US BioTek LABORATORIES

Organic Acids & Environmental Pollutants Interpretation Guide

Table of Contents

Organic Acids Profile 1
Glycolysis Metabolites 3
Pyruvate 3
Lactate 4
Citric Acid Cycle Metabolites 6
Citrate 6
Cis-aconitate 7
Isocitrate 8
Alpha-Ketoglutarate 8
Succinate 9
Fumarate 10
Malate 11
Fatty Acid Oxidation 13
Suberate 13
Adipate 14
Ethylmalonate 14
Methylsuccinate 15
Ketone Metabolites 16
Beta-Hydroxybutyrate 16
Markers of Cofactors Needed 18
Alpha-Ketoisovalerate 18
Alpha-Ketoisocaproate 18
Alpha-Keto-Beta-Methylvalerate 19
Beta-Hydroxyisovalerate 20
Methylmalonate 20
Kynurenate 21
Hydroxymethyl-glutarate 21
Markers of Neurotransmitter Metabolism 22
Homovanillate 22
Vanilmandelate 23
5 HIAA 24
Quinolinate 24
Markers of Detoxification 26
Alpha-Hydroxybutyrate 26
Para-Hydroxyphenyllactate 27
Orotate 27
Pyroglutamate 28
Benzoate 29
Hippurate 29
Markers of Bacterial Metabolism 30
Para-Hydroxybenzoate 30
Para-Hyroxyphenylacetate 30
2-Hydroxyphenylacetate 31
3-Indoleacetate 31
Tricarballylate 32

Environmental Pollutants Profile 33
Xylene 36
3-Methylhippurate 36
2-Methylhippurate 36
Toluene 36
Hippurate 36
Benzoate 36
Benzene 37
t,t-Muconic 37
Trimethylbenzene 37
3,4-Dimethylhippurate 37
Styrene 38
Mandelate 38
Phenylglyoxylate 38
Mandelate + Phenylglyoxylate 38
Phthalates 38
Monoethyl Phthalate 38
Phthalate 38
Quinolinate 38
Paraben 39
Para-Hydroxybenzoate 39
Methyl Tert-butyl Ether 40
Alpha-Hydroxyisobutyrate 40

The US BioTek Organic Acids Profile

Quick Overview

The organic acid test results are based on your personal metabolites (breakdown products) and key factors in your cellular metabolism. Depending on your diet, stress levels, sleep, hydration, medications and current and previously used supplements, the organic acid test report represents both "functional" nutritional status and existing metabolic needs unique onto your biochemistry and current level of nutritional sufficiency.

Your health care provider may choose to further examine your nutritional status, for instance if there is a suggestion that one of your pathways might benefit from iron (Fe), then they may perform a confirmatory test to elucidate such as ferritin, total iron, etc. Likewise if there is a metabolic pathway that may indicate a nutrient need for either B12 or folate, your provider may choose depending on your results to test your MCV (size of red blood cells), larger size may confirm this finding of need for B12 or folate, or they may also measure homocysteine (also a substance naturally made in your body that when increased beyond optimal may suggest low B12/folate).

In short, this organic acid/metabolic test, provides you and your healthcare practitioner a very broad look at the biochemical pathways within the 50 to 100 trillion cells within your body.

How is the Testing Performed?

This test is performed via urinary analysis, since the kidneys are excretory organs. Meaning that it filters your blood and many of the breakdown products (cellular exhaust) of your body are suspended in the urine as the body is cleansed. The technology used by US BioTek Laboratories is the latest LC/MS/MS technology, known for its specificity and enhanced sensitivity. Special attention has been given to achieve reproducible and accurate results, starting with the specimen collection process, heavily researched stability technology used during transport to the lab and the specific preparations guidelines given prior to collecting the laboratory sample.

Why Retest?

Retesting is helpful and important after supplementation and dietary changes to see the impact of enhanced fueling of your individual biochemical pathways and to measure your ability to absorb and assimilate. The report that you have in front of you is much like a Polaroid snapshot (instant picture). Your recent diet, lifestyle, nutritional status and health status are captured within the results. Working with your healthcare provider, you will fuel the pathways that are either high or low, with the goal of providing the "correct fuel" relative to the results and how they correlate with your overall clinical picture in terms of symptoms and how you are feeling.

Understanding Your Results

Your results will be either "Within Range, High or Low": Please look at your test report to identify whether your results were Within Range (normal), High or Low. This test is not intended to diagnose, treat, cure, or prevent any disease or replace the medical advice and/or treatment obtained from a qualified healthcare practitioner. This test does not assess for neonatal inborn errors of metabolism, and is based on stable renal function, and normal renal clearance.

Glycolysis Metabolites

Glycolysis (from glycose, an older term for glucose + -lysis degradation) is the metabolic pathway that converts glucose, into pyruvate. The energy released in this process is used to form the high-energy compounds ATP (adenosine triphosphate) and NADH (reduced nicotinamide adenine dinucleotide).

Pyruvate

↓ Low Results

Nutritional Considerations: Increase complex carbohydrates to decrease glycemic load to ensure proper balance with proteins and fat intake. Support glucose metabolism with B complex, chromium and vanadium.

Ensure there is sufficient intake of vitamin B3 (niacin).

Possible Interfering Factors: Very low carbohydrate diet in susceptible individuals.

Clinical Considerations: Though this finding is not common, a low pyruvate can result in numerous other low metabolite scores. Low energy would be a common symptom of this finding in many patients.

Further examination of daily dietary intake is important in these individuals to make sure a well-balanced diet with sufficient high fiber complex carbohydrates are being consumed. Need to rule out excess lactate that if high warrant further investigation.

Other possible causes can include, high intensity exercise, low oxygen conditions such as asthma or other pulmonary disease, sleep apnea, cardiac insufficiency, ketoacidosis, poorly controlled diabetes and prolonged fasting or severe dieting.

↑ High Results

Nutritional Considerations: Primary consideration including one or more insufficiencies amongst these nutrient factors: B1, B2, B3, B5, Lipoic Acid. Other additional nutrient considerations include CoQ10, Magnesium and Manganese.

Possible Interfering Factors: High Carb diet without adequate co-factors to fuel metabolic needs.

Clinical Considerations: This finding suggests insufficient cofactors to fuel the next metabolic step to fuel the creation of Acetyl-CoA, a critical step in energy production.

In the presence of hypoglycemia, consider possible fructose 1,6-DP Deficiency and Carboxykinase deficiency. Though this organic acid test does not measure for inborn errors of metabolism, this may be a consideration.

In the absence of hypoglycemia, then one may consider pyruvate dehydrogenase deficiency and pyruvate carboxylase deficiency that also warrants further investigation, if not clinically modifiable.

Lactate

↓ Low Results

Nutritional Considerations: Though clinically not common low lactate may arise when insufficient carbohydrates have been consumed, or when pyruvate levels are low. Common nutrients used to support the balance of lactate include: B1, B3, CoQ10, Biotin.

Possible Interfering Factors: Low Pyruvate, Acid/Base Imbalance.

Clinical Considerations: Though not common, a low lactate can arise from insufficient cofactors, particularly vitamin B3.

Insufficient levels of pyruvate can result in low lactate. Clinical observation suggests that excess alkalinity can result in changes in lactate levels, as can excess acidity. Testing urinary pH can be helpful in exploring acidity/alkalinity, as can blood pH.

↑ High Results

Nutritional Considerations: Nutrients that may help support proper lactate metabolism include, B1, B2, B3, B5, Lipoic Acid, CoQ10 and Biotin.

Making sure that blood sugars are controlled, that the diet is sufficiently balanced with carbohydrates, fats and proteins is essential. Prolonged fasting of few days or dieting occur prior to testing may contribute to higher lactate levels, as would vigorous exercise on the borderline of anaerobic.

The heart, brain and most slow twitch fibers are very apt at clearing lactate from the blood to the extent that they prefer lactate as a source of fuel. Note however, that lactate must first be converted into pyruvate before it can be used as a source of energy. Thus making sure that the pyruvate pathway is fueled is essential.

Clearance of lactate from the blood can occur either through oxidation within the muscle fibers in which it was produced or it can be transported to other muscles fibers for oxidation.

Lactate results are the total of D & L-lactate. In most cases L-lactate predominates. Elevated D-lactate can occur if there is dysbiosis.

Possible Interfering Factors: Poor metabolism or excess intake of alcohol.

Clinical Considerations: High lactic acid had been correlated with muscle tenderness and even fibromyalgia like symptoms.

Possible causes can include, high intensity exercise, low oxygen conditions such as asthma or other pulmonary disease, sleep apnea, cardiac insufficiency, ketoacidosis, poorly controlled diabetes and prolonged fasting or severe dieting.

Clinically, some individuals with high lactate will experience anxiousness, nervousness and at times sensation of shortness of breath. Increased water intake can assist in some patients.

It is important to know that if clinical correlation is made with lactic acidosis, medical intervention needs to occur immediately. There are many symptoms related to lactic acidosis which include nausea, vomiting, hyperventilation to remove carbon dioxide, nausea and vomiting, hyperventilation, abdominal pain, lethargy, low blood pressure, rapid pulse, heart rhythm irregularities and acidosis.

Citric Acid Cycle Metabolites

The citric acid cycle — also known as the tricarboxylic acid cycle (TCA cycle), the Krebs cycle is a series of enzyme-catalyzed chemical reactions, which is of central importance in all living cells that use oxygen as part of cellular respiration. In eukaryotic cells, the citric acid cycle occurs in the matrix of the mitochondria.

Citrate

↓ Low Results

Nutritional Considerations: Low levels can be suggestive of insufficiency of one or more of these nutrients: Essential fatty acids, essential amino acids, B1, B2, B3, B6, Lipoic Acid.

Secondary considerations as correlates to individual biochemistry, clinical presentation and nutritional needs include glutathione, manganese, l-arginine.

Clinical consideration is also to augment the use of citrate chelated minerals, such as calcium citrate, as a non-specific example of such a mineral chelate.

Possible Interfering Factors: Inadequate pyruvate or cis-aconitate levels as precursors.

Clinical Considerations: Low levels of citrate can result in altered levels of other citric acid cycle (CAC) levels (Kreb's cycle). Looking at precursor metabolites and overall dietary balance to help ensure proper fueling of the CAC pathway is essential.

A diet low in either fat, protein or carbohydrate can ultimately lead to overburden and overdependence for substrates to optimally fuel this pivotal step in energy and metabolic biochemistry.

If after other changes citrate does not improve glutathione must be considered for testing and support.

↑ High Results

Nutritional Considerations: A high level of citrate often points to insufficient co-factors to ensure proper downstream metabolism of citrate into cis-aconitate.

Common nutrients used include: Essential Amino Acids, Aspartate, Arginine, Magnesium, Manganese, Lipoic Acid.

When cis-aconitate is also high consider n-acetylcysteine (NAC), Iron, Glutathione (GSH).

Possible Interfering Factors: Poor protein digestion or assimilation or protein insufficient diet. Theoretically high intake of citrate rich supplements (ex. calcium citrate).

Clinical Considerations: May be due to poor protein or carbohydrate metabolism. Also excess citric acid in dietary foods, particularly processed foods and supplements can artificially throw off the balance of this metabolite.

Must also rule out heavy metal toxicity such as arsenic, mercury, cadmium, fluoride, bromide, perchlorate and antimony.

Metabolic acidosis and insufficient antioxidant status can be contributory, along with inadequate pancreatic and/or kidney function.

Clinical Note: *It is essential when seeing high citrate levels to re-visit with patient that they avoided citric acid rich foods per patient preparation directions for the test.*

Cis-aconitate

↓ Low Results

Nutritional Considerations: If citrate is low, then fueling the citric acid pathway is essential (see low citrate recommendations).

Common nutrients used to support this pathway include: NAC, Iron citrate, Glutathione, Magnesium, Manganese, B3.

Possible Interfering Factors: Low Citrate and/or Low Pyruvate, antacids, acid blockers, low protein diet, malabsorption.

Clinical Considerations: Important to sustain adequate level of substrate (building block) for next steps in energy pathways, for instance if pyruvate or citrate are low, cis-aconitate often will also be low.

Low level of metabolite often is associated with less than optimal energy, generalized fatigue and decreased muscle strength and endurance.

↑ High Results

Nutritional Considerations: Common nutrients used to optimize this portion of the CAC pathway include: NAC, Iron Citrate, Glutathione, Arginine, B complex.

Additional nutrients sometimes used relative to clinical picture include: Aspartic acid, Manganese, Magnesium and Lipoic acid.

Possible Interfering Factors: Low levels of precursors citrate or isocitrate.

Clinical Considerations: Endogenous and exogenous causes of increased need for glutathione or iron (anemia, chronic disease, malabsorption, etc.) can alter cis-aconitate levels.

Must also rule out heavy metal toxicity such as arsenic, mercury, cadmium, fluoride, bromide, perchlorate and antimony.

Isocitrate

↓ Low Results

Nutritional Considerations: NAC, Fe, Glutathione, low levels of essential amino acids.

Possible Interfering Factors: Antacids, acid blockers, low protein diet, malabsorption.

Clinical Considerations: Low levels may be directly related to low-upstream metabolites, including low levels of either alpha-ketoglutarate or cis-aconitate. Thus fueling these metabolite substrates and co-factors can often bolster a low isocitrate level.

Clinical observations also point to Malabsorption, poorly balanced vegetarian diet, poor standard American diet, low stomach acid, or GI conditions that lead to malabsorption. Also consider digestive enzymes per your healthcare provider.

↑ High Results

Nutritional Considerations: Common nutrient considerations include: Vitamin B3, Magnesium, Manganese, Arginine.

Clinical Observation: *In practice, patients with altered levels of isocitrate invariably have altered cis-aconitate or alpha-ketoglutarate, even if the above metabolites are marginally within the acceptable range. This sets the stage for minor shifts in nutrient status to alter this metabolism of isocitrate.*

Possible Interfering Factors: Methotrexate

Clinical Considerations: If other metabolites are elevated such as cis-aconitate, and citrate, then looking at possible urea metabolism issues may be noteworthy, as reflected in part by BUN (blood urea nitrogen), in some individuals.

Correlate elevated levels of aluminum (due to aluminum inhibition) with elevated isocitrate can offer insights relative to possible etiology.

Alpha-Ketoglutarate

↓ Low Results

Nutritional Considerations: Common nutrients used to support this crucial metabolite that ultimately fuels Succinyl-CoA and ATP production include: Essential Amino Acids; increase EFA intake, B3, arginine.

Inadequately fueled upstream metabolites and lack of co-factors must be addressed.

Possible Interfering Factors: High Palmitic acid dietary intake, high blood triglycerides, lithium use.

Clinical Considerations: Fatigue and altered amino acid status, that possibly can reflect in decreased muscle strength and endurance.

This step of the CAC pathway is essential to optimize to support cellular energy production, low levels of alpha-ketoglutarate may point to suboptimal CAC efficiency, particularly if isocitrate and/or cis-aconitate are elevated.

↑ High Results

Nutritional Considerations: Common nutrients use to support this pathway include: Vitamins B1, B2, B3, B5, Lipoic Acid.

Clinical Note: *Parallel to nutrient repletion, ruling out heavy metal toxicity is essential. Special attention to levels of arsenic, mercury, cadmium, fluoride, bromide, perchlorate and antimony, is essential. Also diabetes, metabolic syndrome, or megaloblastic anemia needs to be addressed if present.*

Possible Interfering Factors: Alpha-ketoglutarate chelated supplements.

Clinical Considerations: Elevated levels can reflect a significant nutrient/co-factor deficit in the ability to move (exit) to one of the final steps prior to energy production.

Often low levels of the same substrates result in elevated levels of pyruvate, the entrance into the CAC.

If pyruvate is also elevated, practical experience points to specific focus on use of B complex, along with Lipoic acid and Magnesium.

Succinate

↓ Low Results

Nutritional Considerations: As with alpha-ketoglutarate, succinate is an immediate precursor metabolite (substrate) for the production of Succinyl-CoA that fuels ATP production.

Common nutrients used in practice to support this metabolite include: Vitamin B2 (riboflavin), Iron (as clinically indicated), CoQ10, Glutamine, branched chain amino acids (Leucine, Isoleucine and Valine).

Clinical Note: *Looking upstream at any other metabolites that may also be low, or suboptimal normal "within range" is essential. Each of these must be optimized to enhance energy production.*

Possible Interfering Factors: Oral contraceptive, hormone replacement and other medications that lower B vitamin levels.

Use of acid blockers that can lower absorption of B12 and other essential nutrients.

Clinical Considerations: Clinical Observation points to increased risk of low succinate levels resulting from excess demand of glutamine due to muscle, GI or immune demand.

Remembering that l-glutamine is a conditional essential amino acid that can become insufficient if either of these metabolic demands become increased.

Even strenuous aerobic exercise or acute illness can cause a relative glutamine drop.

Clinical Note: *After addressing fueling metabolic pathways for succinate and its upstream metabolites, it is essential to address gastrointestinal integrity and absorptive capacity.*

↑ High Results

Nutritional Considerations: High levels may point to low levels of B12. Clinically correlating with possibly higher MCV (mean corpuscular volume), elevated homocysteine or Methylmalonic acid (MMA) is also important.

Common nutrients used to support this pathway include: Magnesium, B2, CoQ10, B12 (methylcobalamin form) and Iron.

Possible Interfering Factors: Lithium, Succinate chelated supplements, excess glutamine intake or bacterial degradation.

Clinical Considerations: Individuals with high levels may suffer from fatigue, myocardial dysfunction, neurodegenerative changes, muscle weakness and ketosis.

Important Clinical Observation: *Individuals with sleep apnea, respiratory disease including COPD and asthma and/or cardiac conditions leading to decreased oxygenation can be contributory and will often be aggravated with a high succinate level.*

Clinically ruling out: *GI Dysbiosis and urinary tract infection even low-grade chronic infection is essential as these can alter the metabolism of the amino acid, l-glutamine, resulting in skewed results.*

Fumarate

↓ Low Results

Nutritional Considerations: Low levels of fumarate have been correlated with lower levels of: Tyrosine and/or Phenylalanine, B6, B2, Arginine, Essential Amino Acids and CoQ10.

Clinical Observation: Use of malic acid supplements (such as magnesium malate) often can help short term as the underlying cause of the low result is clinically determined.

Possible Interfering Factors: Diet low in protein or insufficient in essential amino acid balance.

Use of acid blockers that decrease assimilation/breakdown of ingested protein.

Clinical Considerations: *Some individuals with low level of fumarate may have an increased exacerbation of psoriasis.*

Low levels may correlate with increased fatigue and sense of low energy to perform daily functions.

May wish to look at confirmatory tests for possible low iron status, such as ferritin, TIBC, Total Iron, Transferrin.

Can be symptomatic of poor conversion of phenylalanine to tyrosine or altered urea cycle metabolism.

Important Clinical Note: *Since Phenylalanine and Tyrosine feed into the CAC pathway via fumarate (see Organic Acid in Central Energy Pathways Chart), supplementation with these two amino acids may be particularly indicated for individuals with lower mood, since the catecholamine pathway (dopamine, epinephrine, norepinephrine) is also fueled by these amino acids.*

↑ High Results

Nutritional Considerations: Common nutrients used to support high levels of fumarate include: CoQ10, B2, Fe, B3, B6.

Clinical Note: *Use of the amino acids tyrosine and phenylalanine therapeutically can result in higher fumarate readings as an artifact of fueling this pathway. This is common for individuals using these amino acids to support the catecholamine pathway for mood stability.*

Possible Interfering Factors: Fumarate chelated supplements, lithium, use of tyrosine and phenylalanine supplements.

Yeast overgrowth may yield elevated levels.

Clinical Considerations: If other citric acid cycle metabolites are elevated then need to look at possible presence of cytochrome C oxidase deficiency.

If malate or pyruvate are also elevated, these increased levels may fuel the high fumarate.

Clinical Observation: *It appears that individuals with insulin resistant states such as diabetes II and metabolic syndrome commonly have elevated fumarate. Thus, if clinically indicated performing an HA1c may offer insight.*

Malate

↓ Low Results

Nutritional Considerations: May correlate with low upstream metabolites, oxaloacetate or fumarate.

Common nutritional support includes: Vitamins B3, and B6, Essential Amino Acids.

Clinical Consideration: *May consider to supplement with malate chelated minerals such as magnesium malate until the underlying clinical etiology is fully elucidated.*

Possible Interfering Factors: Low levels of upstream metabolites: oxaloacetate or fumarate.

Clinical Considerations: Can be symptomatic of poor conversion of phenylalanine to tyrosine or altered urea cycle metabolism. Some patients present with fatigue and apathy.

Clinical Observation: *Often patients with fibromyalgia like symptoms respond positively to malate chelated minerals, such as magnesium malate.*

↑ High Results

Nutritional Considerations: With elevated levels of malate can result from elevated pyruvate or oxaloacetate thus requiring attention to these pathways to address the elevated malate. Common supportive nutrients include: Vitamin B3 (niacin), CoQ10.

Possible Interfering Factors: Lithium, Malate chelated supplements.

Clinical Considerations: May be elevated in individuals with metabolic syndrome (pre-diabetes) or overt diabetes. Need to also rule out elevated urea, confirmatory tests may include BUN and Creatinine levels.

Clinical Observation: *Some individuals with yeast overgrowth of the GI tract or systemically will manifest with elevated malate.*

Fatty Acid Oxidation

The burning of stored fat or fats obtained through the diet, known as beta-oxidation, efficiently produces via combination with CoA (coenzyme A) to form acyl-CoA and cyclic shortening of the fatty acyl-CoA by stepwise removal on one acetyl-CoA at a time is critical to produce ATP. It is this pathway that is essential for stored fat or fats obtained via diet, via beta–oxidation to support production of NADH, FADH2 and acetyl co-enzyme A.

Suberate

↓ Low Results

Nutritional Considerations: Clinically if beta-oxidation metabolism is altered, a shift in suberate can occur.

Nutrients used to support this pathway include: Choline, Acetyl-l-Carnitine, CoQ10 and Biotin.

Possible Interfering Factors: Very low serum cholesterol, altered fat metabolism.

Clinical Considerations: This may be related to a mitochondrial defect or altered fat metabolism relative to beta-oxidation performance due either endogenous or exogenous factors.

Clinical Observation: *Some individuals with low suberate note a decrease in mental clarity and memory. If cholesterol is below 140, clinical correlation needs to be considered.*

↑ High Results

Nutritional Considerations: Common nutrients used to support Suberate metabolism include: Vitamin B2, Carnitine or acetyl-l-carnitine, B5, Magnesium.

Possible Interfering Factors: Poorly controlled diabetes, ketosis or oxidative stress yielding acidosis.

Consumption of MCT oil, aspirin therapy, acetaminophen valproic acid, carnitine depleting drugs.

Low caloric diets such as HCG diet, and other low-calorie diets.

Clinical Considerations: Often correlates with metabolic syndrome and/or diabetes. Can be elevated in ketogenic diets or carbohydrate restrictive diets.

Suggestive of possible mitochondrial dysfunction relative to long chain fatty acid metabolism.

Clinical Observation: *In urine samples from ketotic patients; adipic and suberic acid are frequently present in substantial amounts.*

Has been observed also in cases of hepatic disease, hypoxia, malnutrition, high fever, substantial illness, prolonged fasting and fructose intolerance.

Adipate

↓ Low Results

Nutritional Considerations: Nutrients used to support this pathway include: Choline, acetyl-l-carnitine, CoQ10 and Biotin.

Possible Interfering Factors: See low suberate (above).

Clinical Considerations: This may be related to a mitochondrial defect or altered fat metabolism relative to beta-oxidation performance due either endogenous or exogenous factors.

Clinical Observation: *Check to ensure cholesterol is at least 140 mg/dL, low levels may be contributory in some individuals.*

↑ High Results

Nutritional Considerations: Common nutrients used to support Suberate metabolism include: Vitamin B2, Carnitine or acetyl-l-carnitine, B5, Magnesium.

Possible Interfering Factors: Lithium, intake of Jello®.

Clinical Considerations: Symptoms can include fatigue, upper GI upset, blood sugar imbalances-particularly low blood sugars. Inability to optimally metabolize fatty acids is a consideration relative to individual clinical picture.

Ethylmalonate

↓ Low Results

Nutritional Considerations: Supportive nutrients to consider: Carnitine, Biotin.

Possible Interfering Factors: Excess cholesterol suppression.

Clinical Considerations: Clinical Correlation with very low triglycerides and low cholesterol.

↑ High Results

Nutritional Considerations: Supportive nutrients to consider: Carnitine, Vitamin B2, Biotin, Magnesium.

Possible Interfering Factors: High Cholesterol and triglycerides can contribute to increased levels.

Clinical Considerations: Can be suggestive of inability to oxidize fatty acids. If suberate or adipate are elevated this further points to fatty acid metabolic issues worthy of further exploration depending on clinical symptoms.

Elevated urinary Ethylmalonate has been reported in gestational diabetes.

Methylsuccinate

↓ Low Results

Nutritional Considerations: Refer to Suberate.

Clinical Considerations: Refer to Suberate.

↑ High Results

Nutritional Considerations: Refer to Suberate.

Clinical Considerations: Refer to Suberate.

Ketone Metabolites

Ketone metabolites are water-soluble compounds that are produced as by-products when fatty acids are broken down for energy in the liver and kidney. They are used as a source of energy in the heart and brain. In the brain, they are a vital source of energy during fasting.

Beta-Hydroxybutyrate

↓ Low Results

Nutritional Considerations: General supportive nutrients for ketone metabolism include blood sugar supportive nutrients that include: Chromium, Vanadium.

Possible Interfering Factors: Acid blockers or antacids use.

Insufficient caloric and/or quality protein intake.

Clinical Considerations: Sometimes seen in individuals that are exceedingly thin, those with excellent well-balanced diets, very fit individuals and those individuals with low protein and low-fat diets.

↑ High Results

Nutritional Considerations: Common nutrients incorporated in clinical practice to support this pathway include: NAC, Lipoic acid, Glutathione, Vitamins B3, B5, B6, B12, Biotin, MTHF (active folate). Also the addition of Glycine, Chromium and Vanadyl sulfate.

Clinical Note: *Elevated ketone metabolites need to be correlated with potential diabetic symptoms as clinically relevant to help rule out ketoacidosis, though blood levels of ketones should also be checked if this matches the clinical picture. There are non-diabetic etiologies of elevated ketone bodies.*

Also elevated during fasting and when consuming a ketogenic diet.

Possible Interfering Factors: Acetaminophen and other liver metabolized medications with potential of elevated liver enzyme.

Yeast overgrowth, very high cholesterol levels and excess dietary fat intake in some cases.

Clinical Considerations: The following may contribute to increased ketone metabolites: GI Dysbiosis or altered permeability, as well as high demand for glutathione due to health process or toxic exposure may be consideration.

Poor blood sugar regulation. May also suggest decreased carbohydrate intake. Clinical correlations that may be considered when appropriate include the presence of undiagnosed or under treated sleep apnea, hypoxia of all origins, uncompensated high intensity exercise, insufficient protein intake or absorption, excess oxidative stress.

Clinical Note: *High ketones and ketone metabolites can be representative of ketoacidosis/ketosis/lactic acidosis a potentially life-threatening condition. This should be evaluated for all people with diabetes whenever symptoms of illness are present, such as nausea, vomiting, or abdominal pain. These symptoms are often missed because they are similar to elevated blood sugar levels.*

Markers of Cofactors Needed

Vitamins can serve as precursors to many organic cofactors (e.g. vitamins B_1, B_2, B_6, B_{12}, niacin, folate) or as coenzymes themselves (e.g. vitamin C). Minerals are also often play critical roles in metabolic pathways, as do accessory nutrients such as CoQ10. Subsidiary pathways that fuel the Citric Acid Cycle (Kreb's Cycle) must be properly fuels to feed into intermediary metabolites for optimal cellular performance.

Alpha-Ketoisovalerate

↓ Low Results

Nutritional Considerations: Metabolite of branched chain amino acid (BCAA) metabolism (Leucine, Isoleucine and valine).

Important nutritional considerations include: Vitamin B6, Increase protein intake-especially BCAA.

Possible Interfering Factors: Inadequate dietary BCAAs. Poor absorption due to leaky gut or other maladies. Acid blockers and achlorhydria.

Clinical Considerations: Clinically some patients can benefit with higher total protein with emphasis on Branched Chain Amino Acids (BCAA) and a comprehensive B complex with adequate B6.

↑ High Results

Nutritional Considerations: General nutritional support of this pathway generally focuses on the following: Vitamins B1, B2, B3, B5 and B6. Also Lipoic Acid and/or NAC, along with Magnesium.

Possible Interfering Factors: Toxic metal exposure (Arsenic, Antimony, Mercury, Cadmium).

Clinical Considerations: May consider performing toxic metal test if clinically consistent. Can also be very elevated in the case of Maple syrup urine disease, also known as also called branched-chain ketoaciduria, is an autosomal recessive metabolic disorder affecting branched-chain amino acids.

Alpha-Ketoisocaproate

↓ Low Results

Nutritional Considerations: Depending on nutritional status of patient relative to dietary intake of branched chain amino acids the following nutrients are commonly used when BCAA intake is determined to be adequate: Vitamins B1, B2, B3, B5 and B6, along with Lipoic Acid and Magnesium, along with BCAA.

Clinical Note: *If BCAA intake is low, or GI Assimilation is suboptimal, often BCAA supplementation is a primary focus, with the above co-factors added as clinically indicated.*

Possible Interfering Factors: Acid blockers, achlorhydria, and poor amino acid assimilation.

Inadequate dietary intake of BCAAs. Poor GI absorption due to leaky gut or gastrointestinal maladies.

Clinical Considerations: Low levels are suggestive of insufficient BCAA intake and individuals often respond well to B complex augmentation.

↑ High Results

Nutritional Considerations: Nutritional support commonly includes: Vitamins B1, B2, B3, B5 and Lipoic Acid, Magnesium.

Possible Interfering Factors: Need to rule out heavy metal toxicity (Arsenic, Antimony, Mercury, Cadmium).

Clinical Considerations: Clinical review of dietary intake with particular focus on branched chain and total amino acid intake is essential.

Alpha-Keto-Beta-Methylvalerate

↓ Low Results

Nutritional Considerations: Depending on nutritional status of patient relative to dietary intake of branched chain amino acids the following nutrients are commonly used when BCAA intake is determined to be adequate: Vitamins B1, B2, B3, B5 and B6, along with Lipoic Acid and Magnesium, along with BCAA.

Clinical Note: *If BCAA intake is low, or GI Assimilation is suboptimal, often BCAA supplementation is a primary focus, with the above co-factors added as clinically indicated.*

Possible Interfering Factors: Acid blockers, achlorhydria, and poor amino acid assimilation.

Inadequate dietary intake of BCAAs. Poor GI absorption due to leaky gut or gastrointestinal maladies.

Clinical Considerations: Clinically some patients can benefit with higher total protein with emphasis on Branched Chain Amino Acids (BCAA) and a comprehensive B complex with adequate B6.

↑ High Results

Nutritional Considerations: Nutrient commonly used to support this pathway include: Vitamins B1, B2, B3, B5, B6 and, Lipoic Acid, Magnesium, Essential Amino Acids.

Possible Interfering Factors: Need to rule out heavy metal toxicity (Arsenic, Antimony, Mercury, Cadmium).

Clinical Considerations: Possible poor digestion of protein, or insufficient intake of balanced amino acids. Also may reflect inadequate B vitamin levels.

Beta-Hydroxyisovalerate

↓ Low Results

Nutritional Considerations: Depending on nutritional status of patient relative to dietary intake of branched chain amino acids the following nutrients are commonly used when BCAA intake is determined to be adequate: Vitamins B1, B2, B3, B5 and B6, along with Lipoic Acid and Magnesium, along with BCAA.

Clinical Note: *If BCAA intake is low, or GI Assimilation is suboptimal, often BCAA supplementation is a primary focus, with the above co-factors added as clinically indicated.*

Possible Interfering Factors: Acid blockers, achlorhydria, and poor amino acid assimilation.

Inadequate dietary intake or absorption of BCAAs.

Clinical Considerations: Low levels are suggestive of insufficient Branched Chain Amino Acid intake and individuals often well to B complex augmentation.

Urinary Beta-Hydroxyisovalerate is elevated in biotin deficiency.

↑ High Results

Nutritional Considerations: Nutrient commonly used to support this pathway include: Vitamins B1, B2, B3, B5, B6, Biotin and, Lipoic Acid, Magnesium, Essential Amino Acids.

Possible Interfering Factors: Anti-seizure meds, recurrent use of antibiotics-dysbiosis.

Clinical Considerations: Ketosis, protein malnutrition, muscle weakness, poor wound/injury healing may be seen clinically in some individuals.

Methylmalonate

↓ Low Results

Low levels are not frequently correlated with B12 concerns. It should be noted that MMA (methylmalonic acid) is cleared by the kidneys.

↑ High Results

When vitamins B-12 insufficiency occurs methylmalonte levels increase. Elevation should be correlated with serum B-12, after avoiding supplementation for 1 week prior to blood draw and also MCV and

Homocysteine levels for correlation when clinically applicable.

Clinical Considerations: There may be symptoms of altered neurological function, increased MCV when other RBC indices such as folate and iron are also clinically considered simultaneously.

Kynurenate

↓ Low Results

Nutritional Considerations: This pathway is important for tryptophan metabolism. Important nutrients to consider include: Vitamin B1, B3, B6 and Tryptophan.

Clinical Note: *Important to watch for Pellagra symptoms, dementia, diarrhea, dermatitis, etc.*

Possible Interfering Factors: Estrogen Excess, either exogenous or endogenous.

Clinical Considerations: Decreased energy, mental fatigue in some patients.

Clinical Note: *The liver can synthesize niacin from the essential amino acid tryptophan, requiring 30-60 mg of tryptophan to make one mg of niacin.*

↑ High Results

Nutritional Considerations: Common nutrients used to support this pathway include: Vitamin B3, B6, Iron (when clinically indicated), picolinic acid (such as found in minerals as chromium picolinate and other clinically correlated picolinate chelates).

Possible Interfering Factors: Statin Drugs or Possibly Red Rice Yeast. Also Estrogen Excess.

Clinical Considerations: Important to note that high levels can contribute to neurological pathology. High levels of kynurenic acid have been identified in patients suffering from tick-borne encephalitis, schizophrenia and HIV-related illnesses. Often associated with confusion and psychotic symptoms.

Hydroxymethylglutarate

↓ Low Results

Nutritional Considerations: The following nutrients are commonly low and include: Biotin, Carnitine, Vitamin B6, CoQ10, Essential fatty acids.

Clinical Note: *HMG is involved in cholesterol and CoQ10 synthesis. Also involved in leucine (BCAA) metabolism and ketone body synthesis.*

Possible Interfering Factors: Cholesterol lowering medications including statins, Red Rice Yeast and all other causes of low levels of cholesterol.

Clinical Considerations: Clinical observation suggests possible correlation with poor fat digestion.

Markers of Neurotransmitter Metabolism

Each of the catecholamines (Dopamine, Norepinephrine and Epinephrine) and Serotonin metabolites reflect relative upstream status of the respective neurotransmitter. For example, if 5-HIAA is low, this can reflect a correspondingly low level of serotonin or a metabolic pathway defect or co-factor deficit for proper metabolite formation.

Homovanillate

↓ Low Results

Nutritional Considerations: Low levels of homovanillate can be suggestive, relative to clinical presentation of less than optimal dopamine status. Common nutrients used to support this pathway include: Vitamins B2, B3, B6, B12 (methylcobalamin), Folate acid (MTHF), also magnesium and the amino acids Tyrosine, Methionine and SAMe.

Possible Interfering Factors: Haloperidol may lower levels in some individuals.

Clinical Considerations: When low, clinical support of dopamine pathway can be indicated. Symptoms of low dopamine may present clinically with low mood, low emotional response, increased addictive tendencies, and possibly Parkinson's-like symptoms.

↑ High Results

Nutritional Considerations: High levels may indicate of inadequate levels of: Copper, Tyrosine, Vitamin C or B2 to support metabolite creation.

Clinical Note: *In practice often stress and adrenal maladaptation are seen as contributing to high levels. Diet low in tyrosine rich foods or poor protein assimilation can be contributory.*

Homovanillate is typically elevated in patients with catecholamine-secreting tumors.

Possible Interfering Factors: Amphetamines, Cocaine and Crack, etc; use of Parkinson's Medications and aspirin.

Clinical Considerations: Use of substances mentioned in potential interfering factors. Heavy metal burden and exposure such as lead, cadmium, arsenic and mercury.

Symptoms may include agitation, irritability or if longstanding apathy and lack of sustainable contentment. Reflects elevated dopamine catabolism.

Vanilmandelate

↓ Low Results

Nutritional Considerations: Nutrients used to support this metabolite of Norepinephrine include: Vitamin B2, Magnesium, Iron (as clinically indicated), Copper, Vitamin C, Tyrosine.

Clinical Note: *Diet low in tyrosine rich foods or poor protein assimilation can be contributory.*

Possible Interfering Factors: Reserpine (Rauwolfia), Clonidine, MAO Inhibitors, drugs such as imipramine, dopamine.

Clinical Considerations: May suggest poor metabolism to end product, or insufficient fueling and creation of norepinephrine or a preferential shuttling to epinephrine.

Can be associated with symptoms of depression, fatigue, poor stress response and altered sleep capacity.

↑ High Results

Nutritional Considerations: Nutrients used to support this pathway include: Tyrosine as clinically indicated per symptoms (if there are symptoms of sympathetic dominance tyrosine would be contraindicated). If there are signs of too little sympathetic drive some clinicians relative to the individual picture will supplement with very small dosages to see how patient responds while monitoring vitals and overall clinical presentation closely.

Vitamin B6 can also be helpful.

Possible Interfering Factors: Reserpine (Rauwolfia), Clonidine, MAO Inhibitors, drugs such as imipramine, dopamine.

Clinical Considerations: May suggest excess intake of phenylalanine, tyrosine or dopamine agonists, or excess conversion to end metabolite.

Reflects increased Norepinephrine catabolism.

Clinical Note: *Can be increased in pheochromocytoma. Also with the ingestions of certain foods, such as bananas.*

Clinical Observation: *Levels appear elevated frequently with patients undergoing acute or exacerbated chronic stress.*

5 HIAA

↓ Low Results

Nutritional Considerations: Common nutrients used to support this pathway include: Tryptophan or 5 HTP as clinically indicated per symptoms, along with vitamins B2, B6.

Possible Interfering Factors: Poor dietary intake of tryptophan or niacin deficiency.

Clinical Considerations: May suggest insufficient fueling of serotonin pathway or missing co-factors for proper metabolism.

↑ High Results

Nutritional Considerations: Nutrients used to support this pathway if there are signs in a given individual of low serotonin, despite the elevated 5 HIAA include: Tryptophan or 5 HTP as clinically indicated per symptoms at low dosing with close monitoring along with vitamins B and B6 to support pathway).

Clinical Note: *Since the GI tract contains between upwards of 70-80 percent of the body's serotonin looking at GI symptoms including IBS is essential.*

Possible Interfering Factors: Use of medications in the SSRI category, Reserpine, acetaminophen. Excess use of tryptophan or 5 HTP.

Clinical Considerations: Can be suggestive of either high intake of 5 HTP, Tryptophan or higher metabolic demand that needs to be clinically correlated. Certain GI conditions, including carcinoid syndrome, conditions that affect platelet breakdown and function. Also points to elevated serotonin catabolism.

Clinical Important Note: *Though not necessarily present with most elevations of 5 HIAA, knowing the symptoms of serotonin syndrome and ruling out potential presence in a given individual is vitally important.*

Quinolinate

↓ Low Results

Nutritional Considerations: Supplementation with the following nutrients has been used in clinical practice: Vitamins B1, B3, B6 and as clinically indicated tryptophan.

Possible Interfering Factors: Insufficient B vitamins, inadequate tryptophan, use of loop diuretics that can deplete vitamin B1.

Clinical Considerations: It appears that alcoholism, uncontrolled diabetes and use of loop diuretics can be contributory to low levels of quinolinate due to vitamin B1 insufficiency.

↑ High Results

Nutritional Considerations: Antioxidants-Water Soluble and Fat Soluble, Magnesium, B2, B3, B5.

Clinical Note: *This pathway has been proposed to be activated by IFN-gamma and IFN-alpha.*

Possible Interfering Factors: High Phthalate exposure past or present.

Excess exposure to tryptophan or 5HTP is a clinical consideration.

Clinical Considerations: Oxidative stress, neuroinflammation or traumatic brain injury, infections with bacteria, fungal and viral pathogens. Maladaptive 5HTP and tryptophan metabolism.

Markers of Detoxification

These metabolites can be used relative to the clinical picture and individual exposure to offer clinical insight as to which particular pathway may be helpful to fuel and support with dietary changes, control of exposure and nutrient augmentation.

Alpha-Hydroxybutyrate

↓ Low Results

Nutritional Considerations: Low levels can be suggestive of the need to support metabolism with nutrients that include: Threonine, methionine (amino acids) and vitamin B6.

Possible Interfering Factors: Acid blockers or antacids use.

Insufficient caloric and/or quality protein intake.

Poor amino acid assimilation.

Clinical Considerations: Poor digestion or insufficient intake of protein.

Clinical Observations: *Seen in individuals that have adopted modified diets such as vegetarianism without regard to protein balance or other disease states leading to malnutrition such as gastrointestinal disease.*

↑ High Results

Nutritional Considerations: Elevated alpha-hydroxybutyrate metabolites need to be correlated with potential diabetic symptoms as clinically relevant to help rule out ketoacidosis, though blood levels of ketones should also be checked if this matches the clinical picture. There are non-diabetic etiologies of elevated alpha-hydroxybutyrate.

Common nutrients incorporated in clinical practice to support this pathway include: NAC, Lipoic acid, Glutathione, Vitamins B3, B5, B6, B12, MTHF (folate). Also, the addition of Glycine, Chromium and Vanadyl sulfate.

Clinical Note: *Supporting optimal glucose metabolism and blood levels is essential for individuals with elevated levels of alpha-hydroxybutyrate secondary to hyperglycemia. May point to increased hepatic glutathione stress resulting in an increased demand for glutathione production.*

Possible Interfering Factors: Acetaminophen and other liver metabolized medications with potential of elevated liver enzyme.

Yeast overgrowth, very high cholesterol levels and excess dietary fat intake in some cases.

Clinical Considerations: The following may contribute to increased alpha-hydroxybutyrate: GI Dysbiosis or altered permeability, as well as high demand for glutathione due to health process or toxic

exposure may be a consideration. Possible elevation of NADG/NAD+ ratio due to increased lipid oxidation.

Poor blood sugar regulation. May also suggest decreased carbohydrate intake. Clinical correlations that may be considered when appropriate include the presence of undiagnosed or under treated sleep apnea, hypoxia of all origins, uncompensated high intensity exercise, insufficient protein intake or absorption, excess oxidative stress.

Para-Hydroxyphenyllactate

↓ Low Results

Nutritional Considerations: Insufficient Clinical Evidence at this time to offer recommendations.

Possible Interfering Factors: None fully realized.

Clinical Considerations: Insufficient Clinical Evidence at this time to offer recommendations.

↑ High Results

Nutritional Considerations: This carcinogenic metabolite of tyrosine can increase risk under the correct level of susceptibility. Nutrients commonly used to support this pathway include: Vitamin C, Vitamin E, Lipoic acid, NAC and glutathione.

Possible Interfering Factors: Scurvy, liver disease, lactic acidosis.

Clinical Considerations: Inborn errors of metabolism, excess oxidative stress, toxic exposure triggering metabolic response.

Clinical Note: *Elevated levels can increase lipid peroxidation within the liver.*

Orotate

↓ Low Results

Nutritional Considerations: Nutrient that are used in clinical practice to support this pathway include: Essential Amino Acids, Vitamin B5, Magnesium, Potassium, and Arginine.

Possible Interfering Factors: Inadequate dietary intake of protein.

Clinical Considerations: Dysregulation of urea pathway, decreased fueling of oxaloacetate feed into CAC (Kreb's Cycle).

↑ High Results

Nutritional Considerations: When levels are elevated these nutrients are used in clinical practice

relative to the clinical picture: Vitamins B3, B6, MTHF (active folate). Also Magnesium, Glutamine, Glycine, Serine and Arginine.

Possible Interfering Factors: Barbiturates, allopurinol, orotate containing supplements, B vitamin Deficiency, nutrient depleting drugs patient may be taking, including HRT.

Clinical Considerations: When high, may at times reflect liver dysfunction, ammonia excess (correlate with blood urea nitrogen (BUN)). Ammonia excess can result in altered level of consciousness.

Excess lysine intake can negatively alter this pathway.

It may also be worthwhile to measure RBC (Red Blood Cell) magnesium as it can become lowered when orotate is elevated.

Pyroglutamate

↓ Low Results

Nutritional Considerations: When this metabolite is low the following nutrients are often used to support this pathway: Glutathione, NAC and Lipoic acid.

Possible Interfering Factors: Occupational oxidative exposure, aerobic exercise that exceeds antioxidant protection to quench increased reactive oxygen species.

Clinical Considerations: Oxidative stress can trigger low levels or insufficient antioxidant intake relative to systemic burden.

↑ High Results

Nutritional Considerations: Nutrients that may support this pathway include: Glutathione, Lipoic acid, NAC, along with glycine and taurine.

Clinical Note: *Glutamine degradation, hyperammonenia due to urea cycle dysfunction needs to be considered, if correlated with clinical picture and other testing.*

Possible Interfering Factors: Various toxic exposures, ranging from acetaminophen to toluene.

Clinical Considerations: Need to support liver and increase glutathione status in body.

Clinical Observation: *Pregnancy, excess glutamine degradation, renal insufficiency, low protein diet and protein malnutrition can be contributory to altered levels of pyroglutamate. Pyroglutamate is elevated in acetaminophen toxicity and when there is excessive glutathione turnover.*

Benzoate

↓ Low Results

Nutritional Considerations: Insufficient Clinical Evidence at this time to offer recommendations.

Possible Interfering Factors: None known.

Clinical Considerations: Generally, not significant unless, high exposure to organic toxins past or present such as benzene. In such circumstance, testing for benzene levels and other organic toxins is recommended.

↑ High Results

Nutritional Considerations: The most common nutrient used to support this pathway is: Glycine.

High dietary consumption from food preservatives may elevate Benzoate.

Possible Interfering Factors: None known.

Clinical Considerations: It is essential to Support Phase II detoxification pathways and also overall Phase I, II and III as clinically indicated for the individual case.

Hippurate

↓ Low Results

Nutritional Considerations: Depending on clinically correlations with past exposures, the amino acid Glycine.

Possible Interfering Factors: None known.

Clinical Considerations: Generally, not significant unless, high exposure to organic toxins past or present such as benzene. In such circumstance, testing for benzene levels is prudent, as low hippurate may suggest that the liver's Phase II detoxication is not optimally capable of processing possible burden.

↑ High Results

Nutritional Considerations: The nutrient most commonly used to support this pathway is: Glycine.

Possible Interfering Factors: Aspirin, White Willow Bark, Phenylalanine, toluene and other toxic exposures.

Clinical Considerations: GI Overgrowth of flora, Excess Environmental Solvent Exposure (perform environmental pollutant panel), Excess dietary benzoic acid and benzoate intake.

Markers of Bacterial Metabolism

These metabolites are reflective of bacterial metabolism of various nutrients within the body. If high or low they can correlate with various susceptibilities or vulnerabilities of dysregulation of homeostasis.

Para-Hydroxybenzoate

↓ Low Results

Nutritional Considerations: Insufficient Clinical Evidence at this time to offer recommendations.

Possible Interfering Factors: None known.

Clinical Considerations: Clinical relevance has yet to be fully determined.

↑ High Results

Nutritional Considerations: Consider Paraben Metabolic Support Protocol for 3 to 6 months and then retest. If homovanillate or Vanillylmandelate are low this would be suggestive of increased need for tyrosine, depending on clinical presentation.

Clinical Observation: *The use of digestive enzymes, essential fatty acids, fiber, phytonutrients such as those found in green drinks, resveratrol, Glycine, B5 and Pre- and Probiotics are worth clinical consideration.*

Possible Interfering Factors: Tyrosine Supplementation, paraben exposure, metabolite of catechins from green tea.

Clinical Considerations: Excess exposure to parabens may also be a trigger. GI dysbiosis/GI Overgrowth, representing parasitic or bacterial overgrowth.

Clinical Note: *Identifying and eliminating food allergens, minimizing paraben exposure found in cosmetics and body care products. Addressing any GI imbalance including overt pathology and leaky gut syndrome are strong considerations.*

Para-Hydroxyphenylacetate

↓ Low Results

Nutritional Considerations: Nutrients that may be considered: Phenylalanine, essential amino acids.

Possible Interfering Factors: Poor dietary source of protein, poor protein assimilation, use of acid blockers, achlorhydria.

Clinical Considerations: Need to correlate with individual being tested and overall symptoms.

↑ High Results

Nutritional Considerations: Common nutrients include: Vitamin C, MTHF (active folate), tyrosine.

Clinical Note: *Giardiasis, C. difficile and Proteus vulgaris infections of the gut may be implicated in some cases.*

Possible Interfering Factors: Dehydration, Elevated BUN (blood urea nitrogen), excess phenylalanine intake.

Clinical Considerations: Lactose intolerance, insufficient tyrosine, small bowel overgrowth, GI disease processes-including GI pathogenic organisms. Insufficient Liver Function, Kidney Disease (as confirmed via UA, BUN, GFR, Creatinine).

May be present in ischemic disease such as cardiac/pulmonary disease, anemia, sleep apnea.

2-Hydroxyphenylacetate

↓ Low Results

Nutritional Considerations: If low may consider phenylalanine as clinically indicated.

Possible Interfering Factors: None Known.

Clinical Considerations: Need to correlate with clinical picture.

↑ High Results

Nutritional Considerations: Generally basic recommendation is a good Probiotic. Need to correlate with overall toxic burden, GI health and detoxification pathway status of individual.

Possible Interfering Factors: Similar consideration as para-hydroxybenzoate.

Clinical Considerations: May be associated with uremia and BH4 deficiency.

3-Indoleacetate

↓ Low Results

Nutritional Considerations: Insufficient Clinical Evidence at this time to offer recommendations.

Possible Interfering Factors: None Known.

Clinical Considerations: Need to correlate with clinical picture.

↑ High Results

Nutritional Considerations: Generally, the most basic recommendation is a broad spectrum Probiotic.

Possible Interfering Factors: GI Dysbiosis.

Clinical Considerations: Liver Dysfunction, Poor Digestion, Leaky Gut, Decreased ATP Production, GI Disease Processes.

Clinical Note: *General approach is to test for overall GI ecology and potential dysbiosis including bacteria, parasites and yeast.*

Tricarballylate

↓ Low Results

Nutritional Considerations: Insufficient Clinical Evidence at this time to offer recommendations.

Possible Interfering Factors: None Known.

Clinical Considerations: Need to correlate with clinical picture.

↑ High Results

Nutritional Considerations: General considerations include: Probiotics, depending on mineral status consider zinc, calcium, magnesium.

Clinical Considerations: When this metabolite is high, it may bind to calcium, magnesium, zinc and possibly other minerals. It is advisable to look at patient symptoms and confirmatory labs to identify if such an occurrence is present. Overgrowth of bacteria can trigger elevated levels, thus a comprehensive review of GI symptoms, absorption and a stool analysis as indicated may be worth considering.

Many patients, as clinically capable feel better on a lower carbohydrate diet until the cause of this elevated level is identified and addressed.

Environmental Pollutants Profile

Quick Overview

The following environmental pollutant toxin detoxification discussion has been created to offer insights to share with your patient relative to sources of potential exposure currently or cumulatively over past years or decades.

Detoxification support focuses on sustaining homeostasis while addressing the toxic (allostatic load) to assist endogenous detoxication pathways and eliminate the toxic burden. After initiation of detoxification based upon an individual protocol designed by the practitioner, the general recommendation is to retest in 3 to 6 months. It is advisable to discontinue active detoxification for 2 to 4 weeks before retesting to prevent detox induced spikes created by "active accelerated detoxification" that could elevate results erroneously. The following clinical considerations are made with the understanding that the unique insights that only the attending health care provider possesses will modify the protocol so as to fit the patient. Thus you may likely modify this program to best meet your patient's specific dietary and lifestyle needs, other clinical considerations, and to create the most successful approach for their unique biochemistry.

Exposures

Many patients, particularly those that have actively been trying to live a clean and pristine lifestyle in this ever increasingly toxic world, will be baffled as to how they could have such a toxic burden. Here are some educational points to share with patients:

1.) Exposure may be recent, or cummulative from multiple sources including from commuting or secondary exposures, such as work, home, athletic club/gym, or from unknown contamination. If your patient travels or eats out regularly, phthalates and parabens are routinely found in restaurant food, due to packaging. Toxic exposure may have arisen from a regional forest fires, or other exposure to pollutants, and other organic materials, or traffic commutes contributing to benzene and toluene or possibly even from the fruits of their labors via outgassing in new cars, new furniture, new carpet, etc.

2.) It is important to remind patients that their results may also reflect toxic exposures accumulated from years gone by, possibly even their transplacental exposure *in utero*. Many of these organic pollutants (EPPs) are stored readily in adipose (fat) and are released through cellular turnover, weight loss, exercise and even the process of eating foods rich in detoxification nutrients. The goal is to safely, slowly and methodically lessen the burden that involves the "Metabolic 3 Phase DeTox Process" combined with the "Lifestyle 2 Phase Burden Elimination". These will be discussed below in their sections.

Detoxification Considerations

You can share with your patients that they could envision successful detoxification as a targeted goal to lessen the total burden combined with an ongoing routine detox program to keep levels of toxins from re-bioaccumulating. The modular system of detoxification is readily broken into two parallel action steps.

Metabolic 3 Phase DeTox Steps

DeTox Phase 1 and 2: This involve supporting the liver's ability to mobilize and excrete the identified environmental pollutants (EPPs) and other toxins. As seen in the graphic below the liver requires very specific nutrients to fuel detoxification. As seen in the graphic, there is an essential list of nutrients that should be employed to target liver support. Remembering there are hundreds of toxins the world's citizens are exposed too, thus as your patient "detoxes" from their known burdens there will be other substances excreted. This is why broad support of Phase 1 and 2 liver steps is critical. Thus it is important to fuel each pathway with fresh organic veggies and fruits; delivering key phytonutrients and also trace elements. Advising patients of the "Dirty Dozen Foods" not to consume, due to the pesticide and herbicide load is important.

DeTox Phase 3: Seems simple, yet rarely does a patient volunteer or appreciate the importance of their bathroom habits. Patients are encouraged to consume non-fluoridated water that is also free of heavy metals and other pollutants that otherwise further poison biochemical pathways. The recommendation for adults is a minimum of 2 to 3 liters of pristine H2O unless medically contraindicated. The goal is for a patient to note at least 3 urinations during the day that are "near clear" in coloration.

Another vitally important part of detoxification, is stool elimination. As reflected by the Bristol Stool Chart, readily available via a browser search of the world wide web, the goal is to have patients have 2 to 3 meaningful bowel movements per day. Less frequent stool patterns are generally associated with reabsorption of toxins as the stool resides in the colon where toxins readily pass back into the circulation adding "yesterday's waste" to currently daily toxic burden. Essential to remind patients, Phase 1 and 2 help remove the toxins more readily making them available to flush out of the body, in a slow and safe methodical process. Failing to flush the body via adequate hydration and bowel elimination, sabotages the Metabolic 3 Phase DeTox Steps.

Lifestyle 2 Phase Burden Elimination

Becoming aware and playing detective regarding current sources of toxic exposure. If the patient is actively or has actively lost weight recently, this could also lead to a higher total urinary excretion of environmental pollutants (EPPs). Thus, whenever losing weight, an individual should focus on each of the above **Metabolic 3 Phase Detox Steps** and the **Lifestyle 2 Phase Burden Elimination**.

Lifestyle Phase 1: It is vitally important to critically analyze current and past exposures relative to your EPP results. Remembering that to lessen future burdens is already a huge success as it lessens and liberates existing detoxification pathways and "sludging" of the patient's biochemistry. Driving with one's vehicle on re-circulate during the busy commute with windows up unless there is notable off-gassing occurring apparent; then a determination must be made regarding the greater risk. Use of HEPA or

similar air filters at work and in the home can help filter out toxins and also allergens that otherwise burden the body. Not cooking or re-heating foods or leftovers in plastic is important. Additionally, using either a glass container or stainless-steel drinking container instead of plastic water bottles is critical relative to phthalate exposure. Also encourage patients to avoid grapefruit and grapefruit juice during active detoxification as it slows certain liver enzymatic processes. Note, if a patient has been actively consuming grapefruit juice and takes prescription or over the counter medications, stopping the use of grapefruit products may lower select circulating drug levels.
Also, avoiding drinking alcohol, as potent solvent is important during detoxification.

Lifestyle Phase 2: Sweat is one's friend. It is critical however to rinse off quickly after sweating to prevent reabsorption of the toxins that have been released. Afterall transdermal delivery of medications and other substances is a well-known mechanism; toxins can absorb and reabsorb via the skin as well. Many patients with access to a sauna at a gym or far infra-red will use these tools along with "condition appropriate exercise" to sweat out some toxins. This augments and complements the liver detoxification described in Metabolic 3 Phase Detox Steps.

Xylene

3-Methylhippurate & 2-Methylhippurate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

+ Focus on Probiotics and Gut Permeability

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Ensure there is sufficient intake of vitamin B3 (niacin).

Possible Sources of Toxin: Printing, rubber, leather industry, cleaning agents, paint thinner, paints and varnishes. Airplane fuel and vehicle gasoline to improve the octane rating.

Toluene

Hippurate & Benzoate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

+ Focus on Probiotics and Gut Permeability

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Possible Sources of Toxin: Paint thinners, paintbrush cleaners, fingernail polish, glues, lacquers, adhesives, inks, stain removers, some leather tanning processes, vehicle exhaust and added to gasoline to improve octane rating, cigarette smoke, groundwater and also added to gasoline to enhance octane rating.

Benzene

t,t-Muconic

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

Additional Consideration:

Sulforaphane (supplement and broccoli sprouts)

+ Focus on Probiotics and Gut Permeability

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Possible Sources of Toxin: Pesticides, wildfire smoke, cigarette smoke,paint removers, plastics, resins, synthetic fibers, rubber lubricants, dyes, detergents, drugs, vehicle exhaust, pesticides, ground water.

Trimethylbenzene

3, 4-Dimethylhippurate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

+ Focus on Probiotics and Gut Permeability

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Styrene

Mandelate, Phenylglyoxylate, & Mandelate + Phenylglyoxylate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

+ Focus on Probiotics and Gut Permeability

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Possible Sources of Toxin: Cigarette smoke, fiberglass, rubber, insulation, automobile parts, food containers, packaging, household, and building products, carpet backing, pipes, vehicle exhaust, emissions from copy machines.

Phthalates

Monoethyl Phthalate, Phthalate, & Quinolinate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

Additional Considerations:

- Zinc
- Magnesium
- Indole-3-Carbinol (I-3-C) or DIM (also cruciferous vegetables)
- Calcium D-Glucarate

+ Focus on Probiotics and Gut Permeability

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Possible Sources of Toxin: Wall coverings, tablecloths, floor tiles, furniture upholstery, shower curtains, garden hoses, swimming pool liners, rainwear, baby pants, dolls, some toys, shoes, automobile upholstery and tops, food packaging, sheathing for wire and cable, medical tubing, blood storage bags, carpets, paints, glue, insect repellents, hair spray, nail polish, rocket fuel, carpet backing, coating, floor tile, PVC pipes, adhesives, cosmetics, pesticides, toothbrushes, automobile parts, tools, toys, and aspirin.

Paraben

Para-Hydroxybenzoate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

Additional Considerations:

- Milk Thistle and Flavonoids
- Zinc
- Magnesium
- Indole-3-Carbinol (I-3-C) or DIM (also cruciferous vegetables)
- Calcium D-Glucarate

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Possible Sources of Toxin: Personal care products such as soap, shampoo, cosmetics, and perfume.

Methyl Tert-butyl Ether

Alpha-Hydroxyisobutyrate

Detoxification Considerations: Implementing Metabolic 3 Phase Detox Steps and Lifestyle 2 Phase Burden Elimination

- Glutathione
- Alpha-lipoic acid (glutathione precursor)
- Selenium (often in a quality multivitamin or healthy diet)
- Vitamin E (usually in a quality multivitamin)
- Vitamin C – supplement recommended
- Glycine

Additional Considerations:
Activated Charcoal

Consuming abundant pesticide and herbicide-free vegetables and eating lower on the food chain when possible.

Possible Sources of Toxin: Used until 2005 per Congress for new gasoline standards, thus past exposure from this source. Drinking water/groundwater; irrigation contaminates farm produce. MTBE is still used as a gasoline additive in some other countries, including China.

US BioTek Laboratories' Policy

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