
OAT
Organic
Acids
Test
The Great Plains Laboratory, Inc.

The Great Plains Laboratory, Inc.

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."

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Table of Contents

General Overview

The Organic Acids Test provides a snapshot of the metabolism, based on a comprehensive assessment of 76 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.**

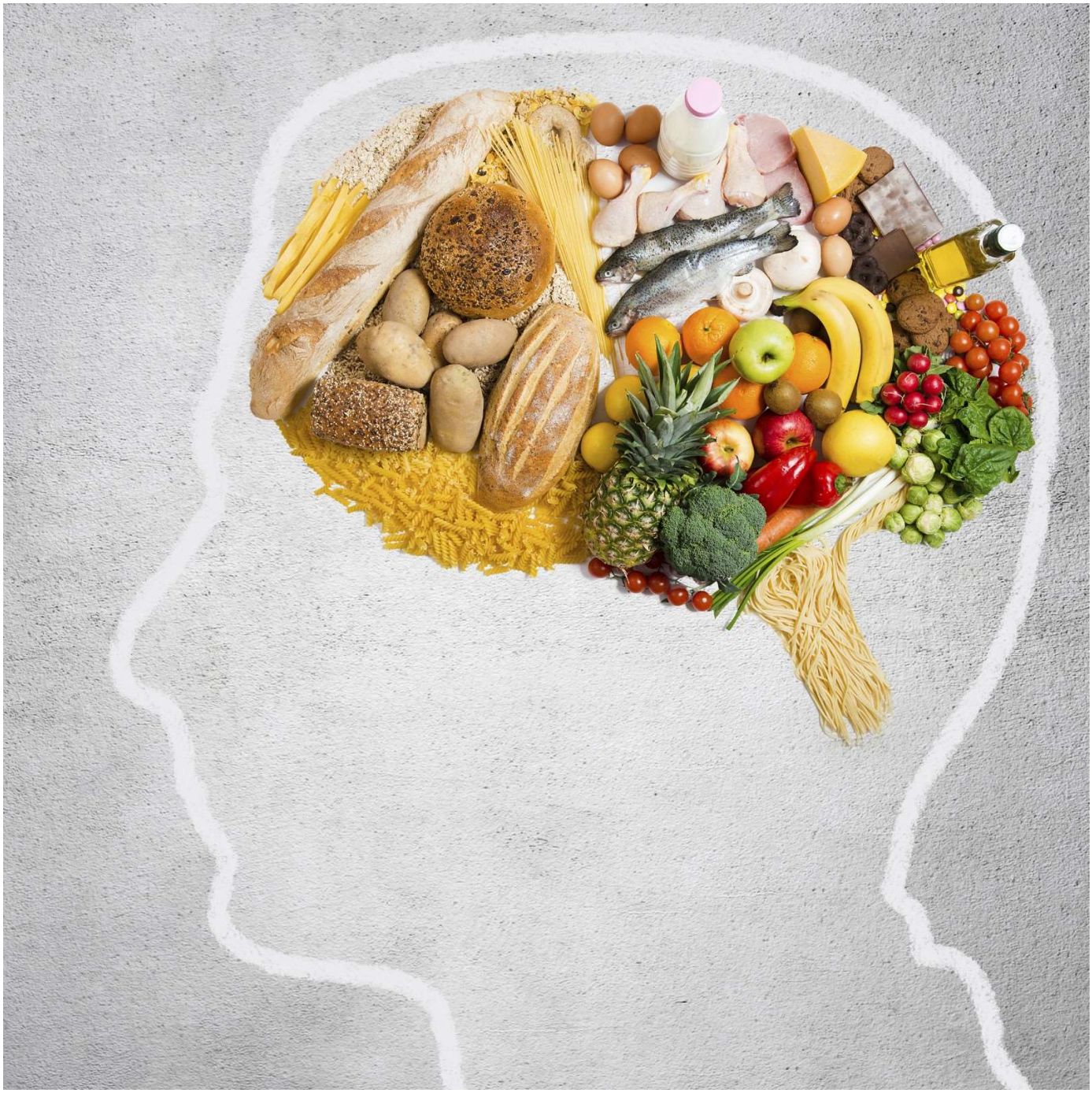
Microbial Organic Acids Test

The Microbial Organic Acids Test (included in the full Organic Acids Test) is ideal for follow-up to the OAT and is recommended for practitioners looking for specific abnormalities of certain microbial balances or to assess treatment efficacy.

We strongly recommend the full OAT as the initial screening test. The Microbial OAT reports 21 components such as markers for beneficial bacteria, harmful bacteria, toxic Clostridia species, Candida species, other yeast and fungal metabolites, and general markers of dysbiosis.

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.

7 | Clinical Significance: Primary Test Areas

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 HPHPA, 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, HVA/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 A_2 Activity Test, Metals Hair Test, Comprehensive Stool Analysis, GPL-TOX Profile, MycoTOX Profile, Vitamin D, and Copper/Zinc Profile.

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 A_2 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

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 Profile, MycoTOX Profile, IgG Food Allergy Test, Phospholipase A_2 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:

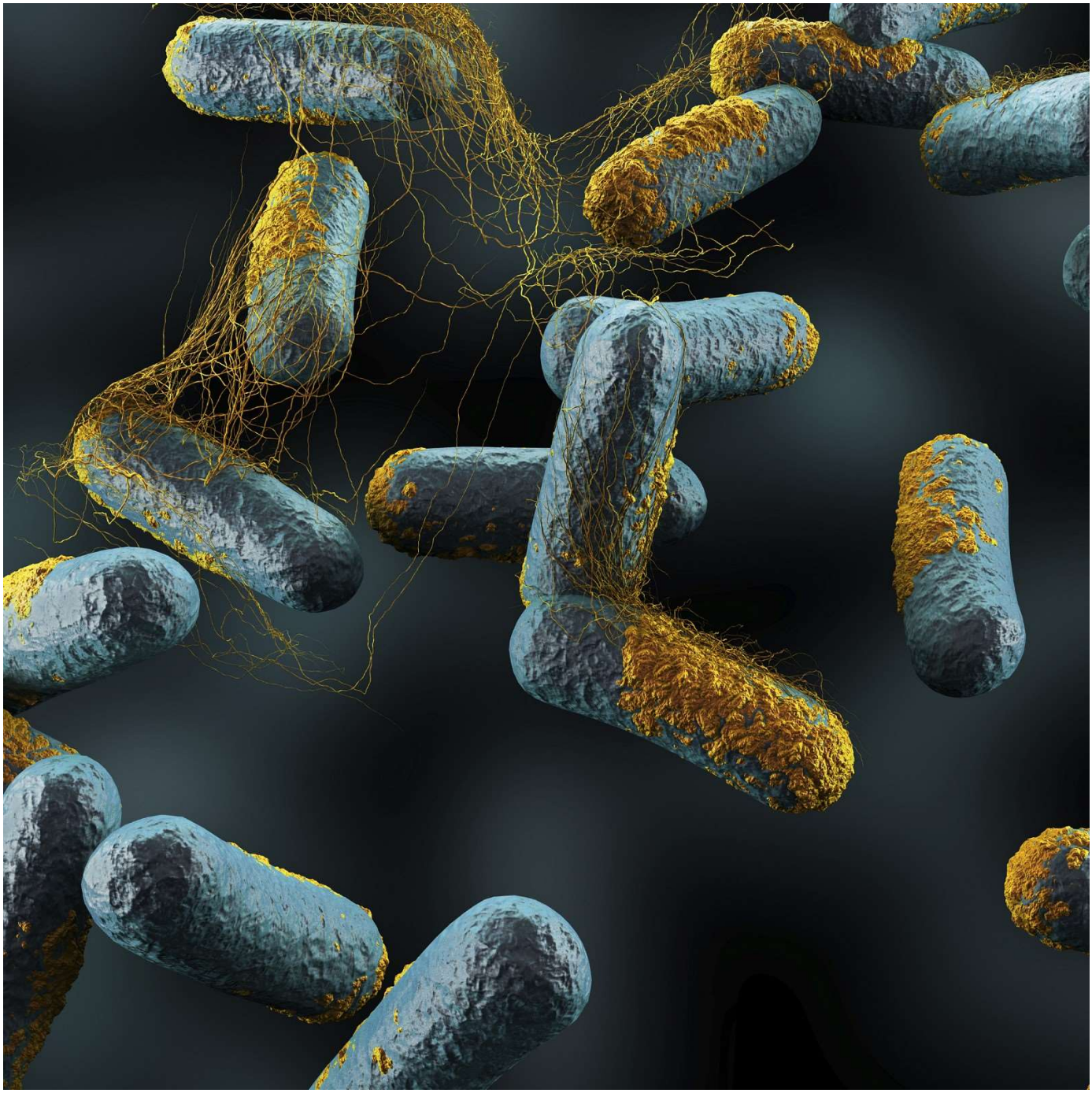
- **All mitochondrial markers**
- **Glycolytic cycle (lactic acid and pyruvic acid)**
- **Yeast and bacteria**
- **Oxalates**
- **Amino acid metabolites**
- **Ketone and fatty acid oxidation**

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.

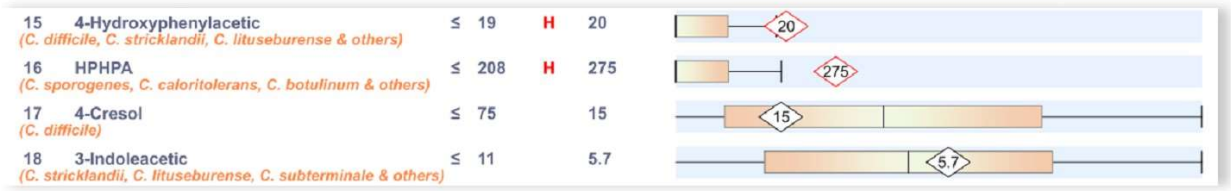
Additional tests recommended for patients with genetic and mitochondrial disorders: GPL-TOX Profile and MycoTOX Profile.



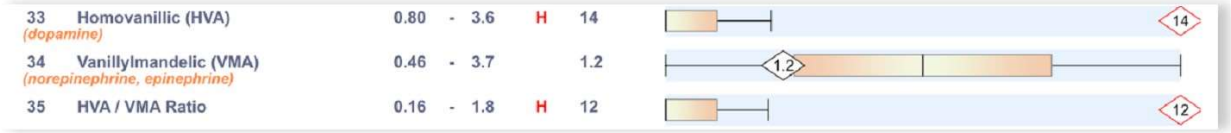
Clostridia

Toxic Effects of Clostridia Metabolites

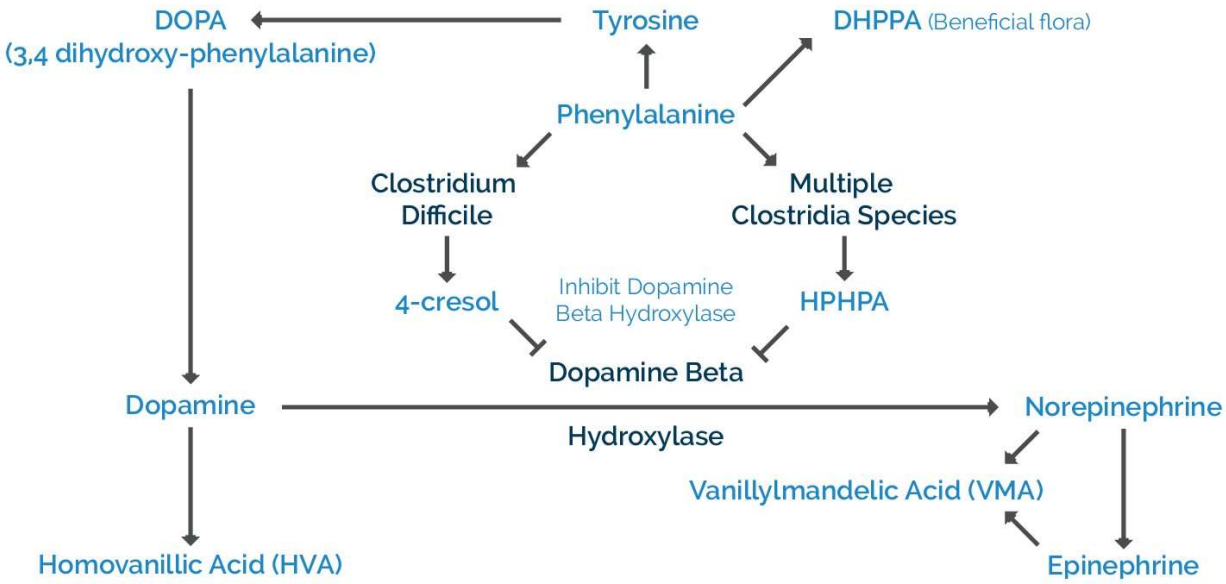
The Great Plains Laboratory Organic Acids Test is very sensitive and can differentiate between harmful and beneficial bacteria, which is unique among tests for Clostridia. It is also the only organic acids test available that measures HPHPA, one of the primary toxic metabolites of Clostridia. In the 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.



19 | Clostridia Overview



Combined Human and Clostridia Metabolic Effects on Neurotransmitters

HPHPA: A History and Case Studies

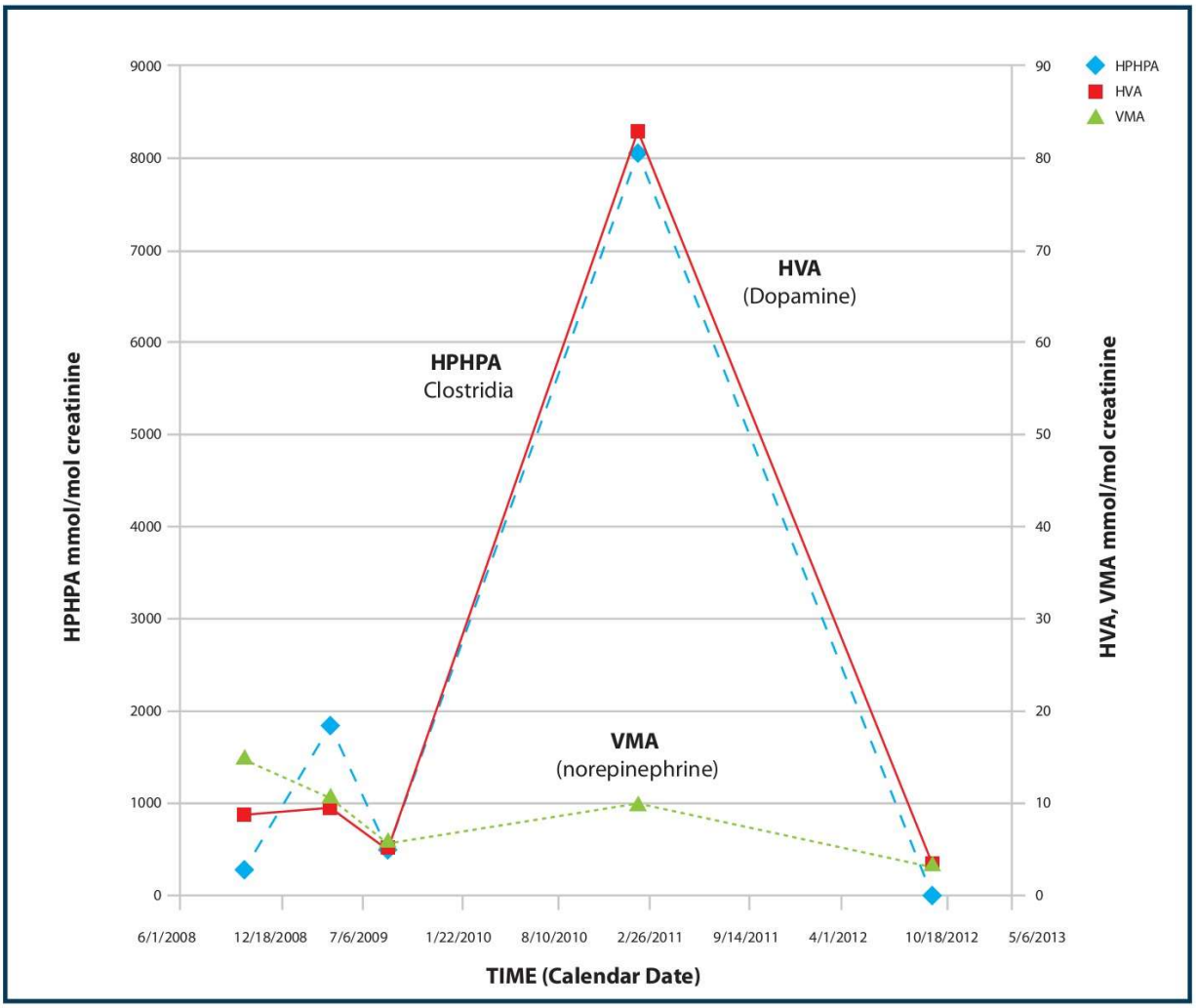
HPHPA (3-(3-Hydroxyphenyl)-3-Hydroxypropionic Acid) was first discovered by M. Armstrong and K. Shaw more than 50 years ago, when they found this compound to be elevated in patients of all types in mental hospitals. The source of this compound is a small number of Clostridia species. William Shaw, Ph.D., 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.


HPHPA
HVA
VMA
HPHPA mmol/mol creatinine
HVA, VMA mmol/mol creatinine
HVA
(Dopamine)
HPHPA
Clostridia
VMA
(norepinephrine)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
90
80
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50
40
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10
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6/1/2008
12/18/2008
7/6/2009
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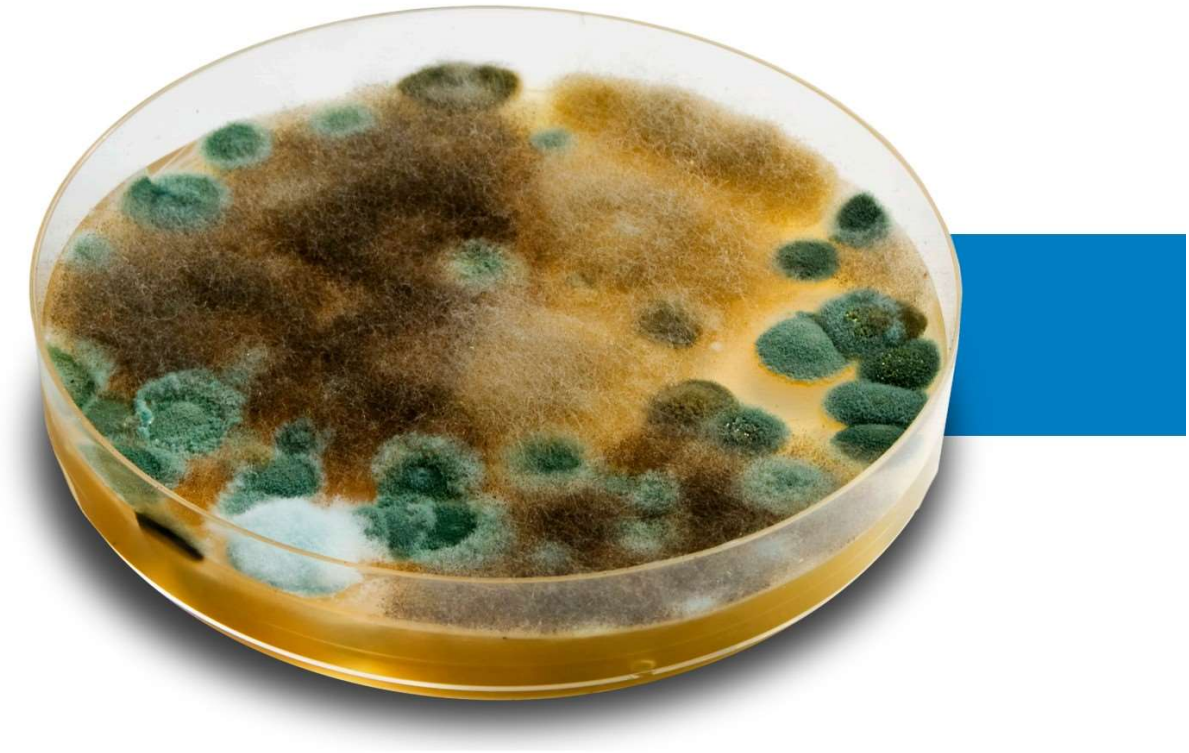
Case Study 2:



Fungus and Mold

Fungal Infections and Mold Exposure

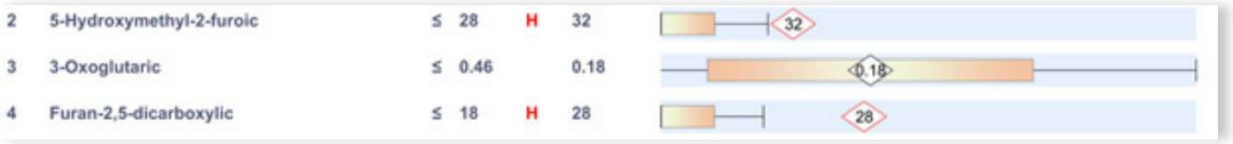
Mycotoxins are the toxic metabolites produced by certain types of fungi. These small molecules from mold are often carried on dust particles or food or are present in water-damaged buildings and homes. Common symptoms of mycotoxin exposure are fatigue, headaches, rashes, food sensitivities, joint pain, and cough. Mycotoxins can induce disease through different routes such as cytotoxicity, immunosuppression, and DNA damage. DNA damage caused by mycotoxins has been shown to be carcinogenic.

Using results from both our MycoTOX Profile and our Organic Acids Test, we have discovered correlations between them and uncovered new routes of treatment for patients with mold exposure. Specifically, there is a strong correlation between mold exposure and patients with autism and Parkinson's Disease.

The OAT offers four distinct areas of information that can assist in the treatment of mycotoxin exposure. These areas are fungal markers, yeast and clostridia markers glutathione markers, and mitochondrial markers. The two most important areas are the fungal markers and yeast and clostridia markers.

We have observed in patients that took both the mycotoxin test and the OAT that two markers in the yeast/fungal section of the OAT were statistically elevated over healthy controls. These two markers are 5-hydroxymethyl-2-furioc and Furan-2,5-dicarboxylic which are both produced by species of *Aspergillus*. Elevations in these two markers could indicate that the patient has a colonization of *Aspergillus* in the body.

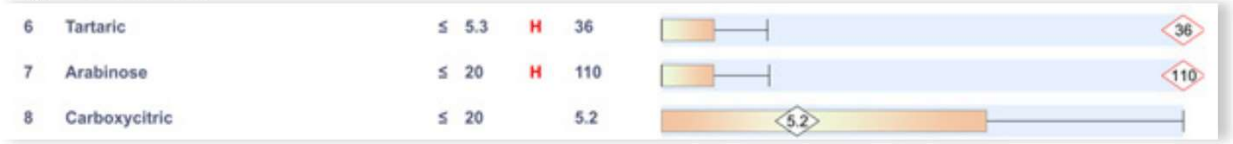
If these two markers are low, that does not rule out possible exposure to other species of mold.



In addition, 90% of patients with elevations in these two markers also have elevations of mycotoxins. This information has proven to be extremely beneficial in determining the best treatment of patients.

The second benefit of using the OAT for patients with possible mycotoxin exposure is the yeast and bacteria markers. Exposure to mycotoxins can lead to the inhibition of T helper cell function and inhibition of antibody synthesis. This can lead to the overgrowth of intestinal pathogens such as Candida or Clostridia. Patients with high levels of mycotoxins have high levels of yeast 75% of the time and Clostridia 40% of the time. In the below example, the patient had both high fungal markers on the OAT and high Ochratoxin on the MycoTOX Profile.

Organic Acids Test:



MycoTOX Profile:

These are serious co-morbidities that can lead to significant health issues. Diagnosis of these issues can lead to improved outcomes.

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:
https://www.upmc.com/-/media/upmc/patients-visitors/education/unique-pdfs/low-oxalate-diet.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

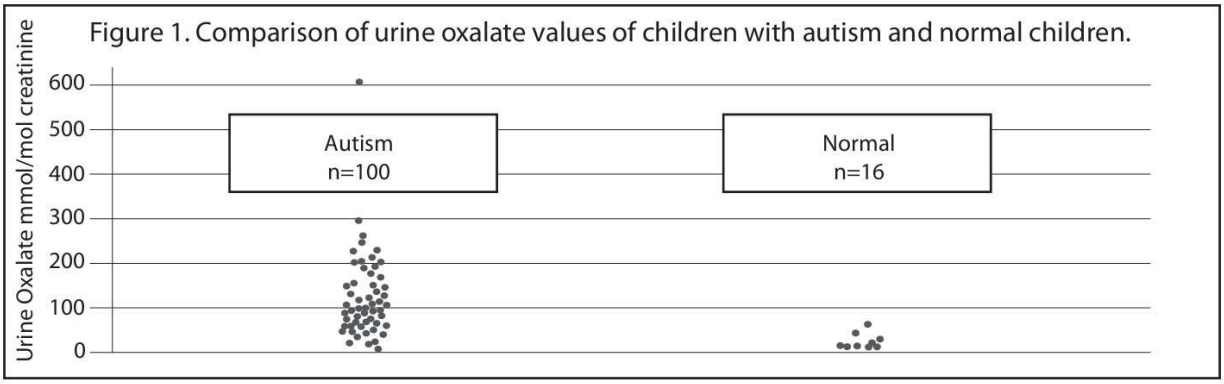
High oxalates in the urine and plasma were first found in people who were susceptible to kidney stones. Many kidney stones are composed of calcium oxalate. Stones can range in size from the diameter of a grain of rice to the width of a golf ball. It is estimated that 10% of males may have kidney stones 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 ± 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.

Figure 1. Comparison of urine oxalate values of children with autism and normal children.



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.**

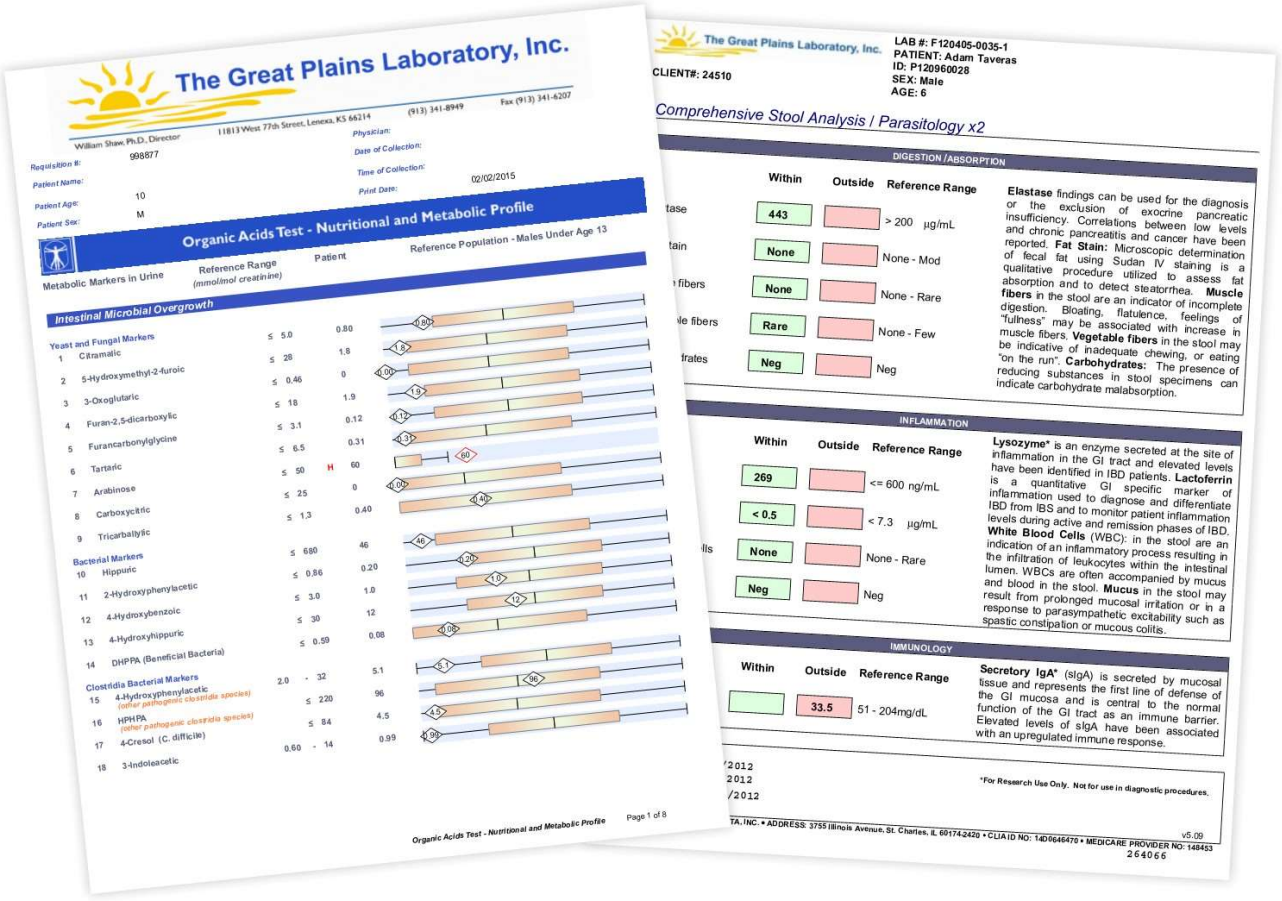
Key Markers

HPHPA (3-(3-Hydroxyphenyl)-3-Hydroxypropionic Acid) Marker for Bacteria, Including Selected Clostridia	Indicates a possible overgrowth of intestinal bacteria, specifically the Clostridia species, *C. botulinum*, *C. sporogenes*, and *C. caloritolerans*. The metabolites of these species can be neurotoxic.
4-cresol Marker for Bacteria, Including Selected Clostridia	Indicates a possible overgrowth of intestinal bacteria, specific 4-cresol producers. 4-cresol is a phenolic product of the Clostridia species, *C. difficile*, and is poorly metabolized in children with autism. High-potency, multi-strain probiotics may help rebalance GI flora.
4-Hydroxyphenylacetic Acid Marker for Bacteria, Including Selected Clostridia	Associated with small intestinal bacteria overgrowth (SIBO) due to its production by *C. difficile*, *C. stricklandii*, *C. lituseburense*, *C. subterminale*, *C. putrefaciens*, and *C. propionicum*.
3-Indoleacetic Acid Marker for Bacteria, Including Selected Clostridia	A tryptophan byproduct of the Clostridia species, *C. stricklandii*, *C. lituseburense*, *C. subterminale*, and *C. putrefaciens*. May indicate a depletion of tryptophan needed for various physiological functions.
3-Hydroxyglutaric Acid Marker for Genetic Disease	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.
3-Methylglutaconic Acid Marker for Mitochondrial Disorder	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.

Tricarballylic Acid Marker for Exposure to Certain Fungal Contamination in Foods	A chemical by-product released from fumonisins during passage through the gastrointestinal tract. Fumonisins are fungal toxins produced primarily by *F. verticillioides*. Elevated levels can be caused by the intake of corn or corn-based food contaminated with fumonisins.
Malic Acid Marker for Mitochondrial Dysfunction	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.
Quinolinic Acid Marker for Inflammation and Neurotoxicity	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.
DHPPA (3,4-Dihydroxyphenylpropionic Acid) Marker for Beneficial Bacteria	Harmless or beneficial bacteria such as *Lactobacilli*, *Bifidobacteria*, and *E. coli* 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.
N-Acetylcysteine (NAC) Marker for Glutathione Precursor & Chelating Agent	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.
Quinolinic Acid / 5-HIAA Ratio Marker for Neurotoxicity and Inflammation	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.

Glyceric Acid Marker for Genetic Disease and Oxalate Metablolism	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.
Oxalic Acid Marker for Oxalate Metabolism	Elevated oxalic acid may be associated with dysbiosis from *Aspergillus*, *Penicillum*, and possible *Candida*, 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.
Methylmalonic Acid (Vitamin B12) Nutritional Marker	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.
Pyridoxic Acid (Vitamin B6) Nutritional Marker	Low values are associated with low B6 status, high oxalates, and/or low neurotransmitters.
Pantothenic Acid (Vitamin B5) Nutritional Marker	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.
Glutaric Acid (Vitamin B2) Nutritional Marker	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.

Sample Report



The Great Plains Laboratory, Inc.

William Shaw Ph.D., Director — 11813 West 77th Street, Lenexa, KS 66214 — (913) 341-8949 — Fax (913) 341-6207

Requisition #: 998877
Patient Name:
Patient Age: 10
Patient Sex: M
Physician:
Date of Collection:
Time of Collection:
Print Date: 02/02/2015

Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient	Reference Population - Males Under Age 13
Intestinal Microbial Overgrowth			
Yeast and Fungal Markers			
1 Citramalic	≤ 5.0	0.80	
2 5-Hydroxymethyl-2-furoic	≤ 28	1.8	
3 3-Oxoglutaric	≤ 0.46	0	
4 Furan-2,5-dicarboxylic	≤ 18	1.9	
5 Furancarbonylglycine	≤ 3.1	0.12	
6 Tartaric	≤ 6.5	0.31	
7 Arabinose	≤ 50 H	60	
8 Carboxycitric	≤ 25	0	
9 Tricarballylic	≤ 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 HPHPA (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.

CLIENT#: 24510

LAB #: F120405-0035-1
PATIENT: Adam Taveras
ID: P120960028
SEX: Male
AGE: 6

Comprehensive Stool Analysis / Parasitology x2

DIGESTION /ABSORPTION

	Within	Outside	Reference Range
tase	443		> 200 µg/mL
tain	None		None - Mod
fibers	None		None - Rare
le fibers	Rare		None - Few
frates	Neg		Neg

Elastase findings can be used for the diagnosis or the exclusion of exocrine pancreatic insufficiency. Correlations between low levels and chronic pancreatitis and cancer have been reported. **Fat Stain:** Microscopic determination of fecal fat using Sudan IV staining is a qualitative procedure utilized to assess fat absorption and to detect steatorrhea. **Muscle fibers** in the stool are an indicator of incomplete digestion. Bloating, flatulence, feelings of "fullness" may be associated with increase in muscle fibers. **Vegetable fibers** in the stool may be indicative of inadequate chewing, or eating "on the run". **Carbohydrates:** The presence of reducing substances in stool specimens can indicate carbohydrate malabsorption.

INFLAMMATION

	Within	Outside	Reference Range
	269		<= 600 ng/mL
	< 0.5		< 7.3 µg/mL
lls	None		None - Rare
	Neg		Neg

Lysozyme* is an enzyme secreted at the site of inflammation in the GI tract and elevated levels have been identified in IBD patients. **Lactoferrin** is a quantitative GI specific marker of inflammation used to diagnose and differentiate IBD from IBS and to monitor patient inflammation levels during active and remission phases of IBD. **White Blood Cells** (WBC): in the stool are an indication of an inflammatory process resulting in the infiltration of leukocytes within the intestinal lumen. WBCs are often accompanied by mucus and blood in the stool. **Mucus** in the stool may result from prolonged mucosal irritation or in a response to parasympathetic excitability such as spastic constipation or mucous colitis.

IMMUNOLOGY

	Within	Outside	Reference Range
		33.5	51 - 204mg/dL

Secretory IgA* (sIgA) is secreted by mucosal tissue and represents the first line of defense of the GI mucosa and is central to the normal function of the GI tract as an immune barrier. Elevated levels of sIgA have been associated with an upregulated immune response.

/2012
2012
/2012

*For Research Use Only. Not for use in diagnostic procedures.

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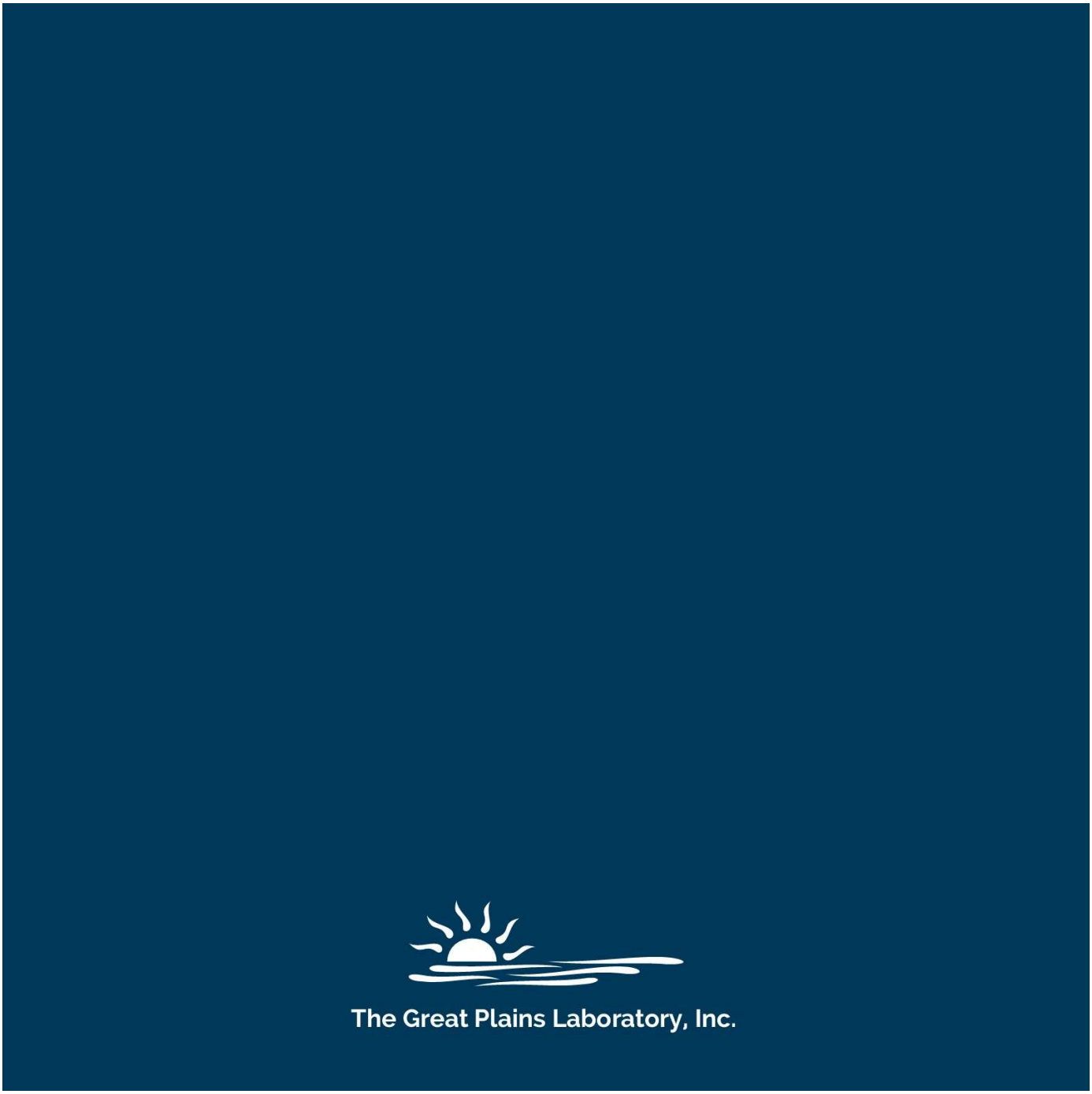
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