



The Great Plains Laboratory, Inc.

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The Great Plains Laboratory, Inc. (GPL) is a research-based clinical laboratory that offers testing for nutritional factors in chronic illnesses worldwide. Our company was founded in 1996 and is currently serving more than 100 countries. We provide a variety of metabolic tests that are not routinely available through other laboratories, and have tested more than 200,000 patients with autism and other related disorders. Our goal is to help people achieve their maximum potential through quality laboratory testing, knowledgeable staff, and excellent customer service.

Our Mission

“Our mission is to improve health treatment outcomes for chronic illnesses by providing the most accurate, reliable, and comprehensive biomedical analyses available - using the latest technology and proven techniques – and by providing education to patients, families, and health care practitioners.”



First in Nutritional and Environmental Medicine

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General Overview

The Organic Acids Test provides a snapshot of the metabolism, based on a comprehensive assessment of 74 unique urinary metabolites. These small, discarded organic acid molecules are by-products of human cellular activity, the digestion of foods, and the metabolism of gastrointestinal flora. Specimens from individuals with a chronic illness, allergic condition, or neurological disorder often have one or more abnormal organic acids. Some organic compounds are produced by an overgrowth of gastrointestinal yeast and/or bacteria species due to impaired immune function or exposure to broad-spectrum antibiotics. Identification of yeast or bacterial overgrowth, paired with successful treatment can eradicate or markedly reduce patients' symptoms and significantly increase the likelihood of recovery.

The Great Plains Laboratory's Organic Acids Test is the most comprehensive test of its kind. It evaluates yeast and bacterial overgrowth, vitamin and antioxidant levels, fatty acid metabolism, neurotransmitter levels, inborn errors of metabolism (including oxalate levels), mitochondrial function, oxidative stress, detoxification, and much more. For a full list of all markers in the Organic Acids Test, see our brochure, *The Clinical Significance of the Organic Acids Test*, or visit the Organic Acids Test page on our web site, www.GreatPlainsLaboratory.com.





Specimen Requirements:

10 mL of first morning urine before food or drink is suggested. Patients should avoid apples, grapes (including raisins), pears, cranberries and their juices 24 hours prior to specimen collection.



Clinical Significance: Primary Test Areas

Yeast & Bacteria

The Organic Acids Test (OAT) from The Great Plains Laboratory, Inc. offers the most complete and accurate evaluation of intestinal yeast and bacteria available. ***It is the only OAT that distinguishes between beneficial and harmful bacteria.*** It also detects specific toxic metabolites of Clostridia bacteria, which are commonly missed by conventional culture methods, including unique markers for 4-cresol and HPHPA. The toxins released by toxic Clostridia metabolites can inhibit key neurotransmitters in the brain, including the conversion of dopamine to norepinephrine, leading to or exacerbating the symptoms of a variety of neuropsychiatric and behavioral disorders, such as depression, bipolar disorder, and autism. Clostridia infection is also associated with gastrointestinal disorders, including irritable bowel syndrome, Crohn's disease, and ulcerative colitis. Overgrowth of *Candida albicans*, perhaps the most common form of yeast in the body, can build up toxins that are associated with fibromyalgia, migraines, chronic fatigue syndrome, poor concentration or "brain fog", onset or magnification of symptoms of depression and psychosis. *Candida* can also become invasive, attaching to the intestinal wall, and causing "leaky gut" syndrome, which can magnify food allergies, impede absorption of vitamins and minerals, and cause a variety of intestinal disorders. Factors which can cause intestinal yeast overgrowth include oral antibiotic use, excessive sugars in the diet, mold or other toxic environmental exposure, selective or combined immune deficiencies, and genetic irregularities. Excess *Candida* burdens mitochondrial function and produces elevated levels of oxalates.

Once any yeast or bacterial abnormalities are detected, there are a variety of treatment options available, including antifungal or antibacterial products, probiotic supplementation, vitamins, antioxidants, and dietary modification. Patients and physicians have reported significant improvement upon treatment, including decreased fatigue, regular bowel movements, increased energy and alertness, increased concentration, improved verbal skills, less hyperactivity, better sleep patterns, and decreased abdominal pain.

Nutrition: Vitamins & Antioxidants

The Organic Acids Test includes several nutritional markers, showing essential vitamin and antioxidant levels, including vitamins B12, B6, B5, B2, and C, Coenzyme Q10, N-Acetylcysteine, and Biotin (Vitamin H). Deficiencies of these vitamins and antioxidants are affiliated with a variety of chronic health issues.

A diet lacking in adequate nutrients affects our overall health. Many people with chronic illnesses and mental health disorders show significant deficiencies of important vitamins and other nutrients. Malnutrition due to deficiencies in specific micronutrients impairs the immune system. The most consistent abnormalities are seen in cell-mediated immunity, complement system function, cytokine production, and antibody affinity.

More information about specific conditions related to these deficiencies and recommended supplementation for treatment can be found in our **Clinical Significance of the Organic Acids Test** brochure.

Fatty Acid Metabolism

The Organic Acids Test measures eight specific ketones and fatty acid metabolites. Elevated levels of these fatty acids can be indicators of protein malnutrition, type I diabetes, severe GI *Candida* overgrowth, various genetic disorders, and cause hypoglycemia and lethargy. More information about specific conditions related to fatty acid metabolism defects and recommended supplementation for treatment can be found in our **Clinical Significance of the Organic Acids Test** brochure.

Neurotransmitters

The Organic Acids Test measures levels of HVA (homovanillic acid) and VMA (vanillylmandelic acid), the metabolites of the neurotransmitters, dopamine and epinephrine/norepinephrine. It also measures the ratio of the two metabolites. Elevated HVA and decreased VMA may be caused by Clostridia infection or lead toxicity. An elevated ratio is often the result of decreased conversion of dopamine to norepinephrine by the enzyme, dopamine beta-hydroxylase. This inhibition is commonly caused by Clostridia by-products, including HPPHA, 4-cresol, and 4-hydroxyphenylacetic acid, which are also measured in the OAT.

The Organic Acids Test also reports levels of quinolinic acid. Increased values of this marker may be caused by chronic inflammation from microbial infections, central nervous system degeneration, excessive tryptophan supplementation, and even exposure to phthalates. Quinolinic acid is considered neurotoxic at very high levels due to over stimulation of nerve cells, leading to premature nerve cell death.

Mitochondrial Function

Mitochondria are the energy factories in our body and contribute to metabolizing biochemicals needed for optimum health, such as synthesis of certain hormones, cholesterol metabolism, neurotransmitter metabolism, and ammonia metabolism.

The Organic Acids Test has several markers for mitochondrial function, including six Krebs cycle metabolites and two specific amino acid metabolites. Increased values of these metabolites can indicate mitochondria energy pathway dysfunction and deficiencies in a variety of important vitamins and enzymes needed for optimal mitochondrial health.

For more information on recommended supplementation to support mitochondrial function, see our **Clinical Significance of the Organic Acids Test** brochure.

Inborn Errors of Metabolism

The Great Plains Laboratory, Inc. is the only lab that includes markers for oxalate metabolism in the Organic Acids Test. Elevated oxalates may indicate the genetic diseases, hyperoxaluria type I and type II. Build-up of oxalates can cause kidney stones. Oxalates can also deposit in the bones, eyes, thyroid gland, and other tissues. They may also cause pain and inflammatory conditions such as fibromyalgia and vulvodynia (vulvar pain). For information on possible treatments for oxalate issues, see the section in this book on oxalates. The OAT also includes markers for other inborn errors of metabolism, specifically for metabolites of the glycolytic cycle.

Detoxification and Oxidative Stress

The Organic Acids Test includes important indicators of the body's detoxification abilities, including those for glutathione levels. Glutathione is one of the most important and powerful antioxidants, and is often deficient in autism and other chronic conditions.

When an individual is prone to oxidative stress, they are also more susceptible to opportunistic pathogens. These pathogens can hinder, either directly or indirectly, proper digestion and create further oxidative stress in the body. Unless addressed, this vicious cycle will continue to inhibit the various chemical pathways necessary for proper neurological and immune function.

Another important marker included in the Organic Acids Test for detoxification is orotic acid. High levels of orotic acid can be caused by dysbiosis. Elevations of this marker are most commonly associated with ammonia toxicity. Elevated ammonia may result from drug toxicity to the liver, viral liver infection, or inborn errors of ammonia metabolism. Ammonia excess affects brain tissue, causing symptoms such as headaches, insomnia, confusion, inability to concentrate, anxiety, and even delirium.



Applications for Select Disorders

Organic Acids: Autism and PDD

The following markers are highly correlated with autism and PDD:

- **Yeast and bacteria (especially arabinose, citramalic acid, tartaric acid, HPHPA, 4-cresol, and DHPPA)**
- **Oxalates (specifically oxalic, glyceric, and glycolic acids)**
- **Mitochondrial function (including succinic, fumaric, malic, 2-oxoglutaric, aconitic, and citric acids)**
- **Neurotransmitter function (HVA, VMA, HVM/VMA ratio, and quinolinic acid)**
- **Nutritional (markers relevant to autism treatment such as vitamins B6 and B12 and markers for detoxification)**

Eliminating yeast overgrowth can be an effective method of reducing autistic symptoms. Microbial overgrowth can be measured by urinary organic acids analysis of yeast and bacteria metabolites. The test also helps to identify indicators of methylation problems associated with autism.

Many children on the autism spectrum have an overgrowth of certain Clostridia species, which produce compounds such as HPHPA (3-(3-hydroxyphenyl)-3-hydroxypropionic acid) and 4-cresol. HPHPA and 4-cresol may disrupt dopamine metabolism by interfering with the enzyme, dopamine beta-hydroxylase. HPHPA is a potent toxin with profound neurological effects in autism, which can cause moodiness, tantrums, extreme anxiety, aggression, self-injurious behavior, and digestive problems.

The Great Plains Laboratory is the only lab that measures oxalates as part of an organic acids test. A great deal of research in recent years indicates that oxalate treatment is at the core of autism treatment. For more information about oxalates and autism, please turn to page 27.

Additional tests recommended for patients with autism: IgG Food Allergy Test, Advanced Cholesterol Profile, Phospholipase A₂ Activity Test, Metals Hair Test, Comprehensive Stool Analysis, GPL-TOX, Vitamin D, Copper/Zinc Profile, and GPL-SNP1000 .

Organic Acids: Neuropsychiatric and Neurological Conditions

The following markers are highly correlated with neuropsychiatric and neurological conditions:

- **Yeast and bacteria (especially arbinose, tartaric acid, HPHPA, 4-cresol, and DHPPA)**
- **Neurotransmitter function (HVA, VMA, HVA/VMA ratio, and quinolinic acid)**
- **Mitochondrial function (especially 3-hydroxyglutaric acid)**
- **Oxalates (all markers)**
- **Nutritional (especially B12, B6, B5, vitamin C, CoQ10, N-Acetylcysteine, and biotin)**

Proper treatment of Clostridia overgrowth, which produces excessive HPHPA and 4-cresol has markedly reduced or eliminated symptoms in patients with schizophrenia, OCD, depression, and other mental health disorders by balancing neurotransmitter levels. For more information about Clostridia and neuropsychiatric disorders, please turn to page 21 for a complete case study and useful statistics.

Overgrowth of yeast is associated with depression, memory impairment, behavioral disorders, low energy levels, hyperactivity, and a burdened immune system. Severe yeast overgrowth can impede vitamin and mineral absorption, leading to excess oxalate levels, and inadequate health.

High levels of quinolinic acid are implicated in Alzheimer's disease, Huntington's disease, depression, dementia, and other psychiatric and neurological conditions.

Additional tests recommended for patients with psychiatric and neurological disorders: GPL-TOX, IgG Food Allergy Test, Phospholipase A₂ Activity Test, Gluten /Casein Peptide Test, and Vitamin D Test.

Organic Acids: Mitochondrial and Genetic Disorders

The following markers are highly correlated with mitochondrial and genetic disorders:

- All mitochondrial markers
- Glycolytic cycle (lactic acid and pyruvic acid)
- Yeast and bacteria
- Oxalates
- Amino acid metabolites
- Ketone and fatty acid oxidation

The Organic Acids Test detects levels of malic acid, which, when elevated simultaneously with citric, fumaric, and alpha-ketoglutaric acids, strongly suggests cytochrome C oxidase deficiency, indicating dysfunction in the mitochondrial energy pathways.

The marker, 3-methylglutaconic acid in high values indicates a reduced ability to metabolize the amino acid, leucine. This abnormality is found in the genetic disease, methylglutaconic aciduria and in mitochondrial disorders.

Another marker in the Organic Acids Test indicating genetic disease is 3-hydroxyglutaric acid. This metabolite is associated with glutaric aciduria type I, which is caused by a deficiency of glutaryl CoA dehydrogenase, an enzyme involved in the breakdown of lysine, hydroxylysine, and tryptophan. In this specific disorder, other organic acids such as glutaric and glutaconic acids will be elevated as well.

Additional tests recommended for patients with genetic and mitochondrial disorders: GPL-TOX and GPL-SNP1000.

Organic Acids: Chronic Gastrointestinal and Inflammatory Disorders

The following markers are highly correlated with chronic gastrointestinal and inflammatory disorders:

- Yeast and bacteria (especially arabinose, tartaric acid, HPHPA, 4-cresol, and DHPPA)
- Neurotransmitter function
- Nutritional markers (especially glutaric and methylcitric acids) and quinolinic acid

Additional tests recommended for patients with chronic gastrointestinal and inflammatory disorders: IgG Food Allergy Test, Phospholipase A₂ Activity Test, and Gluten/Casein Peptide Test.

“After identifying a low serotonin level on an Organic Acids Test (a hallmark functional medicine test), a severely depressed and suicidal man began taking 100mg of 5HTP twice a day (5HTP is the direct precursor to serotonin). After two days, he said his depression virtually disappeared and he was no longer suicidal. I love when I can identify a biochemical glitch and someone can have such a profound emotional turn around.”

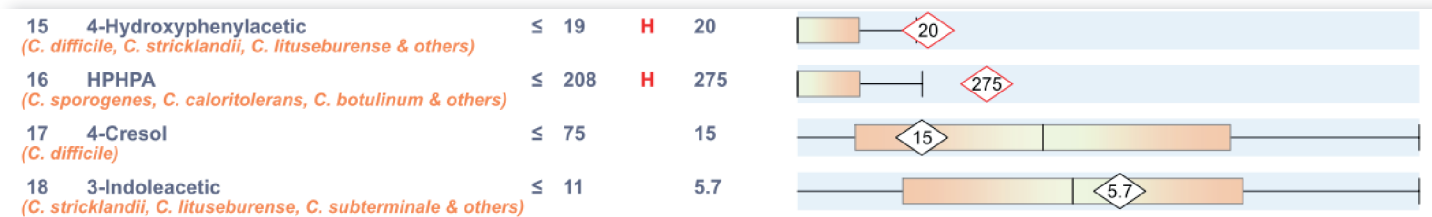
-Dr. Josh Friedman



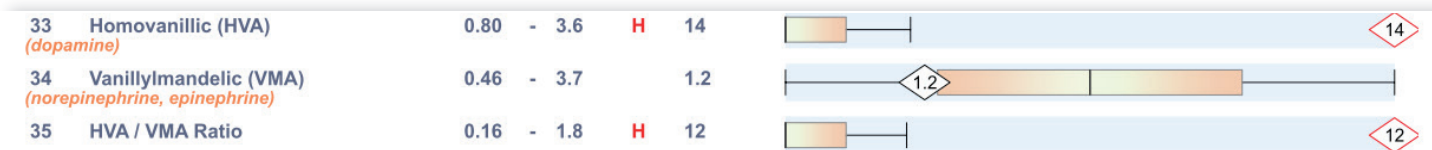
Clostridia

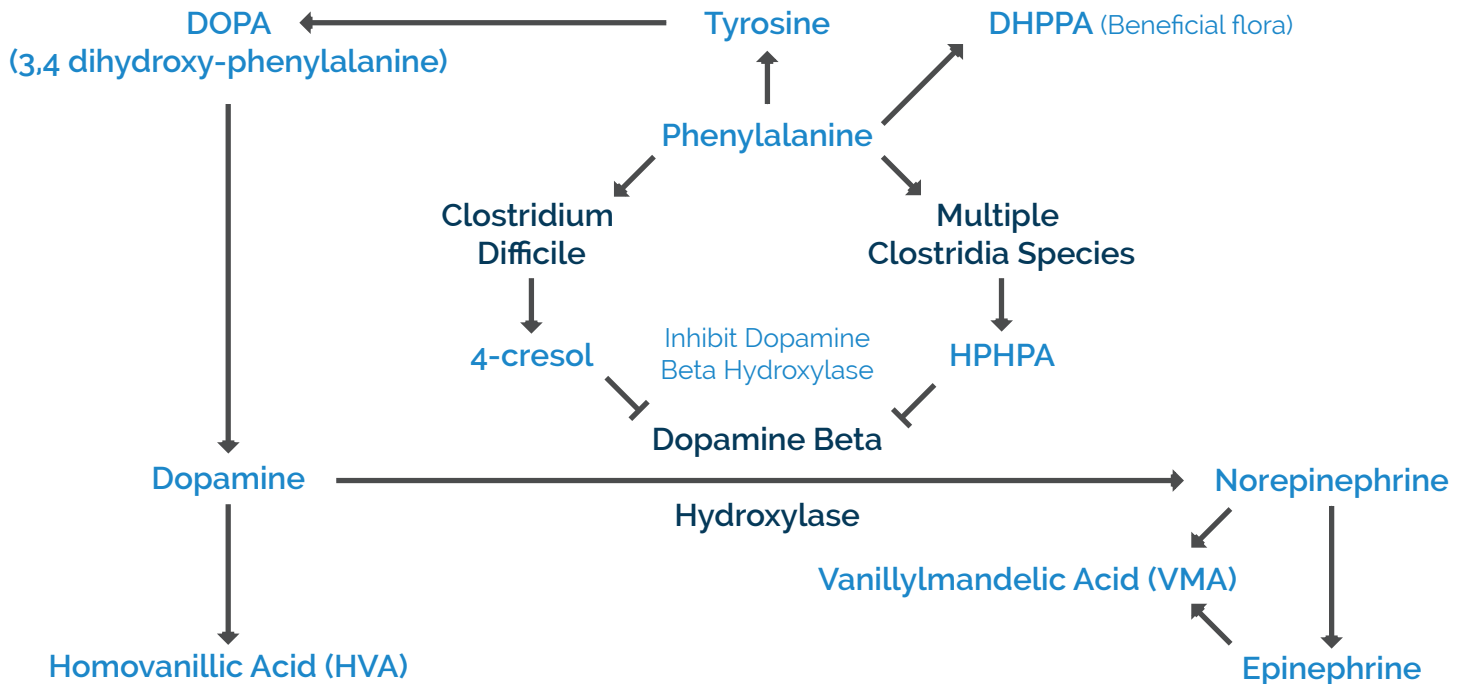
Toxic Effects of Clostridia Metabolites

The Great Plains Laboratory Organic Acids Test is very sensitive and can differentiate between harmful and beneficial bacteria, which is unique among tests for Clostridia. It is also the only organic acids test available that measures HPHPA, one of the primary toxic metabolites of Clostridia. In the sample results below, the patient has a high level of HPHPA, but a low level of 4-cresol, the main marker for *C. difficile*. Other tests that only measure 4-cresol, and not HPHPA, would have missed this harmful bacterial overgrowth.



Another benefit to The Great Plains Laboratory Organic Acids Test is that it evaluates Clostridia metabolites that can inhibit metabolism of important neurotransmitters. As shown in the sample results below, the test measures homovanillic acid (HVA), a metabolite of dopamine, as well as vanillylmandelic acid (VMA), a metabolite of norepinephrine and epinephrine. Clostridia bacteria can produce toxins that may inhibit the conversion of dopamine to norepinephrine. This can lead to a build-up of dopamine and a disruption in the dopamine to norepinephrine ratios. By assessing these metabolites, the Organic Acids Test is able to better determine the possible underlying cause of many different conditions.





Combined Human and Clostridia Metabolic Effects on Neurotransmitters

HPHPA: A History and Case Studies

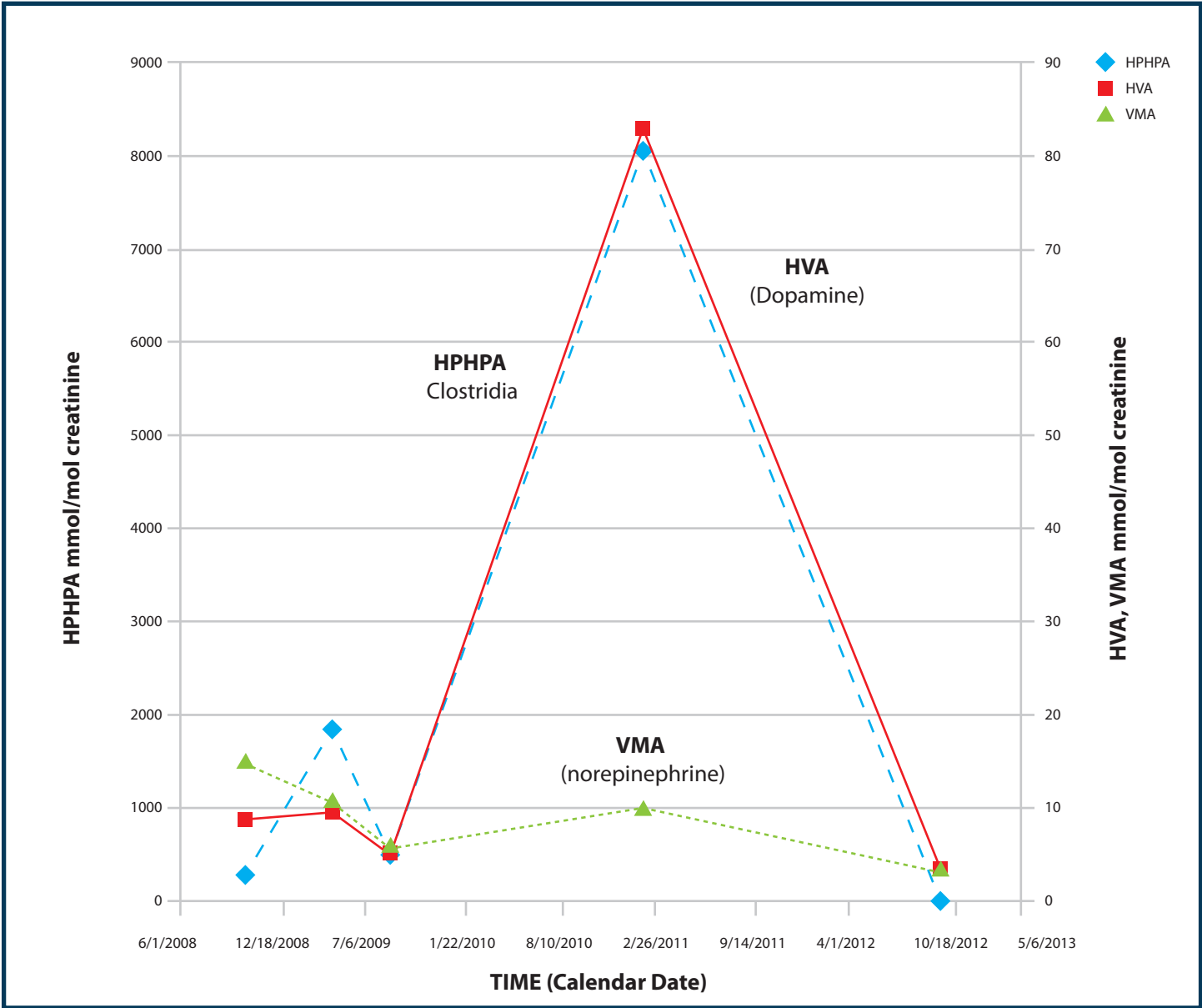
HPHPA (3-(3-Hydroxyphenyl)-3-Hydroxypropionic Acid) was first discovered by M. Armstrong and K. Shaw more than 50 years ago, when they found this compound to be elevated in patients of all types in mental hospitals. The source of this compound is a small number of Clostridia species. William Shaw, Ph.D., Director of The Great Plains Laboratory, Inc., re-discovered this compound in many patients with psychiatric diseases during research at a major pediatric hospital. Significant decreases in symptoms of schizophrenia, autism, seizure disorders, tic disorders, depression, chronic fatigue syndrome, and AD(H)D have been reported after testing for and treating these specific Clostridia infections. A number of physicians have indicated that this marker is one of the most clinically significant biochemical markers that they use for symptom management. For more information on the history of HPHPA, go to: www.GreatPlainsLaboratory.com

Case Study 1:

A patient with severe chronic fatigue and depression was tested for organic acids, which revealed a high concentration of HPHPA, indicating Clostridia overgrowth of the gastrointestinal tract. Symptoms had persisted for a year-and-a-half and the patient had been on complete disability. Treatment with Clostridia-specific antibiotics resulted in a marked decrease (from 1,444 to 13 mmol/mol creatinine) in HPHPA and complete clearing of depression symptoms and chronic fatigue. The patient was able to get off of disability and return to work after less than a month of treatment.

Case Study 2:

The graph on page 22 shows the correlation between HPHPA, harmful Clostridia, and dopamine in a patient diagnosed with extremely severe autism. The Great Plains Laboratory tracked the patient's levels of Clostridia over time, and after successful treatment with oral Vancomycin, the patient's Clostridia levels dropped to near zero and levels of HVA (the dopamine metabolite) returned to normal. Once a Clostridia infection is found, a routine Microbial Organic Acids Test (MOAT) every three months is recommended to check for possible recurring infections.



Case Study 2:



Oxalates

What are Oxalates?

The Organic Acids Test by The Great Plains Laboratory, Inc. is the only OAT on the market that evaluates levels of oxalates in urine. Oxalate (and its acid form, oxalic acid), is an organic acid that is primarily derived from three sources: the diet, fungus (such as *Aspergillus* and *Penicillium*), possibly *Candida*, and also human metabolism. Oxalic acid is the most acidic organic acid in body fluids and is used commercially to remove rust from car radiators. Antifreeze (ethylene glycol) is toxic primarily because it is converted to oxalate in the body. Two different types of genetic diseases are known in which oxalates are high in the urine, hyperoxalurias type I and type II, which can also be determined from the Organic Acids Test.

Foods especially high in oxalates are often foods thought to be otherwise healthy, including spinach, beets, chocolate, peanuts, wheat bran, tea, cashews, pecans, almonds, berries, and many others. People now frequently consume “green smoothies” in an effort to eat “clean” and get healthy, however, they may actually be sabotaging their health. The most common components of green smoothies are spinach, kale, Swiss chard, and arugula, all of which are loaded with oxalates. These smoothies also often contain berries or almonds, which have high amounts of oxalates as well. Oxalates are not found in meat or fish at significant concentrations. Daily adult oxalate intake is usually 80-120 mg/d. A single green smoothie with two cups of spinach contains about 1,500 mg of oxalate, a potentially lethal dose. A complete list of high oxalate foods is available on the internet at:

<http://patienteducation.upmc.com/Pdf/LowOxalateDiet.pdf>

“If oxalic acid is very high in the blood being filtered by the kidney, it may combine with calcium to form crystals that may block urine flow and cause severe pain. However, such crystals may also form in the bones, joints, blood vessels, lungs, eyes, skin, heart, thymus, skeletal muscle, joints, fat, teeth, mouth, nerves, and even the brain.”

-William Shaw, Ph.D.

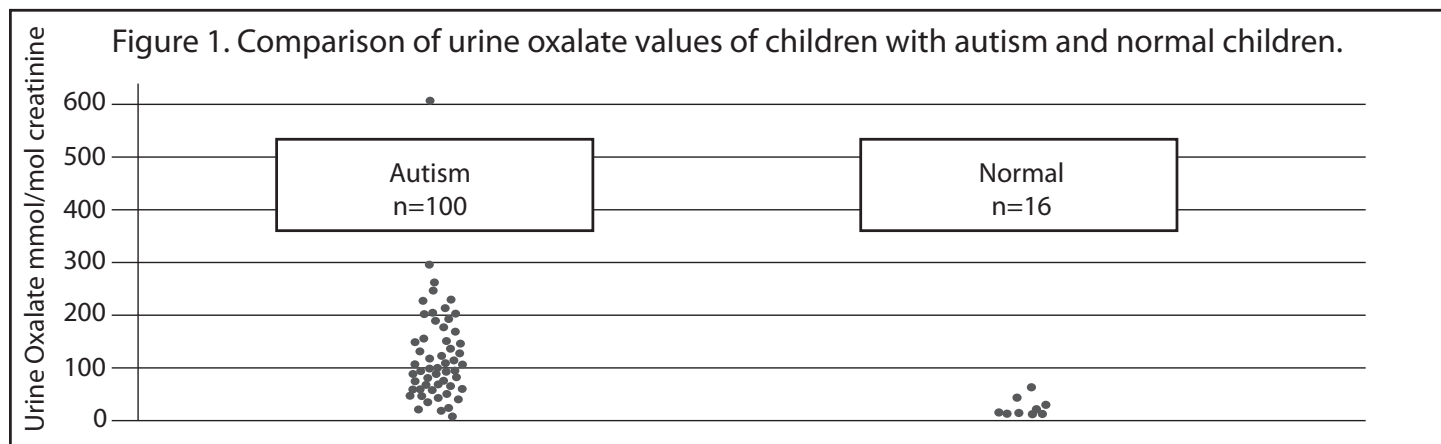
The Dangers of Oxalates

High oxalates in the urine and plasma were first found in people who were susceptible to kidney stones. Many kidney stones are composed of calcium oxalate. Stones can range in size from the diameter of a grain of rice to the width of a golf ball. It is estimated that 10% of males may have kidney stones some time in their life. Because many kidney stones contain calcium, some people with kidney stones think they should avoid calcium supplements. However, the opposite is true. When calcium is taken with foods that are high in oxalates, oxalic acid in the intestine combines with calcium to form insoluble calcium oxalate crystals that are eliminated in the stool. This form of oxalate cannot be absorbed into the body. When calcium is low in the diet, oxalic acid is soluble in the liquid portion of the contents of the intestine (called chyme) and is readily absorbed from the intestine into the bloodstream. If oxalic acid is very high in the blood being filtered by the kidney, it may combine with calcium to form crystals that may block urine flow and cause severe pain.

In addition to kidney disease, individuals with fibromyalgia and women with vulvar pain (vulvodynia) may suffer from the effects of excess oxalates. Oxalate crystals may also form in the bones, joints, blood vessels, lungs, thyroid, and even the brain, possibly impeding their proper function. In addition, oxalates in the bone may crowd out the bone marrow cells, leading to anemia and immunosuppression. Oxalate crystals cause pain and damage to various tissues, due to their sharp, physical structure, and may also increase inflammation. Iron oxalate crystals may cause significant oxidative damage and diminish iron stores needed for red blood cell formation. Oxalates may also function as chelating agents and may chelate many toxic metals, such as mercury and lead. Unlike other chelating agents, oxalates trap heavy metals in the tissues, leading to metal toxicity. Oxalates also interfere with the Krebs cycle's glucose metabolism and can inhibit absorption of essential minerals necessary for optimum health.

Oxalates and Autism

Studies show that oxalates in the urine are much higher in individuals with autism than in non-autistic children. In the figure below, it shows that 36% of the children on the autism spectrum had values higher than 90 mmol/mol creatinine, the value consistent with a diagnosis of genetic hyperoxalurias, while none of the non-autistic children had values this high. 84% of the children on the autism spectrum had oxalate values outside the normal range (mean \pm 2 sd). None of the children on the autistic spectrum had elevations of the other organic acids associated with genetic diseases of oxalate metabolism, indicating that oxalates are high due to external sources.



A low-oxalate diet is being used extensively to treat children with autism and other disorders. Researcher, Susan Owens discovered that the use of a diet low in oxalates markedly reduced symptoms in children with autism and PDD. For example, the mother of an autistic son reported that he became more focused and calm, that he played better, that he walked better, and had a reduction in leg and feet pain after being on a low oxalate diet. Prior to the diet, her child could hardly walk up the stairs. After the diet, he walked up the stairs very easily. Many children with autism throughout the world are now being placed on this diet with good results.

How Can Oxalates Be Treated?

- Implement a low-oxalate diet. This may be especially important if the individual has had *Candida* for long periods of time and there is high tissue oxalate buildup.
- Use antifungal drugs to reduce yeast and fungi that may be causing high oxalates. Children with autism frequently require years of antifungal treatment. Arabinose, a marker used for years for yeast/fungal overgrowth in the Organic Acids Test is correlated with high amounts of oxalates.
- Supplements of calcium and magnesium citrate can reduce oxalate absorption from the intestine. Citrate is the preferred calcium form to reduce oxalate because citrate also inhibits oxalate absorption from the intestinal tract.
- N-Acetyl glucosamine supplements can stimulate the production of the intercellular cement, hyaluronic acid, to reduce pain caused by oxalates.
- Chondroitin sulfate can prevent the formation of calcium oxalate crystals.
- Vitamin B6 is a cofactor for one of the enzymes that degrades oxalate in the body and has been shown to reduce oxalate production.
- Excessive fats in the diet may cause elevated oxalates if the fatty acids are poorly absorbed because of bile salt deficiency. If taurine is low, supplementation with taurine may help stimulate bile salt production (taurocholic acid), leading to better fatty acid absorption and diminished oxalate absorption.
- Probiotics may be very helpful in degrading oxalates in the intestine. Individuals with low amounts of oxalate-degrading bacteria are much more susceptible to kidney stones. Both *Lactobacillus acidophilus* and *Bifidobacterium lactis* have enzymes that degrade oxalates.
- Increase intake of essential omega-3 fatty acids, commonly found in fish oil and cod liver oil, which reduces oxalate problems. High amounts of the omega-6 fatty acid, arachidonic acid, are associated with increased oxalate problems. Meat from grain fed animals is high in arachidonic acid.
- Supplements of vitamin E, selenium, and arginine have been shown to reduce oxalate damage.
- Increase water intake to help eliminate oxalates.



Key Markers

<p>HPHPA (3-(3-Hydroxyphenyl)-3-Hydroxypropionic Acid) Marker for Bacteria, Including Selected Clostridia</p>	<p>Indicates a possible overgrowth of intestinal bacteria, specifically the Clostridia species, <i>C. botulinum</i>, <i>C. sporogenes</i>, and <i>C. caloritolerans</i>. The metabolites of these species can be neurotoxic.</p>
<p>4-cresol Marker for Bacteria, Including Selected Clostridia</p>	<p>Indicates a possible overgrowth of intestinal bacteria, specific 4-cresol producers. 4-cresol is a phenolic product of the Clostridia species, <i>C. difficile</i>, and is poorly metabolized in children with autism. High-potency, multi-strain probiotics may help rebalance GI flora.</p>
<p>4-Hydroxyphenylacetic Acid Marker for Bacteria, Including Selected Clostridia</p>	<p>Associated with small intestinal bacteria overgrowth (SIBO) due to its production by <i>C. difficile</i>, <i>C. stricklandii</i>, <i>C. lituseburense</i>, <i>C. subterminale</i>, <i>C. putrefaciens</i>, and <i>C. propionicum</i>.</p>
<p>3-Indoleacetic Acid Marker for Bacteria, Including Selected Clostridia</p>	<p>A tryptophan byproduct of the Clostridia species, <i>C. stricklandii</i>, <i>C. lituseburense</i>, <i>C. subterminale</i>, and <i>C. putrefaciens</i>. May indicate a depletion of tryptophan needed for various physiological functions.</p>
<p>3-Hydroxyglutaric Acid Marker for Genetic Disease</p>	<p>A metabolite associated with the genetic disease, glutaric aciduria type I, which is due to a deficiency of glutaryl CoA dehydrogenase, an enzyme involved in the breakdown of lysine, hydroxylysine, and tryptophan. In this disorder, other organic acids (glutaric and glutaconic) will be elevated. Treatment includes special diets low in lysine and supplementation with carnitine or acetyl-L-carnitine.</p>
<p>3-Methylglutaconic Acid Marker for Mitochondrial Disorder</p>	<p>Significant increase is due to a reduced ability to metabolize the amino acid, leucine. This abnormality is found in the genetic disease, methylglutaconic aciduria, and in mitochondrial disorders. 3-methylglutaric acid may also be elevated. Supplementation with coenzyme Q10, NAD+, L-carnitine and acetyl-L-carnitine, riboflavin, nicotinamide, biotin, and vitamin E may be useful.</p>

<p>Tricarballic Acid Marker for Exposure to Certain Fungal Contamination in Foods</p>	<p>A chemical by-product released from fumonisins during passage through the gastrointestinal tract. Fumonisins are fungal toxins produced primarily by <i>F. verticillioides</i>. Elevated levels can be caused by the intake of corn or corn-based food contaminated with fumonisins.</p>
<p>Malic Acid Marker for Mitochondrial Dysfunction</p>	<p>When malic acid is simultaneously elevated with citric, fumaric, and alpha-ketoglutaric acids, it strongly suggests cytochrome C oxidase deficiency, indicating dysfunction in the mitochondrial energy pathways.</p>
<p>Quinolinic Acid Marker for Inflammation and Neurotoxicity</p>	<p>Quinolinic acid is an organic acid derived from the amino acid, tryptophan, and can be neurotoxic at high levels. Excitotoxic substances like quinolinic acid may stimulate nerve cells so much that the nerve cells die. Brain toxicity due to quinolinic acid has been implicated in Alzheimer's disease, autism, Huntington's disease, stroke, dementia, depression, HIV-associated dementia, and schizophrenia.</p>
<p>DHPPA (3,4-Dihydroxyphenylpropionic Acid) Marker for Beneficial Bacteria</p>	<p>Harmless or beneficial bacteria such as <i>Lactobacilli</i>, <i>Bifidobacteria</i>, and <i>E. coli</i> mediate the breakdown of chlorogenic acid to 3,4-dihydroxyphenylpropionic acid (DHPPA). High values of DHPPA are associated with increased amounts of these bacteria in the gastrointestinal tract.</p>
<p>N-Acetylcysteine (NAC) Marker for Glutathione Precursor & Chelating Agent</p>	<p>N-acetylcysteine is a powerful antioxidant that acts to increase the glutathione reserves in the body. It is found in body fluids, but is also used as a nutritional supplement. It reduces the toxicity of drugs like acetaminophen (Tylenol) and protects against toxicity of mercury and other heavy metals. Low levels could indicate a glutathione deficiency.</p>
<p>Quinolinic Acid / 5-HIAA Ratio Marker for Neurotoxicity and Inflammation</p>	<p>A high ratio of quinolinic acid to the tryptophan metabolite, 5-hydroxyindoleacetic acid, indicates excessive inflammation due to recurrent infections, excessive tryptophan intake, immune overstimulation, excessive adrenal production of cortisol, or excessive exposure to phthalates.</p>

<p>Glyceric Acid Marker for Genetic Disease and Oxalate Metabolism</p>	<p>Glyceric acid is elevated in genetic hyperoxaluria type II. Normal values of glyceric acid rule out genetic causes of significant elevation of oxalic acid in urine.</p>
<p>Oxalic Acid Marker for Oxalate Metabolism</p>	<p>Elevated oxalic acid may be associated with dysbiosis from <i>Aspergillus</i>, <i>Penicillium</i>, and possible <i>Candida</i>, or from high doses of vitamin C. If yeast and/or fungal markers are elevated, antifungal therapy may reduce oxalates. Elevated oxalic acid may also result from anti-freeze (ethylene glycol) poisoning.</p>
<p>Methylmalonic Acid (Vitamin B12) Nutritional Marker</p>	<p>Slightly elevated methylmalonic acid is commonly associated with vitamin B12 deficiency, or other factors such as pernicious anemia, GI bacterial metabolism, malabsorption, or gastroenteritis in very young infants. Very elevated values may indicate a genetic disorder.</p>
<p>Pyridoxic Acid (Vitamin B6) Nutritional Marker</p>	<p>Low values are associated with low B6 status, high oxalates, and/or low neurotransmitters.</p>
<p>Pantothenic Acid (Vitamin B5) Nutritional Marker</p>	<p>High pantothenic acid indicates high recent intake of pantothenic acid. Since some individuals may require very high doses of pantothenic acid, high values do not necessarily indicate the need to reduce pantothenic acid intake.</p>
<p>Glutaric Acid (Vitamin B2) Nutritional Marker</p>	<p>Elevation indicates riboflavin deficiency (vitamin B2), a common factor in moderate urinary increases of glutaric acid. Other possible factors include fatty acid oxidation defects and metabolic effects of valproic acid, or celiac disease. The probability of a genetic disease is higher with very high values. The use of dietary supplements containing riboflavin and coenzyme Q10 may improve clinical symptoms. This compound may be elevated in about 10% of children with autism.</p>

Sample Report

The Great Plains Laboratory, Inc.
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 Requisition #: 998877 | Physician: | Date of Collection: | Time of Collection: 02/02/2015 | Print Date: | Patient Age: 10 | Patient Sex: M

Organic Acids Test - Nutritional and Metabolic Profile

Reference Population - Males Under Age 13

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient
Intestinal Microbial Overgrowth		
Yeast and Fungal Markers		
1 Citramalic	≤ 5.0	0.80
2 5-Hydroxymethyl-2-furolic	≤ 28	1.8
3 3-Oxoglutaric	≤ 0.46	0
4 Furan-2,5-dicarboxylic	≤ 18	1.9
5 Furan-carboxylglycine	≤ 3.1	0.12
6 Tartaric	≤ 6.5	0.31
7 Arabinose	≤ 50	60 H
8 Carboxycitric	≤ 25	0
9 Tricarballic	≤ 1.3	0.40
Bacterial Markers		
10 Hippuric	≤ 680	46
11 2-Hydroxyphenylacetic	≤ 0.86	0.20
12 4-Hydroxybenzoic	≤ 3.0	1.0
13 4-Hydroxyhippuric	≤ 30	12
14 DHPPA (Beneficial Bacteria)	≤ 0.59	0.08
Clostridia Bacterial Markers		
15 4-Hydroxyphenylacetic (other pathogenic clostridia species)	2.0 - 32	5.1
16 HPPHA (other pathogenic clostridia species)	≤ 220	96
17 4-Cresol (C. difficile)	≤ 84	4.5
18 3-Indoleacetic	0.60 - 14	0.99

Organic Acids Test - Nutritional and Metabolic Profile Page 1 of 8

The Great Plains Laboratory, Inc.
 Requisition #: 998877 | Patient Name: | Physician: | Date of Collection: | Reference Population - Males Under Age 13

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient
Oxalate Metabolites		
Glyceric	0.74 - 13	2.6
Glycolic	27 - 221	102
Oxalic	35 - 185	36
Polytic Cycle Metabolites		
Glucuronic	2.6 - 48	5.7
Uronic	0.32 - 8.8	1.8
Pyruvic Markers - Krebs Cycle Metabolites		
Pyruvic	≤ 23	8.0
Malic	≤ 1.8	0.16
Pyruvic	≤ 2.3	0.24
Tartaric	≤ 96	5.2
Pyruvic	9.8 - 39	8.1 L
Pyruvic	≤ 597	104
Pyruvic Markers - Amino Acid Metabolites		
Pyruvic	0.01 - 0.97	0.18
Tartaric	≤ 16	0.15
Pyruvic	≤ 6.9	0.53
Pyruvic Metabolites		
Pyruvic Metabolites (A)		
Pyruvic	0.49 - 13	2.5
Pyruvic (MA)	0.72 - 6.4	2.1
Pyruvic (Nephrine)	0.23 - 2.8	1.2
Pyruvic (5-HIAA)	≤ 11	0.56
Pyruvic	0.48 - 8.8	1.6
Pyruvic	≤ 4.2	0.72
Pyruvic	≤ 2.5	2.8 H

Organic Acids Test - Nutritional and Metabolic Profile Page 2 of 8



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