis, starvation, genetic fatty acid oxidation disorders, chronic alcohol consumption, intake of MCT oil, and other metabolic conditions. • Adipic, suberic, and sebacic acids are elevated in medium-chain acyl-CoA dehydrogenase (MCAD) deficiency. Sebacic acid is also seen in multiple acyl-CoA dehydrogenase deficiency (MADD). • Evaluate intake of high-adipate foods such as beets, sugarcane, jams, jellies, and Jell-O®. • Elevated pimelic acid is seen in biotin deficiency. See β-hydroxyisovaleric acid in Nutrition section. • Sebacic acid is used in plasticizers, lubricants, hydraulic fluids, and cosmetics. Consider environmental exposure.	• Low is the expected finding.

CARNITINE DEPLETION

Carnitine is a metabolic cofactor that helps transport long-chain fatty acids into the mitochondria so that they can undergo beta oxidation to produce ATP.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Glutaric Acid (Glutarate)	• Produced in the breakdown of lysine or tryptophan and utilizes carnitine when produced.	» Increased glutaric acid is associated with secondary carnitine deficiency.	• Low is the expected finding.

KETONES

The presence of ketones implies the body is using fat for fuel, commonly seen during fasting, a high-fat or ketogenic diet, or prolonged exercise. Ketones are produced in the liver from fatty acid oxidation from adipose tissue.

MARKER	DESCRIPTION	IF HIGH	IF LOW
β-Hydroxybutyric Acid (3-Hydroxybutyrate) (β-Hydroxybutyrate)	• β-hydroxybutyric acid is a ketone and a byproduct of fatty acid metabolism and makes up ~70% of ketones produced in liver mitochondria. • Urine ketones reflect serum ketones.	• Increased in fasting, starvation or very low carbohydrate diets, strenuous exercise, and metabolic issues. • B3 is a nutrient cofactor for β-hydroxybutyrate dehydrogenase, and needs may be increased during ketogenesis. • Non-diet causes include diabetes, corticosteroid or growth hormone deficiency, excess alcohol or salicylates, and several inborn errors of metabolism.	• Low is the expected finding.

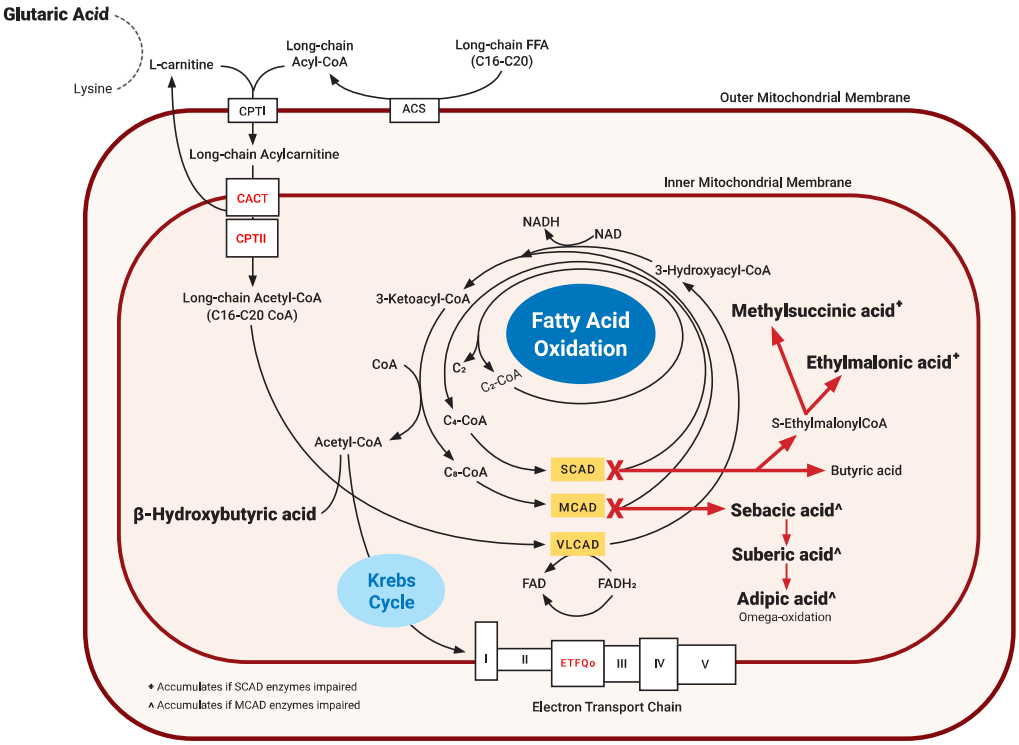


Figure 5. Fatty Acid Oxidation

NUTRITION

Vitamins act as nutrient co-factors in metabolic functions. Vitamin levels are dependent on adequate dietary intake, intestinal absorption, and commensal bacteria. Diet, GI health, and gut bacteria should be evaluated when vitamin needs are identified.

B-COMPLEX VITAMINS: B1, B2, B3, B5, Lipoic Acid (LA)

MARKER	DESCRIPTION	IF HIGH	IF LOW
Branched-Chain Alpha Keto Acids (BKCD) • α-Ketoisovaleric Acid • α-Keto-β-Methylvaleric Acid • α-Ketoisocaproic Acid • α-Ketoglutaric Acid • Pyruvic Acid	• All enzymes in this section are dependent on B-complex vitamins, primarily B1 (thiamin). • 3 branched-chain α-keto dehydrogenase (BCKD). • Alpha-ketoglutarate dehydrogenase. • Pyruvate dehydrogenase.	» Need for B-complex vitamins, including vitamin B1, B2, B3, B5, and lipoic acid (LA). » Vitamin B1 needs magnesium for absorption and activation.	• Low is the expected finding.

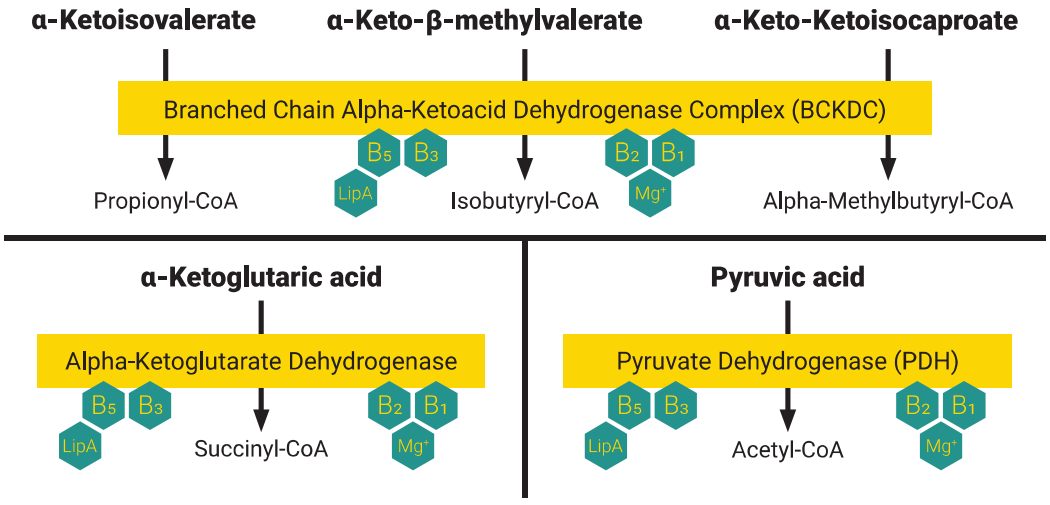


Figure 6. B-Complex Markers: B1, B2, B3, B5, Lipoic Acid (LA)

VITAMIN B12 (COBALAMIN)

MARKER	DESCRIPTION	IF HIGH	IF LOW
Methylmalonic Acid (MMA) (Methylmalonate)	• Urine methylmalonic acid (MMA) correlates with serum vitamin B12 deficiency. • Vitamin B12 is required for the conversion of MMA to succinyl CoA. When B12 is insufficient, MMA will accumulate and spill over into urine.	• Identifies a functional need for vitamin B12. The following may impact B12 levels: » Low dietary intake (vegan/vegetarian diets), low stomach acid, impaired digestion and absorption, gut dysbiosis, dehydration, older age, and renal function. » Disease states such as celiac disease, liver disease, and pernicious or megaloblastic anemia. » Medications such as metformin, proton pump inhibitors, and histamine H2 blockers.	• Low is the expected finding.

FOLATE (VITAMIN B9)

MARKER	DESCRIPTION	IF HIGH	IF LOW
Formiminoglutamic Acid (Formiminoglutamate or FIGLU)	• FIGLU is the intermediate metabolite in the pathway that converts histidine to glutamic acid. • Folate is naturally occurring while folic acid is the major synthetic form of vitamin B9.	• Identifies a need for folate. • Folate is dependent on vitamin B12 for methylation – check methylmalonic acid (MMA) level.	• Low is the expected finding.

VITAMIN B6

MARKER	DESCRIPTION	IF HIGH	IF LOW
Pyridoxic Acid* (4-Pyridoxate)	• Identifies levels of vitamin B6 intake. • Pyridoxic acid is a catabolic product of B6 excreted in urine. • Urine pyridoxic acid correlates with plasma pyridoxal 5'-phosphate (PLP) and red blood cell (RBC) PLP. • Levels vary according to B6 intake and respond quickly to supplementation/ repletion (1–2 weeks).	• Very high levels may identify excess B6 intake.	• Very low levels (<dl on the report) may indicate B6 need.
Xanthurenic Acid (Xanthurenate)	• Xanthurenic acid is a metabolite of the breakdown of tryptophan. • Can elevate early in B6 deficiency and is considered a functional marker of B6 status.	• Identifies a need for B6. • Elevated levels can be due to a block in a B6 dependent pathway.	• Low is the expected finding.

BIOTIN

MARKER	DESCRIPTION	IF HIGH	IF LOW
β-Hydroxyiso-valeric Acid (3-Hydroxyisovaleric Acid)	• Increased urinary excretion of 3-hydroxyisovaleric acid is used as an indicator of biotin deficiency.	• Identifies a need for biotin. • Pimelic acid in the Fatty Acid Oxidation section may also be elevated. • Ketogenic diets have been associated with biotin deficiencies. • Biotin needs are increased in smokers.	• Low is the expected finding.

PLANT COMPONENTS

MARKER	DESCRIPTION	IF HIGH	IF LOW
Quercetin	• Quercetin is a flavonoid that has antimicrobial properties. • Urinary quercetin has been suggested as a marker of absorbed quercetin.	• Assess diet. Quercetin is found in plants such as tea, onions, cruciferous vegetables, and dark berries. • Can consider quercetin supplement.	• Low levels may indicate a diet low in quercetin-rich foods.
Tartaric Acid (Tartarate)	• Tartaric acid is an analog of malic acid and can inhibit its production – may impact Krebs cycle function.	• Assess diet. Tartaric acid is found naturally in some foods, primarily grapes and wine. » It is a "biomarker" of red wine intake. • Commonly used as a food additive due to its antioxidant properties. • *Candida* spp. cells grown in a lactic acid medium produced tartaric acid. » Elevated levels do not confirm *Candida* spp. overgrowth.	• Diet may be low in grapes or wine. • Tartaric acid can be utilized by gut bacteria as a carbon source.

SUGAR INTAKE

MARKER	DESCRIPTION	IF HIGH	IF LOW
Fructose	• Fructose is a naturally occurring sugar found in fruits and honey. • High-fructose corn syrup (HFCS) is a sweetener made from corn starch and is in many processed foods. • The body can generally metabolize small doses of fructose, especially when consumed over time or during a meal. • Research suggests a relationship between the rise in metabolic diseases and increased consumption of fructose.	• Identifies increased fructose intake. • Increased fructose, primarily from HFCS in non-natural sources (sugar-sweetened beverages and processed foods). • Fruit and honey are natural sources. • Elevated fructose levels should be further investigated and modified if excessive. Monitor for metabolic function. • Excess fructose is associated with nonalcoholic fatty liver disease (NAFLD), increased advanced glycation end products (AGEs), metabolic inflammation, lipid dysregulation, dysbiosis, compromised renal function, disordered eating, and cognition.	• Identifies lower fructose intake. • Low is the expected finding.

STRESS & MOOD

Stress can lead to alterations in catecholamine and serotonin turnover metabolites. Tracking these metabolites provides insights into the physiological impact of stress on neurotransmitter dynamics.

CATECHOLAMINE TURNOVER

Metabolite of tyrosine breakdown (catabolism).

MARKER	DESCRIPTION	IF HIGH	IF LOW
Homovanillic Acid (HVA)* (Homovanillate)	• Homovanillic acid (HVA) is a major metabolite derived from the breakdown of dopamine, one of the key catecholamine neurotransmitters in the body. • HVA represents dopamine turnover. • The conversion of dopamine to HVA occurs via monoamine oxide (MAO) and catechol-O-methyltransferase (COMT). • Dopamine is converted to norepinephrine via dopamine-beta-hydroxylase (DBH).	• Higher levels represent increased dopamine turnover. • Seen in anxiety, stress, autism spectrum disorder (ASD), and sleep apnea. • Represents increased catecholamine activity/stress. » Consider stress reduction techniques. » Consider nutrients to support COMT and methylation (vitamin B12, B6, folate, and magnesium) and MAO deamination (vitamin B2). • Higher levels seen in an impaired ability to convert dopamine to norepinephrine via DBH. » Consider cofactors (copper and vitamin C). • HVA is also a metabolite of microbial bioactivity of flavonoids – consider GI-MAP to check dysbiosis. • Elevated levels will be seen with medications influencing dopamine metabolism such as Parkinson's disease medications.	• Low HVA levels are related to low dopamine or low dopamine turnover. Very low levels on the report (<dl) may indicate reduced dopamine turnover. • Ensure nutrients and cofactors for dopamine synthesis, such as tyrosine, phenylalanine, iron, vitamin B6, and tetrahydrobiopterin (BH4). • Ensure adequate nutrients for COMT methylation (vitamin B12, B6, folate, and magnesium) and MAO deamination (vitamin B2). • Low levels are associated with higher scores on the Beck Depression Inventory-II. • Lower levels seen with pesticide exposure.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Vanillylmandelic Acid (VMA) (Vanillylmandelate)	• Vanillylmandelic acid (VMA) is the major metabolite derived from the breakdown of epinephrine and norepinephrine, key catecholamine neurotransmitters in the body. • VMA represents epinephrine and norepinephrine turnover.	• Higher levels represent increased epinephrine/ norepinephrine turnover. • Elevated levels are typically seen with stress and chronic stress where there is a consistent release of catecholamines. » Consider stress reduction techniques. » Consider support with magnesium. • Higher levels seen in post-traumatic stress disorder (PTSD) and anxiety.	• Low levels are associated with lower stress and less anxiety. • Lower levels can result from impaired pathways: » Dopamine conversion to norepinephrine via DBH (copper and vitamin C). » Breakdown of epinephrine and norepinephrine via COMT methylation (vitamin B12, B6, folate, and magnesium) and MAO deamination (vitamin B2).
HVA/VMA Ratio	• Dopamine is converted to norepinephrine via Dopamine-beta-hydroxylase (DBH) enzyme. • The HVA/VMA ratio reflects the balance of dopamine and norepinephrine epinephrine. • Impaired DBH has been implicated in addiction, ADHD, Alzheimer's disease. Schizophrenia.	• Decreased conversion of dopamine to norepinephrine, primarily due to impaired DBH enzyme. » Consider DBH cofactors- copper, vitamin C. • High levels seen with genetic polymorphisms (SNPs) on DPH enzyme resulting in reduced activity. • *p*-Cresol, produced from tyrosine fermentation via 4-Hydroxyphenylacetic Acid is a potent inhibitor of DBH.	• Low levels reflect sufficient conversion of dopamine to norepinephrine and indicates normal pathway function.

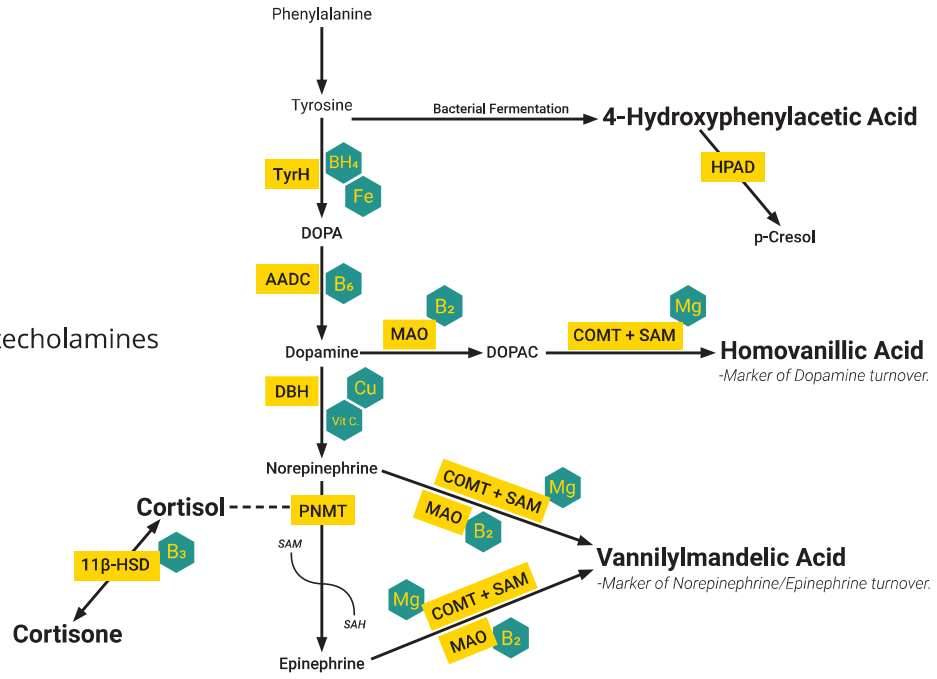


Figure 7. Tyrosine Catecholamines

SEROTONIN TURNOVER

Metabolites of tryptophan breakdown (catabolism).

MARKER	DESCRIPTION	IF HIGH	IF LOW
5-Hydroxy-indoleacetic Acid* (5-HIAA)*	• 5-hydroxyindoleacetic acid (5-HIAA) represents serotonin turnover. • First morning 5-HIAA correlates with 24-hour in urine.	• Higher levels represent more serotonin turnover/ breakdown. • High levels are seen in those taking SSRI medications or 5-HTP supplements. • 5-HIAA may increase after eating foods high in 5-HTP such as bananas, pineapple, tomatoes, kiwi fruit, and walnuts.	• Low levels may indicate inadequate serotonin production. • Very low levels (<dl on the report) may indicate decreased serotonin turnover and need for support. • Low levels are associated with depression and anxiety. • Consider 5-HTP supplementation and/or increase dietary sources.
Picolinic Acid (Picolinate; PA)	• A tryptophan metabolite. • Aids in maintaining balance between neurotoxic and neuroprotective states. • Can aid in zinc absorption.	• Can increase with viral infections. • Produced under inflammatory conditions (IFN-gamma). • May identify re-routing of the tryptophan pathway to prevent build-up of quinolinic acid. » Picolinic acid has antagonistic properties towards the toxic effects of quinolinic acid.	• Low is the expected finding. • Can be decreased in nephritis. • May identify utilization of tryptophan into the Krebs cycle for energy use.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Kynurenic Acid (Kynurenate; KA)	• A product of tryptophan catabolism. • Kynurenic acid is an N-methyl-D-aspartate (NMDA) antagonist.	• Can be neuroprotective against increased quinolinic acid. • A long term B6 deficiency may result in elevated levels, along with xanthurenic acid. Check B6 in the Nutrition section. • Exercise may increase kynurenic acid.	• A moderate B6 deficiency resulted in slight decreases in kynurenic acid with tryptophan load.
Quinolinic Acid (Quinolinate; QA)	• A product of tryptophan catabolism. • Quinolinic acid is an NMDA receptor agonist and acts as an excitotoxin.	• Excessive quinolinic acid is considered to be neuroinflammatory and is seen in autism spectrum disorder (ASD), suicidal patients, viral infections, metabolic syndrome, and more. » Increased neuroinflammation from QA can be modulated by the neuroprotective properties of KA. • Avoid phthalate exposure. Phthalates structurally mimic tryptophan metabolites. High phthalate exposure can increase QA by decreasing the quinolinate phosphoribosyl transferase (QPRT) enzyme. • Inflammation can increase QA by decreasing the QPRT enzyme – consider antioxidants such as vitamin D, polyphenols, EPA/DHA, and magnesium. Avoid phthalates and alcohol.	• Low is the expected finding. • Low levels have been noted in niacin deficiency.
Quinolinic Acid/ Kynurenic Acid Ratio (QA/KA Ratio)	• Quinolinic acid and kynurenic acid have opposing neuroactive properties and alterations in their balance may play a role in neurodegenerative and neuropsychiatric diseases.	• Elevated levels are neuroinflammatory and excitotoxic. » Consider antioxidants, magnesium, and exercise.	• Healthy subjects had a decreased quinolinic acid/ kynurenic acid ratio.

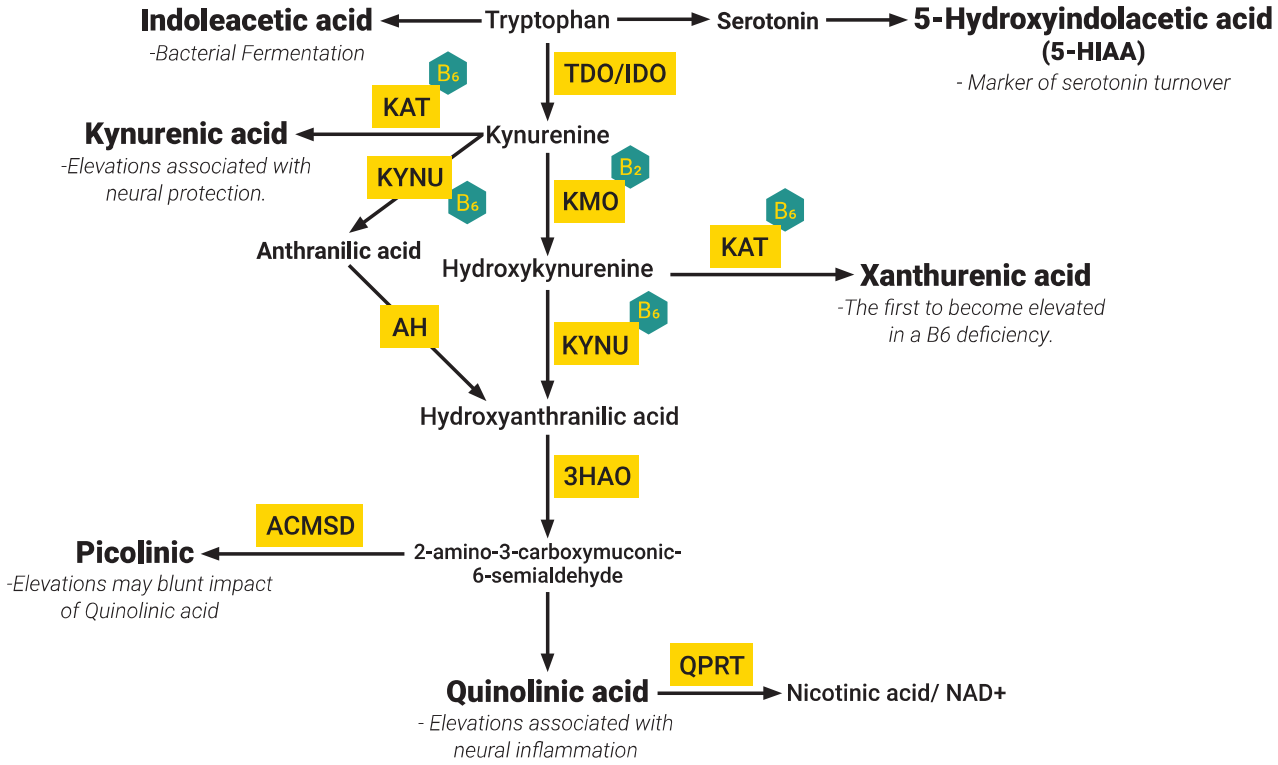


Figure 8. Tryptophan: Serotonin Turnover. Tryptophan's main pathway is the kynurenine pathway, which favors quinolinic acid since it results in essential NAD+ production. Excess quinolinic acid is associated with neural inflammation, while kynurenic acid is neuroprotective. Alterations in their balance may play a role in neurodegenerative and neuropsychiatric diseases. Picolinic acid has immunomodulatory properties. The balance can be modulated with anti-inflammatory support, vitamin B6 and B2 supplementation, and reduced exposure to toxicants such as phthalates. Only 1–2% of tryptophan is metabolized to serotonin, which is broken down to 5-hydroxyindolacetic acid (5-HIAA) or converted to melatonin.

STEROID HORMONES

MARKER	DESCRIPTION	IF HIGH	IF LOW
Cortisol	• Cortisol is a major active glucocorticoid, which regulates glucose metabolism. • The hypothalamic-pituitary-adrenal axis (HPA) regulates cortisol synthesis and release. • 11β-hydroxysteroid dehydrogenase (11β-HSD) mediates the interconversion between active cortisol and inactive cortisone. » Inflammatory markers such as CRP and TNFα may upregulate 11β-HSD1 activity.	• Higher in acute stress, depression, bipolar, schizophrenia, dyslipidemia, hypertension, hyperglycemia, Cushing syndrome, pregnancy, hydrocortisone use, smoking, excess licorice, caffeine or high-calorie food intake. • Elevated cortisol can alter or disrupt the function of the digestive system, reproductive system, immune system, and growth processes. • Cortisol clearance depends on irreversible metabolic inactivation in the liver and urinary excretion. • Levels can be reduced with the establishment of sleep-wake cycles, massage therapy, exercise, exposure to nature, supplements such as magnesium and omega-3 fatty acids, herbs such as ashwagandha, lemon balm, and chamomile, an anti-inflammatory diet, and gut microbiome support.	• Low levels have been associated with post-traumatic stress disorder (PTSD), low blood pressure, infections, chronic glucocorticoid use, or adrenal issues. • Lower values are generally seen later in the day. • Values may be lower in kidney disease.
Cortisol/Cortisone Ratio	• The cortisol/cortisone ratio identifies 11β-HSD activity.	• A higher cortisol to cortisone ratio identifies 11β-HSD1 activity, which reactivates cortisone to active cortisol. • A higher cortisol/cortisone ratio is seen in chronic stress, inflammation, Cushing syndrome, mineralocorticoid excess, and ectopic ACTH syndrome	• A lower cortisol to cortisone ratio identifies 11β-HSD2 activity, which converts cortisol to inactive cortisone to prevent overstimulation by cortisol. • 11β-HSD2 is present in kidney, sweat glands, and intestinal epithelium. • Increased 11β-HSD2 activity is associated with obesity and increased oral glucose tolerance test (OGTT).

TOXIC IMPACTS

Markers of oxidative stress, toxin exposure, antioxidant defense, renal function, and metabolic health, aid in understanding overall physiological status and potential health risks.

OXIDATIVE DAMAGE

Oxidative stress is an imbalance of free radicals and antioxidants that can lead to cell and tissue damage. It occurs naturally and plays a role in aging.

MARKER	DESCRIPTION	IF HIGH	IF LOW
8-Hydroxy-2'-Deoxyguanosine **(8-OHdG or 8-OH-2-DG)**	• A DNA repair product. High levels identify oxidative damage to DNA. Found with arsenic exposure, insomnia, schizophrenia, and bipolar disorder.	• Increased oxidative stress: » Evaluate lifestyle, such as poor diet, exposure to smoke, smog, metal-containing particulate matter, ionizing radiation (UV light), high intake of charbroiled foods, excessive exercise, and more. » Consider antioxidant foods and supplements. • 8-OHdG has been associated with chronic inflammation, nutrient deficiency, cancer, atherosclerosis, and diabetes.	• Low is the expected finding.

TOXINS

Exposure to natural and man-made hazardous substances.

MARKER	DESCRIPTION	IF HIGH	IF LOW
2,3,4-Methyl-hippuric Acid (2,3 or 4-Methylhippurate)	• Methylhippuric acid is a metabolite and marker of xylene exposure – a petroleum product commonly used as a solvent. • Xylene is mainly metabolized in the liver via oxidation of methyl groups, followed by conjugation with glycine to yield hippuric acid.	• High levels of xylene have been noted in mitochondrial fatty acid beta-oxidation disorders, and have nervous, reproductive, immune, hepatic and respiratory effects. • Reduce exposure to tobacco smoke, gasoline, paint, varnish, shellac, and air fresheners. • Consider methylation support and glycine supplementation. • Check benzoic and hippuric acid in Microbial Metabolites section to determine adequate glycine conjugation.	• Low is the expected finding.
Mandelic Acid & Benzoylform (Phenylglyoxylic Acid)	• Mandelic acid and benzoylform are major metabolites of styrene and ethylbenzene exposure.	• Avoid exposure: » Inhalation of tobacco smoke, off-gassing of building materials and consumer products, and vehicle and industrial emissions account for over 90% of styrene exposure in the general population. » Polystrenes from food packaging and containers can leach into foods. » Levels are higher in smokers.	• Low is the expected finding. • A diet higher in vegetables and fruit is associated with decreased levels.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Glucaric Acid (Glucarate, D-Glucaric Acid or Saccharic Acid)	• Produced by cytochrome P450 activity. • It is an indicator of induced hepatic metabolization (clearance) of xenobiotics. • Glucaric acid is available as a dietary supplement in the form of calcium D-glucarate.	• Increases with phase 1 detoxification (P450 activity). • Increases with exposure to toxins, polychlorinated biphenyls (PCBs), alcohol, smoking, and medications such as acetaminophen. Evaluate for sources. • Vegetarians may have higher levels. Glucaric acid is found in grapefruit, apples, oranges, and cruciferous vegetables. » Glucaric acid from plant-based foods may act as a nontoxic β-glucuronidase inhibitor.	• Low is the expected finding.

GLUTATHIONE STATUS

Glutathione (GSH) is a major endogenous antioxidant that can neutralize reactive oxygen species. GSH is made up of three amino acids: glycine, cysteine, and glutamic acid.

MARKER	DESCRIPTION	IF HIGH	IF LOW
α-Hydroxybutyric Acid (Alpha-Hydroxybutyrate)	• Formed from the breakdown of alpha-ketobutyrate, in the production of glutathione. • α-hydroxybutyric acid may represent the rate of glutathione synthesis.	• Represents increased glutathione synthesis and thus a high potential need for glutathione support. • Consider supplementation with glycine or serine, N-acetylcysteine (NAC), B3, or glutathione.	• Low is the expected finding. • May be lower in ulcerative colitis and Crohn's disease.
α-Ketobutyric Acid (Alpha-Ketobutyrate)	• α-ketobutyric acid is produced from cystine during glutathione production, along with hydrogen sulfide (H2S) as a by-product. • α-ketobutyric acid is reversibly converted to α-hydroxybutyric acid. • Identifies cysteine formation.	• Can be increased in glutathione production.	• Low is the expected finding.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Pyroglutamic Acid (Pyroglutamate)	• Pyroglutamic acid is the last step of the glutathione cycle and is a marker of impaired glutathione production when elevated.	• Identifies cysteine insufficiency or glycine availability needed for glutathione production. Consider supplementation with: » Glycine or serine » Check benzoic acid for glycine use. » NAD+ precursor (like tryptophan and niacin) » NAC • Seen in drug-induced inhibition of glutathione synthetase, such as from acetaminophen. • Increased during oxidative stress, acidosis, sepsis, nonalcoholic fatty liver disease (NAFLD), and inborn errors.	• Low is the expected finding.

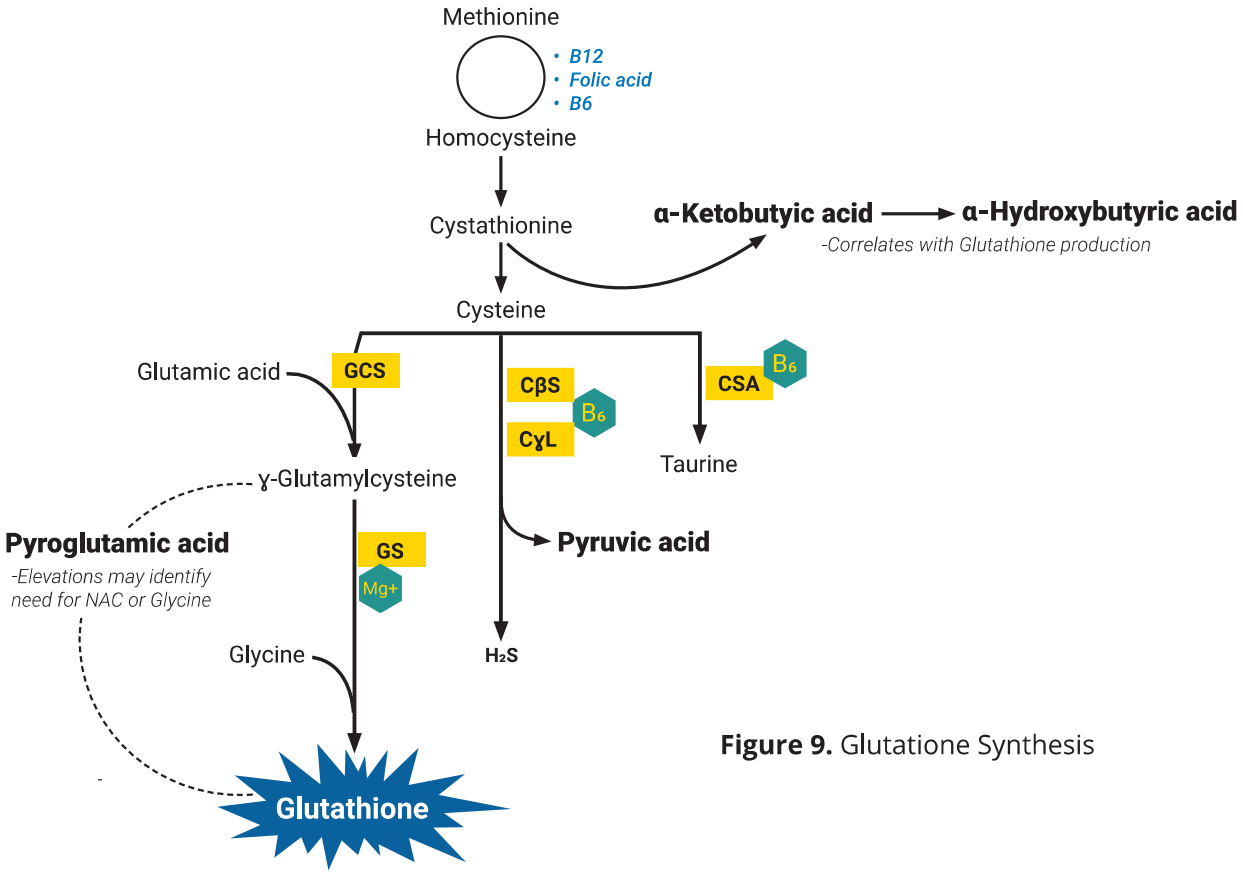


Figure 9. Glutathione Synthesis

KIDNEY IMPACTS

Kidney or renal functions include acid-base balance, regulating fluid, sodium, potassium, and clearing toxins, absorption of glucose and amino acids, regulation of blood pressure, and activation of vitamin D.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Orotic Acid (Orotate)	• Urinary excretion of orotic acid is an intermediate in pyrimidine biosynthesis (nitrogenous bases in DNA and RNA) and is increased in many urea cycle disorders. • Urea cycle disorders result in problems with ammonia clearance. • It has been noted as a carrier for zinc, magnesium, and carnitine.	• Elevated in urea cycle disorders. • May identify arginine or ornithine depletion – consider arginine supplementation. • Orotic acid is found in bovine milk and dairy products and root vegetables.	• Low is the expected finding.
Urine pH	• Urine pH measures acidity and ranges from 0 to 14. A pH of 7 is neutral, a pH result below 7 is acidic and above 7 is alkaline. • A common "normal" reference range for urine pH is 6.0–7.5, but the value is not generally clinically meaningful within the range of 4.5–8.0.	• Higher pH = alkaline. • A plant-based diet (high intake of fruits, nuts, and vegetables) is associated with an alkaline pH. • Kidney stones, urinary tract infection, and kidney issues are associated with a more alkaline environment.	• Lower pH = acidic • A diet high in animal protein, sodas, processed foods, and cereal grains is associated with a more acidic pH. • Diabetic ketoacidosis, diarrhea, and starvation.
Albumin (Microalbumin)	• Albumin is not normally found in the urine. • Albumin is associated with endothelial dysfunction. » Temporary dysfunction can occur with fever, dehydration, urinary tract infection (UTI), and after vigorous exercise.	• Elevated albuminuria has benign causes and may evaluate for cardiovascular disease, diabetes, kidney disease, cerebral, cardiac, and renal microcirculations. • Recommendations for follow-up include three measurements one month apart. • High in males, African Americans, Asians, smokers, people with higher muscle mass, urinary tract infections, or genital leakage.	• Low is the expected finding.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Phosphate	• Phosphate is a charged particle (ion) that contains the mineral phosphorus. • Maintaining phosphate homeostasis helps regulate intestinal absorption from the diet, the rate of bone turnover, and urinary excretion. » Urine levels are considered a marker of intestinal phosphate absorption.	• Seen with an increased intake of processed foods and drinks, increased hyper-parathyroidism, kidney stones, and long-term antacid use. • Phosphate toxicity has been associated with the "diseasome of aging."	• Low levels are seen with low vitamin D levels and exogenous insulin use.
Creatinine	• A marker of kidney function. • Creatinine is filtered out of the blood by the kidneys at a constant rate. • Creatinine level is impacted by kidney function, muscle mass, age, gender, and ethnicity. • Creatinine identifies urine concentration; markers on the OAp are normalized to creatinine.	• Identifies higher muscle mass or dehydration. • Elevated creatinine (urine or blood) can indicate kidney issues. Follow up with glomerular filtration rate (GFR).	• Lower value is seen in kidney disease, overhydration, or in those with lower mucle mass.
Aldosterone	• Aldosterone's primary function is to impact kidney sodium absorption and potassium excretion, which can impact blood pressure.	• Check blood pressure for subclinical hypertension and the presence of sleep apnea. • Clinical evidence has established strong associations between aldosterone excess, resistant hypertension, and obstructive sleep apnea.	• Low is the expected finding.

OXALATE METABOLISM

Oxalate homeostasis is maintained by a complex interplay of metabolic pathways, the microbiome, epithelial oxalate transporters, and adequate oxalate excretion.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Oxalic Acid (Oxalate)	• Oxalic acid is a uremic toxin. • Urinary levels represent both dietary oxalic acid and endogenous production. • Dietary oxalic acid is associated with kidney disease, cardiovascular conditions, cellular and systemic inflammation, and diabetes. • Endogenous oxalic acid production occurs primarily in the liver.	• Consider diet: » Higher-oxalate foods include spinach, brassica vegetables, rhubarb, legumes, beets, berries, potatoes, chocolate, nuts, beer, black tea, and coffee. » Cooking method can lower oxalate level: boiling > steaming > baking. » Avoid a high acid load diet – see urine pH. » Consume calcium-rich foods or beverages simultaneously with oxalate-containing foods to decrease oxalate absorption. • Evaluate glutathione and oxidative stress markers. • Consider supplements: » Vitamin B6 supplementation may reduce oxalic acid. » Ascorbic acid (vitamin C) supplementation can increase oxalic acid production. » Hydroxyproline accounts for 15% of oxalic acid – avoid collagen supplementation. • Check gut microbiome. Oxalate degradation is primarily performed by *Oxalobacter formigenes.* • Evaluate kidney markers.	• Low is the expected finding.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Glyceric Acid (Glycerate)	• Produced in the oxalate metabolism pathway via the glyoxylate reductase/ hydroxypyruvate reductase (GRHPR) enzyme. » Primary hyperoxaluria type 2 (PH2) is a GRHPR deficiency mutation.	• May increase with metabolic issues. The production of glyceric acid is favored under adverse physiological conditions (imbalanced glucose or pH). • Can induce acidosis. • Consider B3 and Mg+ support. • Increased levels of glyceric acid with elevated oxalic acid can identify inborn errors such as PH2.	• Low is the expected finding.
Glycolic Acid (Glycolate)	• Produced from: » Glyoxal via advanced glycation end products (AGEs) from oxidative stress – this conversion uses glutathione. » Interconverts with glyoxylate which can become oxalic acid. Glycolic acid is the main producer of glyoxylate. » Some can come from fructose breakdown (estimated ~12%).	• Check B6 and glutathione markers and oxidative stress – support accordingly. • Increased with inborn errors such as primary hyperoxaluria type 1 (PH1). • Increased with excess hydroxyproline from collagen catabolism. • Elevated glycolic acid and lactic acid seen with ethylene glycol intoxication.	• Low is the expected finding.

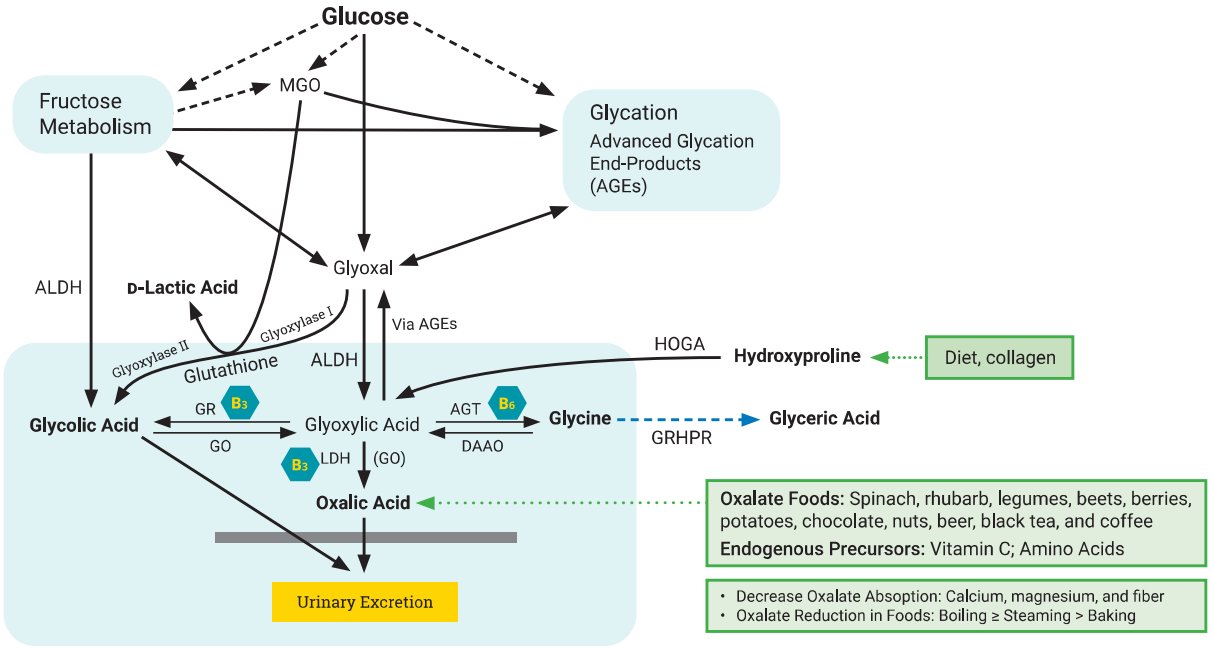


Figure 10. Glyoxylate Cycle

MICROBIAL METABOLITES

Microbial metabolites are the byproducts of gut microbial action on compounds that reach the colon.

MICROBIAL METABOLITE OF TRYPTOPHAN

MARKER	DESCRIPTION	IF HIGH	IF LOW
Indoleacetic Acid **(Indole-3 acetic acid, Indoleacetate, IA or IAA)**	• A derivative of indole. • Indoles are microbial metabolites of tryptophan. • Produced via fermentation by *Bifidobacterium* spp., *Bacteroides* spp., *Bacillus* spp., *Pseudomonas* spp., *Escherichia* coli, and *Clostridium* spp. • Dysbiosis can induce disruptions in tryptophan catabolism which contribute to disorders such as inflammatory conditions, neuropsychiatric diseases, metabolic syndrome, and cancer.	• Elevated levels have been associated with inflammatory dysbiosis. • If elevated, check total protein and tryptophan intake, overall digestion, and gut dysbiosis/ overgrowth. • Ensure adequate fiber in the diet to balance protein intake. » Check gut bacteria via GI-MAP. » Tryptophan-rich foods include cruciferous vegetables, red meat, fish, cheese, beans and eggs.	• Lower levels have been associated with dysbiosis. » Lower levels have been associated with long-term obesity, liver disease, inflammatory bowel disease (IBD), and diabetes. • Identifies decreased synthesis or increased utilization of indoleacetic acid. » Inflammation may reduce available tryptophan. » Check overall protein intake and/or level of gut bacteria via GI-MAP.

MICROBIAL METABOLITE OF PHENYLALANINE & TYROSINE

MARKER	DESCRIPTION	IF HIGH	IF LOW
4-Hydroxy-phenylacetic Acid (4-Hydroxy-phenylacetate or p-Hydroxyphenylacetic Acid)	• 4-hydroxyphenylacetic acid is a product of tyrosine or tyramine (a breakdown product of tyrosine). • Produced via fermentation by *Clostridium* spp., *Klebsiella* spp., *Pseudomonas* spp., and *Proteus* spp. • *Clostridium difficile* is a bacteria known to decarboxylate 4-hydroxyphenylacetic acid to produce *p*-cresol.	• If elevated, check for high protein or tyrosine/ tyramine intake. » Fermented foods such as sausages, marmite, soybean products, fish sauce, beers, and wine. • Check digestion and for gut dysbiosis/overgrowth. • Limited research has correlated 4-hydroxyphenylacetic acid with small intestinal bacterial overgrowth (SIBO).	• Check for low protein or tyrosine intake and/ or if gut bacteria is low (insufficiency dysbiosis). • Quercetin has been proposed to reduce free radicals of 4-hydroxyphenylacetic acid.
Phenylacetic Acid (Phenylacetate or PAA)	• Phenylacetic acid a product of phenylalanine fermentation by *Bacteroides* spp., *Pseudomonas* spp., *Escherichia coli, Bifidobacterium* spp., and *Lactobacillus* spp. • Phenylethylamine (PEA) from food is quickly metabolized into phenylacetic acid by monoamine oxidase (MAO). Symptoms such as a headache are noted with impaired conversion. • Phenylacetic acid is used to scavenge glutamine.	• Check for high protein intake and phenylalanine intake, digestion, and for gut dysbiosis/overgrowth. • High levels have been found in Crohn's disease, dysbiosis, nephritis, hepatitis, and phenylketonuria (PKU). • Can be a uremic toxin at very high levels. • On OMX, check glutamine – supplement if needed.	• Lower levels are generally expected and correlate with higher *Faecalibacterium prausnitzii.* • Lower levels are found in depression and in children with obesity.

Microbial fermentation of colonic protein and amino acids is called proteolytic fermentation. Fermentation of aromatic amino acids, tryptophan, phenylalanine, and tyrosine are known to have significant impacts on health and function. Common proteolytic metabolites such as, p-cresol, indoles, phenol, and ammonia, and thier metabolites, are considered harmful at elevated concentrations in the colon. Imblances of these markers can identify impaired digestion or increased endogenous production (increased mucus or bleeding), inadequate fiber or excess protein intake, or imbalanced gut microbes.

MICROBIAL METABOLITES

Microbial metabolites can come from bacterial action on plant bioactive compounds, such as polyphenols that reach the large intestine. Many different classes of polyphenols, such as flavonids and anthocyanides, give rise to specific microbial metabolites. Urinary polyphenol metabolites are potential biomarkers of dietary intake and bacterial balance. Substreates, such as benzoic acid which comes primarily from diet, can help identify bacterial activity, and level of glycine conjugation.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Benzoic Acid (Benzoate)	• Benzoic acid is a fermentation product of gut bacteria that act on dietary polyphenols such as *Escherichia coli, Bifidobacterium* spp., and *Lactobacillus* spp. • Benzoic acid can inhibit pathogenic microorganisms. • Benzoic acid conjugates with glycine to become hippuric acid – thus benzoic acid levels generally remain low.	• Check diet and gut bacterial levels. » Benzoic acid is found in broccoli, pepper (*Capsicum annuum*), fruits, and as a preservative. » Levels increase with intake of fruit juice, tea, and wine. • If levels are elevated, support with glycine supplementation – pantothenic acid (B5) may increase glycine conjugation.	• Low is the expected finding.
Hippuric Acid (Hippurate)	• The human body converts benzoic acid to hippuric acid for excretion. Benzoic acid is conjugated with glycine to form hippuric acid. • Hippuric acid is a normal urinary metabolite associated with microbial degradation of certain dietary components.	• Hippuric acid has been positively associated with gut diversity and better health. • Higher levels are seen with a Mediterranean diet. • Levels of hippuric acid rise with the consumption of fruit juice, tea, and wine, which are converted from benzoic acid. • Associated with *Clostridia* spp.	• Altered gut microbiota, low diversity, or insufficiency dysbiosis result in decreased hippuric acid. • High benzoic acid with low hippuric acid is associated with poor liver health.

MARKER	DESCRIPTION	IF HIGH	IF LOW
3,4-Dihydroxy-hydrocinnamic Acid (3,4-Dihydroxyphenylpropionate, DHCA, 3,4-DHPPA)	• An abundant phenolic compound formed primarily by the microbial action of *Clostridium* spp., *Escherichia coli, Bifidobacterium* spp., *Lactobacillus* spp., and *Eubacterium* spp. on dietary polyphenols, as well as on dopamine, phenylalanine, tyrosine, and tryptophan. • 3,4-DHPPA has antioxidant properties and significantly inhibits the secretion of pro-inflammatory cytokines.	• Associated with higher intake of polyphenols. Coffee is an abundant source. » Other food sources include red beetroot, common beet, and olives. • Highly correlated with high homovanillic acid (HVA). • Associated with higher bacterial levels.	• Associated with lower intake of polyphenols or lower levels of gut bacteria (insufficiency dysbiosis).
3,5-Dihydroxy-benzoic Acid (3,5-DHBA)	• A bacterial product produced by microbial action on polyphenols. • A metabolite of alkylresorcinol.	• Associated with higher intake of polyphenols. • Highly correlated with the intake of whole-grains and cereals. » Alkylresorcinols are a naturally occurring type of phenolic lipid found in high concentrations in the outer layer and bran of cereal grain, primarily wheat and rye. • Associated with higher bacterial levels.	• Associated with lower intake of polyphenols, specifically whole grains, or lower levels of gut bacteria (insufficiency dysbiosis).
4-Hydroxybenzoic Acid (p-Hydroxybenzoate or 4-HB)	• A hydroxybenzoic acid derivative formed by the microbial action of the total microbiota, *Clostridium* spp., *Eubacterium* spp., polyphenols, and aromatic amino acids. • Associated with ubiquinone (CoQ10) biosynthesis.	• Associated with higher intake of polyphenols, primarily anthocyanidins, and exposure to parabens. • Associated with increased follicle stimulating hormone (FSH).	• Associated with lower intake of polyphenols or lower levels of gut bacteria (insufficiency dysbiosis).

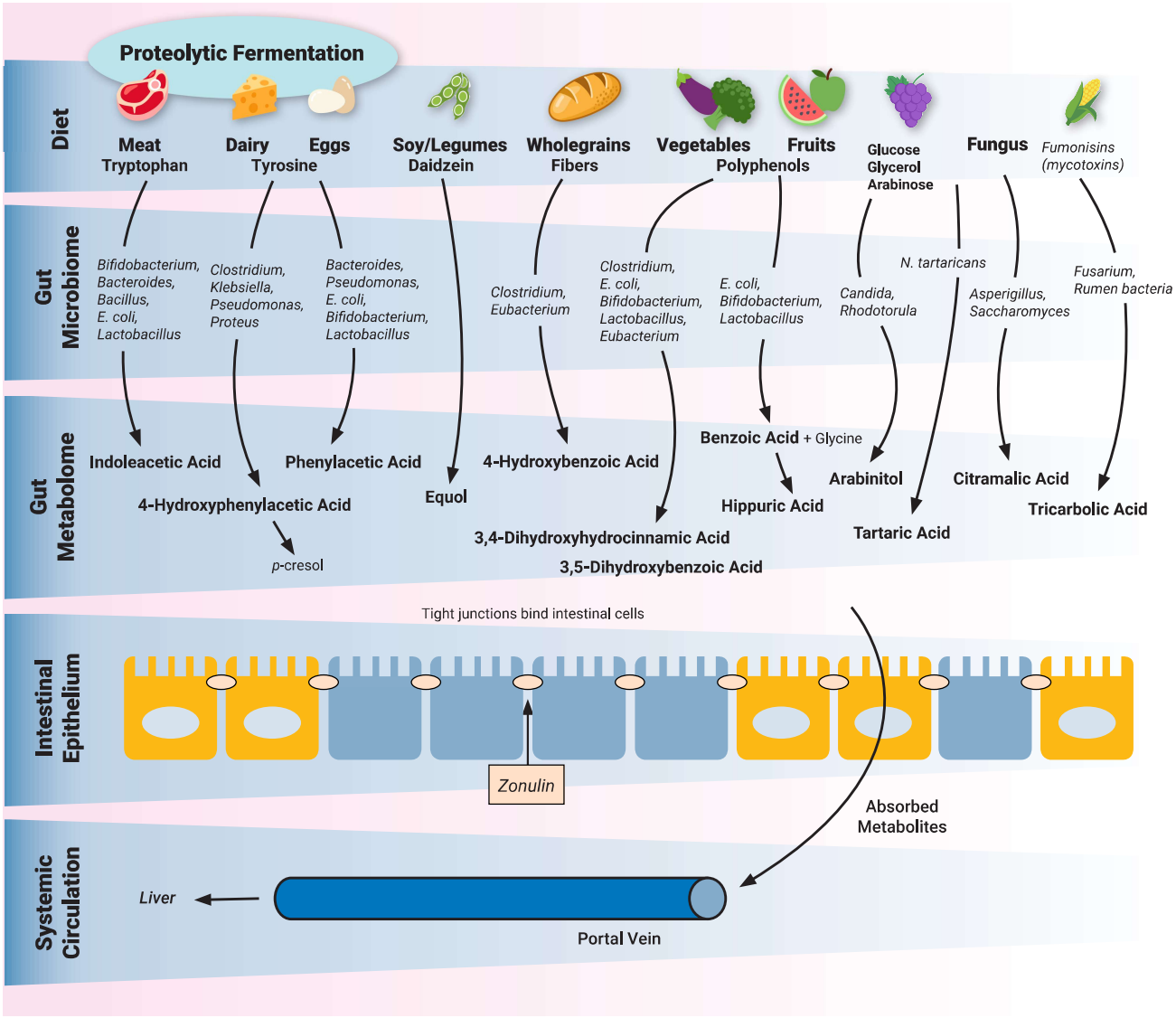


Figure 11. Microbial metabolites are the byproducts of gut microbial action on compounds that reach the colon. Undigested carbohydrate (fibers/starch) and protein (amino acids) are the major substrates available to the microbiota for fermentation, though phytonutrients, such as polyphenols also play a large part. Gut microbes include both bacteria and fungi. Many factors can influence the fermentation process including, dietary intake, adequacy of digestion, lifestyle habits, individual colonic bacterial and fungal patterns, and degree of gut dysbiosis.

ISOFLAVONE MICROBIAL METABOLITES

Endogenously produced from daidzein (soy isoflavone) and can interact with estrogen receptors to produce estrogenic or anti-estrogenic effects.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Equol	• Equol is a beneficial bacterial metabolite of daidzein and can have estrogenic and antioxidant activity.	• Higher isoflavone and/or daidzein intake. • Daidzein is found in soy-foods, such as tofu, tempeh, and miso. It is also found in pistachio nuts. • Higher with elevated bacterial levels. • Isoflavone metabolites are associated with significant health benefits.	• Lower isoflavone and daidzein intake. • Associated with lower bacterial levels. • Equol non-producer. • Women with premenstrual syndrome (PMS) are more likely to be equol non-producers.

FUNGAL ASSESSMENT

Gut microbes include bacteria and fungi. Fungi, like bacteria, produce metabolites. Fungal metabolites can identify level of fungal activity and have been associated with dysbiosis.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Arabinitol (Arabitol)	• A fungal metabolite from *Candida* spp., *Rhodotorula* spp., and other types of yeast. • Can biotransform arabinose, glucose, or glycerol to arabinitol.	• Elevated arabinitol should be further evaluated for yeast overgrowth. » High dietary intake of sugar or high-fructose corn syrup (HFCS) may increase arabinitol levels. • Arabinitol is used as a natural sweetener, a dental caries reducer, a sugar substitute, and a color stabilizer. • Evaluate for gastrointestinal yeast and dysbiosis. • Consider support with commensal fungal species such as *Saccharomyces boulardii.*	• Low is the expected finding.

MARKER	DESCRIPTION	IF HIGH	IF LOW
Citramalic Acid (Citramalate)	• A urinary marker of microbial dysbiosis. • Produced by fungus and bacteria such as *Saccharomyces* spp., *Propionibacterium* spp., and *Aspergillus niger.* • It is an analog of malic acid (a Kreb cycle intermediate) and can inhibit its production – may impact Krebs cycle function.	• May indicate increased fungal activity or dysbiosis. • Found in a range of foods including apples, citrus, and fermented foods such as red wine. • Evaluate for gastrointestinal yeast and dysbiosis.	• Low is the expected finding. • Low intake of fruits such as apples, citrus, and fermented foods.
Tricarballylic Acid (Tricarballlylate)	• Tricarballylic acid is dicarboxylic acid. • Potential sources include: » Fumonisins, a group of mycotoxins produced by the *Fusarium* genus. Commonly found on corn or corn-derived products. » Certain aerobic bacteria found in the gut-notable *Firmicutes* phylum.	• *Salmonella ruminantium* and *Wolinrlls succinogenes* are known to produce tricarballylic acid in animal studies. • Positively correlated with the *Firmicutes* phylum. » Evaluate for gastrointestinal yeast and dysbiosis. • Detection of tricarballylic acid can indicate the presence of fumonisins (mycotoxins) from maize (corn) in the gastrointestinal tract. » Tricarballylic acid chelates magnesium. » Consider magnesium and B2 if elevated.	• Low is expected finding. • *Salmonella enterica* can use tricarballylate as a carbon and energy source.
Tartaric Acid (Tartarate)	• Tartaric acid is an analog of malic acid and can inhibit its production – may impact Krebs cycle function.	• Assess diet. Tartaric acid is found naturally in some foods, primarily grapes and wine. » It is a "biomarker" of red wine intake. • Commonly used as a food additive due to its antioxidant properties. • *Candida* spp. cells grown in a lactic acid medium produced tartaric acid. • Elevated levels do not confirm *Candida* spp. overgrowth.	• Low is the expected finding. • Diet may be low in grapes or wine. • Tartaric acid can be utilized by gut bacteria as a carbon source.

OAp

ORGANIC ACIDS PROFILE

SUPPORT INFO

877-485-5336

METHODOLOGY

LC-MS/MS – Organic Acids Urine.
The newer testing results in significant increases in sensitivity & specificity, and increased reproducibility.

SPECIMEN REQUIREMENTS

Urine Sample — First morning void (FMV) in specimen cup provided and shipped frozen.

TEST ORDERING OPTIONS

- OAp - Organic Acids Profile™

Optional Ordering Options

- OMX™ - Urine & Plasma
- AAp - Amino Acids Profile™
- GI-MAP® | GI Microbial Assay Plus

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