The Great Plains Laboratory, Inc.

William Shaw, Ph.D., Director 11813 West 77th Street, Lenexa, KS 66214 (913) 341-8949 Fax (913) 341-6207 www.GPL4U.com

New Urine Test for Toxic Organic Chemical Exposure

Toxic Chemicals: A Major Cause of Developmental Disorders and Chronic Illnesses

Every day, we are exposed to hundreds of toxic chemicals through products like pharmaceuticals, pesticides, packaged foods, household products, and environmental pollution. As we have become more accustomed to chemical-laden products, and as our environment has become more contaminated, we have been confronted with an accelerating rate of chronic illnesses like cancer, heart disease, chronic fatigue syndrome, chemical sensitivity, autism spectrum disorders, ADD/AD(H)D, autoimmune disorders, Parkinson's disease, and Alzheimer's disease.

Because exposure to environmental pollutants has been linked to many chronic diseases, The Great Plains Laboratory has created GPL-TOX, a toxic organic exposure profile that screens for the presence of 168 different toxic chemicals including organophosphate pesticides, phthalates, benzene, xylene, vinyl chloride, pyrethrin insecticides, and others. This profile also includes Tiglyglycine (TG), a marker for mitochondrial disorders resulting from mutations of mitochondrial DNA. These mutations can be caused by exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies.

Advantages of the GPL-TOX Profile

1. **William Shaw, Ph.D., Director of The Great Plains Laboratory, is board-certified in both clinical chemistry and toxicology by The American Board of Clinical Chemistry.**
2. **Tests for 11 unique toxic pollutants and screens for a total of 168 toxic compounds, all from a single urine sample.**
3. **Includes markers for both environmental pollutants and mitochondrial function metabolites, and is an ideal screening for patients with suspected toxic exposure or other chronic illnesses.**
4. **Uses the power of advanced mass spectrometry (MS/MS), which is needed to detect lower levels of certain genetic, mitochondrial, and toxic chemical markers, that conventional mass spectrometry often misses.**

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Common Sources of Household Toxins

Pyrethrins

Pyrethrins are widely used in both indoor and outdoor insecticides, inlcuding bug spray, bug bombs, and flea and tick products. Pyrethrin is made synthetically, but it also occurs naturally in chrysanthemum flowers. Although considered safer for human exposure than organophosphates as insecticides, pyrethrins have been associated with increased incidences of AD(H)D, autism, and premature death. Inhaling high levels of pyrethrins or pyrethroids may bring about asthmatic breathing, sneezing, nasal stuffiness, headache, nausea, incoordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensation. Individuals who have ragweed sensitivity are especially vulnerable to allergic reactions to these products.

Benzene

Benzene is a by-product of all types of combustion. It is found in cigarette smoke, gasoline fumes, motor vehicle exhaust, and industrial processesing facilities. Benzene also outgasses from synthetic materials (carpet, drapes, and furniture), glues, and detergents. Benzene causes hematological abnormalities as well as being mutagenic and carcinogenic. High exposure to benzene may cause nausea, vomiting, dizziness, poor coordination, central nervous system depression, and even death.

Phthalates

The most common group of toxins found in our environment.

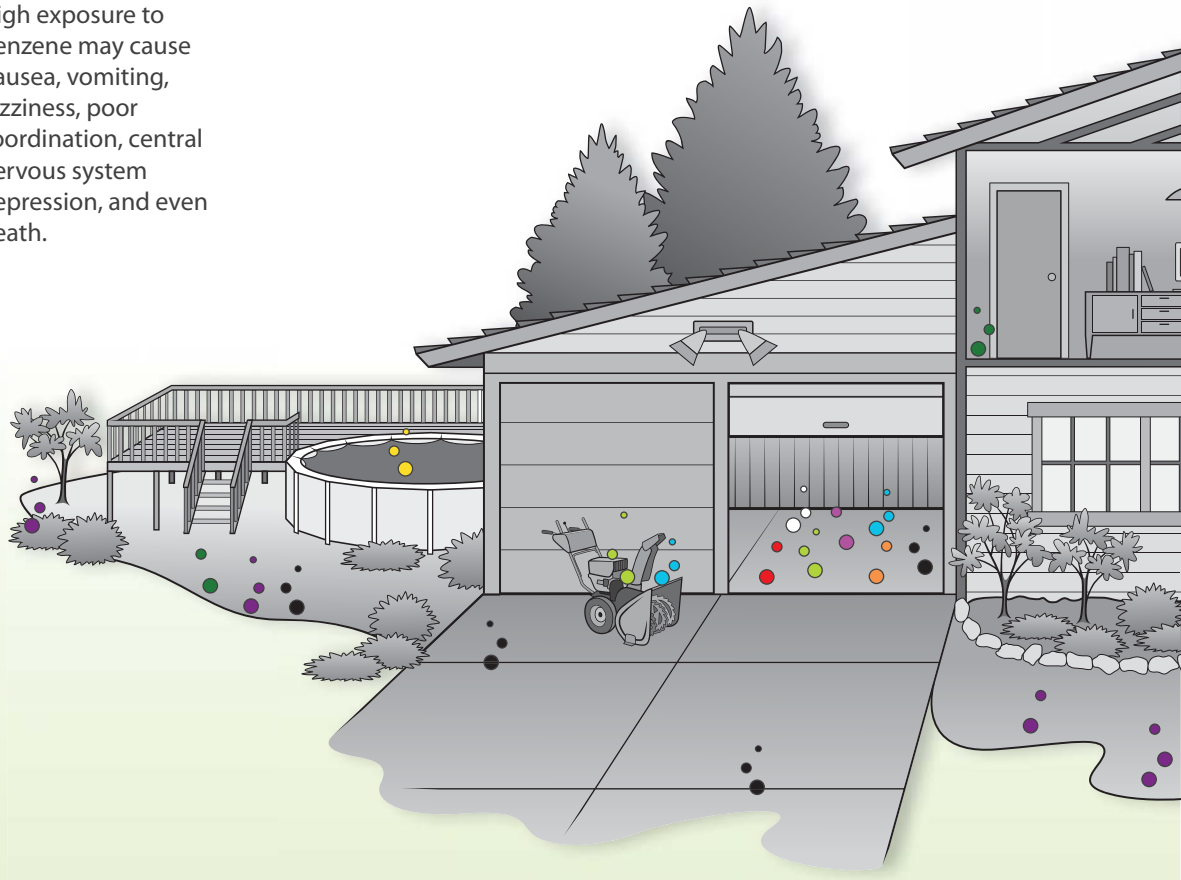
Found in bath products, skin care and beauty products, cosmetics, nail polish, perfumes, detergents, cleaning products, plastic food containers, baby/child products (teething rings, sippy cups, etc.) oral drug coatings, paper coatings, printing inks, and varnishes.

Xylenes

Xylenes (dimethylbenzenes) are found not only in common products such as paints, lacquers, pesticides, cleaning fluids, fuel and exhaust fumes, but also in perfumes and insect repellents.

Styrene

Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food-packaging materials.



Organophosphates

Organophosphates are one of the most toxic groups of substances used throughout the world.

They are most commonly used in insecticides, herbicides, and lice shampoos, as well as in nerve agents.

MTBE and ETBE

MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, and inhalation or skin exposure to gasoline or its vapors and exhaust fumes.

Solvents

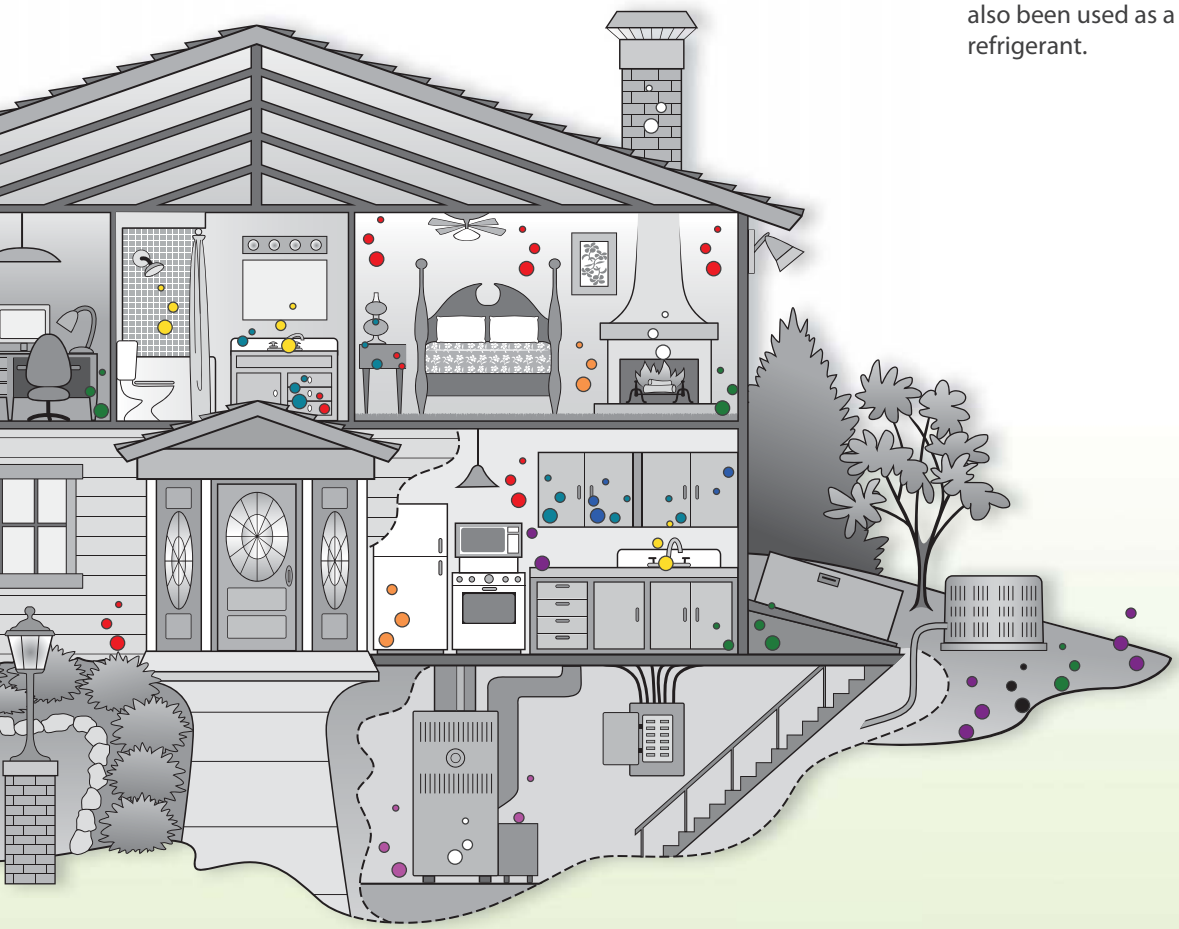
Products that contain solvents include paint, ink, coatings, automotive products, paint thinners, household cleaners and stain removers, dry cleaning fluid, adhesives, pharmaceuticals, nail polish remover, and microelectronics.

Vinyl Chloride

Vinyl chloride is released by industries or formed by the breakdown of other chlorinated chemicals can enter the air and drinking water supplies. Smaller amounts of vinyl chloride are used in furniture and automobile upholstery, wall coverings, housewares, and automotive parts. Vinyl chloride has also been used as a refrigerant.

2,4-D

2,4-Dichololor-phenoxyacetic Acid is most commonly used in agriculture of genetically modified foods, and as a weed killer for lawns. Genetically modified soybeans and corn that are resistant to 2,4-D and glyphosate (the main toxic chemical in the herbicide, Roundup™) have been approved in the U.S. and Canada, along with the coinciding herbicide, Enlist Duo™, which includes both herbicides. Dermal or oral exposure to 2,4-D has been associated with neuritis, weakness, nausea, abdominal pain, headache, dizziness, peripheral neuropathy, stupor, seizures, brain damage, and impaired reflexes. 2,4-D is also a known endocrine disruptor, and can block hormone distribution and cause glandular breakdown.



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Environmental Pollutants Tested by GPL-TOX

Phthalates

Perhaps the most widespread group of toxic chemicals found in our environment. Phthalates are commonly found in after shave lotions, aspirin, cosmetics, detergents, foods microwaved with plastic covers, oral pharmaceutical drugs, intravenous products prepared in plastic bags, hair sprays, insecticides, insect repellents, nail polish, nail polish remover, skin care products, adhesives, explosives, lacquer, janitorial products, perfumes, paper coatings, printing inks, safety glass, and varnishes. Phthalates have been implicated in reproductive damage, depressed leukocyte function, and cancer. Phthalates have also been found to impede blood coagulation, lower testosterone, and alter sexual development in children. Low levels of phthalates can feminize the male brain of the fetus, while high levels can hyper-masculinize the developing male brain.

Vinyl Chloride

Vinyl chloride is an intermediate in the synthesis of several commercial chemicals, including polyvinyl chloride (PVC). Exposure to vinyl chloride may cause central nervous system depression, nausea, headache, dizziness, liver damage, degenerative bone changes, thrombocytopenia, enlargement of the spleen, and death.

Benzene

Benzene is an organic solvent that is widespread in the environment. Benzene is a by-product of all sources of combustion, including cigarette smoke, and is released by outgassing from synthetic materials, and is a pollutant released by numerous industrial processes. Benzene is an extremely toxic chemical that is mutagenic and carcinogenic. High exposures to benzene cause symptoms of nausea, vomiting, dizziness, lack of coordination, central nervous system depression, and death. It can also cause hematological abnormalities.

Pyrethrins

Pyrethrins are widely used as insecticides. Exposure during pregnancy doubles the likelihood of autism. Pyrethrins may affect neurological development, disrupt hormones, induce cancer, and suppress the immune system.

Xylenes

Xylenes (dimethylbenzenes) are solvents found not only in common products such as paints, lacquers, pesticides, cleaning fluids, fuel and exhaust fumes, but also in perfumes and insect repellents. Xylenes are oxidized in the liver and bound to glycine before eliminated in urine. High xylene levels may be due to the use of certain perfumes and insect repellents. High exposures to xylene create an increase in oxidative stress, causing symptoms such as nausea, vomiting, dizziness, central nervous system depression, and death. Occupational exposure is often found in pathology laboratories where xylene is used for tissue processing.

Endocrine Disruptors in the Workplace, Hair Spray, Folate Supplementation, and Risk of Hypospadias: Case-control Study

Gillian Ormond,1,2 Mark J Nieuwenhuijsen,2,3 Paul Nelson,4 Mireille B Toledano, 2 Nina Iszatt,2 Sara Geneletti,2 and Paul Elliott2

1Department of Epidemiology and Public Health, University College Cork, Cork, Ireland; 2Department of Epidemiology and Public Health, Imperial College London, London, UK; 3Center for Research in Environmental Epidemiology (CREAL), IMIM, CIBERESP, Barcelona, Spain; 4Independent Public Health

Styrene

Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food-packaging materials. The ability of styrene monomer to leach from polystyrene packaging to food has been reported. Occupational exposure due to inhalation of large amounts of styrene adversely impacts the central nervous system, causes concentration problems, muscle weakness, tiredness and nausea, and irritates the mucous membranes of the eyes, nose, and throat.

Organophosphates

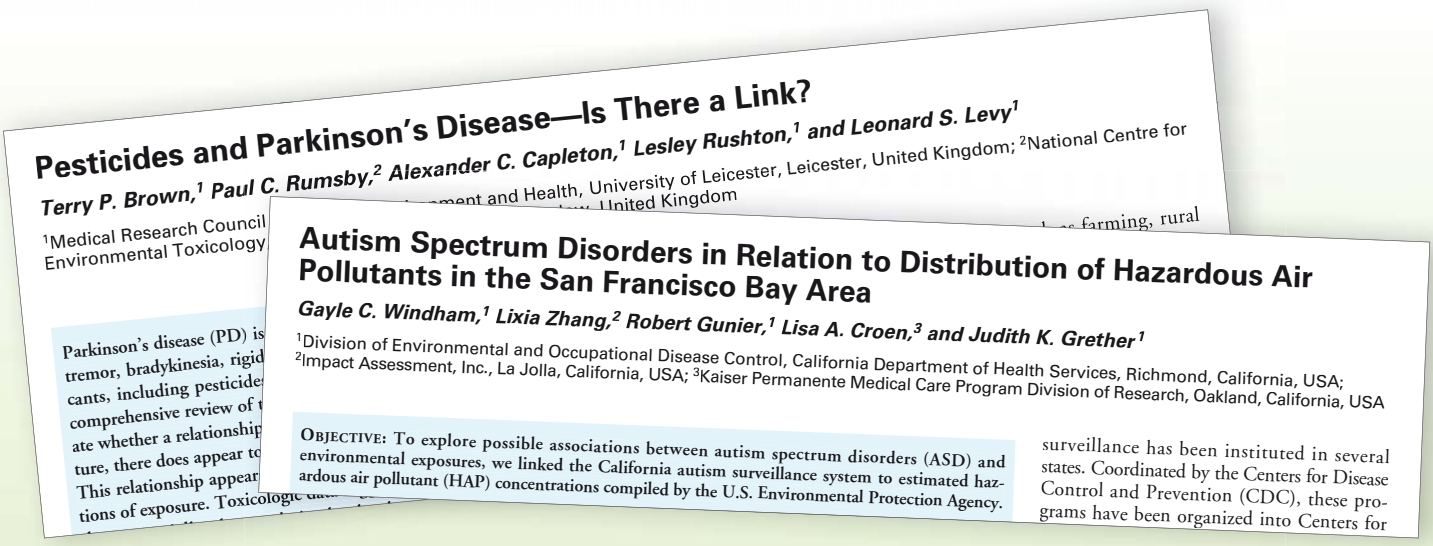
Organophosphates are one of the most toxic groups of substances used throughout the world. They are often used as biochemical weapons and terrorist agents, but are most commonly used in pesticide formulations. Organophospates are inhibitors of cholinesterase enzymes, leading to overstimulation of nerve cells, causing sweating, salivation, diarrhea, abnormal behavior, including aggression and depression. Children exposed to organophosphates have more than twice the risk of developing pervasive developmental disorder (PDD), an autism spectrum disorder. A study done in the San Francisco Bay area found that in California agricultural areas, children born to mothers living within 500 meters of fields where organochlorine pesticides were used were more than 6 times more likely to develop autism than children whose mothers did not live near such fields. ASD risk increased with the poundage of organochlorines applied and decreased with distance from field sites. Maternal organophosphate exposure has been associated with various adverse outcomes including having shorter pregnancies and children with impaired reflexes.

MTBE and ETBE

MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, and inhalation or skin exposure to gasoline or its vapors and exhaust fumes. MTBE has been demonstrated to cause hepatic, kidney, and central nervous system toxicity, peripheral neurotoxicity, and cancer in animals. Since the metabolites of these compounds are the same, ETBE may be similarly toxic.

2,4-Dichlorophenoxyacetic Acid (2,4-D)

A very common herbicide that was a part of Agent Orange, used by the United States during the Vietnam War to increase visibility for war planes, by destroying plant undergrowth and crops. It is most commonly used in agriculture on genetically modified foods, and as a weed killer for lawns. Exposure to 2, 4-D via skin or oral ingestion is associated with neuritis, weakness, nausea, abdominal pain, headache, dizziness, peripheral neuropathy, stupor, seizures, brain damage, and impaired reflexes. 2, 4-D is a known endocrine disruptor, and can block hormone distribution and cause glandular breakdown.



Pesticides and Parkinson's Disease—Is There a Link?

Terry P. Brown,[1] Paul C. Rumsby,[2] Alexander C. Capleton,[1] Lesley Rushton,[1] and Leonard S. Levy[1]

[1]Medical Research Council Environmental Toxicology ... ment and Health, University of Leicester, Leicester, United Kingdom; [2]National Centre for ... United Kingdom

Parkinson's disease (PD) is ... tremor, bradykinesia, rigid... cants, including pesticides... comprehensive review of t... ate whether a relationship... ture, there does appear to... This relationship appear... tions of exposure. Toxicologic ...

Autism Spectrum Disorders in Relation to Distribution of Hazardous Air Pollutants in the San Francisco Bay Area

Gayle C. Windham,[1] Lixia Zhang,[2] Robert Gunier,[1] Lisa A. Croen,[3] and Judith K. Grether[1]

[1]Division of Environmental and Occupational Disease Control, California Department of Health Services, Richmond, California, USA; [2]Impact Assessment, Inc., La Jolla, California, USA; [3]Kaiser Permanente Medical Care Program Division of Research, Oakland, California, USA

OBJECTIVE: To explore possible associations between autism spectrum disorders (ASD) and environmental exposures, we linked the California autism surveillance system to estimated hazardous air pollutant (HAP) concentrations compiled by the U.S. Environmental Protection Agency.

... surveillance has been instituted in several states. Coordinated by the Centers for Disease Control and Prevention (CDC), these programs have been organized into Centers for

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GPL-TOX is Recommended for the Following Disorders:

- Alzheimer's Disease
- Amyotrophic Lacteroclerosis (ALS)
- Anorexia Nervosa
- Anxiety Disorder
- Apraxia
- Arthritis
- Asthma
- Attention deficit (ADD)
- Attention deficit with hyperactivity (ADHD)
- Autism
- Autoimmune disorders
- Bipolar disorder
- Cancer
- Cerebral palsy
- Chronic fatigue syndrome
- Crohn's disease
- Depression
- Developmental disorder
- Down Syndrome
- Epilepsy
- Failure to thrive
- Fibromyalgia
- Genetic diseases
- Irritable bowel syndrome
- Learning disability
- Mitochondria disorder
- Multiple sclerosis
- Obsessive compulsive disorder (OCD)
- Occupational exposures
- Parkinson's disease
- Peripheral neuropathy
- Schizophrenia
- Seizure disorders
- Systemic lupus erythematosus
- Tic disorders
- Tourette syndrome
- Ulcerative colitis

Specimen Requirements:

5 mL of the first morning urine before food or drink is suggested.

Mitochondrial Disorders

The GPL-TOX profile tests for Tiglyglycine (TG), one of the most specific markers for mitochondrial disorders resulting from mutations of mitochondrial DNA. These mutations can result from exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies. Mitochondria are important in all cells in the body, but are especially important to organs that utilize large amounts of energy, such as the muscles, heart, and brain. The mitochondria also have several other important functions in the cell, including steroid synthesis, calcium regulation, free radical production, and the induction of apoptosis or programmed cell death, all of which are involved in the pathogenesis of numerous disorders. The marker used in the GPL-TOX profile indicates mitochondrial dysfunction by monitoring a metabolite that is elevated in mitochondrial deficiency of cofactors such as NAD+, flavin-containing coenzymes, and Coenzyme Q10. Disorders associated with mitochondrial dysfunction include autism, Parkinson's disease, and cancer.

Metabolites Tested by GPL-TOX

2-Methylhippuric Acid (2MHA) **3-Methylhippuric Acid (3MHA)** **4-Methylhippuric Acid (4MHA)**	These are metabolites of xylenes, solvents found in paints, lacquers, cleaning agents, pesticides, and gasoline. Exposure to xylenes generates methylhippuric acid isomers. Avoid/reduce exposure to these substances.
N-acetyl phenyl cysteine (NAP)	NAP is a metabolite of benzene. Benzene is a solvent that is widespread in the environment. It is found in cigarette smoke and gasoline, and is a byproduct of all types of combustion, including motor vehicle exhaust. Treatment consists of removing sources of exposure.
Phenylglyoxylic Acid (PGO)	Exposure to environmental styrene may slightly increase phenylglyoxylic and mandelic acid. Reduce exposure by eliminating the use of plastic and styrofoam containers for cooking, reheating, eating or drinking. Elimination of styrene can be accelerated by supplementing with glutathione and N-acetyl cysteine (NAC).
2-Hydroxyisobutyric Acid (2HIB)	2-Hydroxyisobutyric acid is formed endogenously as a product of branched-chain amino acid degradation and ketogenesis. This compound is also the major metabolite of gasoline octane enhancers such as MTBE and ETBE. Elevated levels indicate environmental exposure and very high values have been reported in genetic disorders.
Monoethyl Phthalate (MEP)	MEP from diethyl phthalate is the most abundant phthalate metabolite found in urine. Diethyl phthalate is used in plastic products. Elevated values indicate exposure from various possible sources. Elimination of phthalates may be accelerated by sauna treatment.
Dimethylphosphate (DMP) **Diethylphosphate (DEP)**	DMP and DEP are major metabolites of many organophosphate pesticides. Reduce exposure by eating organic foods and avoiding use of pesticides in your home or garden. Living near agricultural areas or golf courses and areas regularly sprayed with pesticides will increase exposure. Elimination of organophosphates can be accelerated by sauna treatment.
3-Phenoxybenzoic Acid (3PBA)	3-Phenoxybenzoic acid is a metabolite of pyrethroid insecticides. Elimination can be accelerated by sauna treatment.
Thiodiglycolic Acid (TDG)	TDG is a major metabolite of vinyl chloride and may indicate exposure to several important commercial compounds, including polyvinyl chloride from certain plastic bottles. Elevated urinary values of TDG may also be found after ingestion of large amounts of fresh onion, or after vitamin B12 administration, due to stimulation of sulfur amino acid metabolism.
2,4-Dichlorophenoxyacetic Acid (2,4-D)	2,4-D was an ingredient in Agent Orange, and is most commonly used in agriculture of genetically modified foods, and as a weed killer for lawns. Reduce exposure by eating organic foods and avoiding use of pesticides in your home or garden.
Tiglylglycine (TG)	TG is a marker for mitochondrial dysfunction. Mutations of mitochondria DNA may result from exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies.

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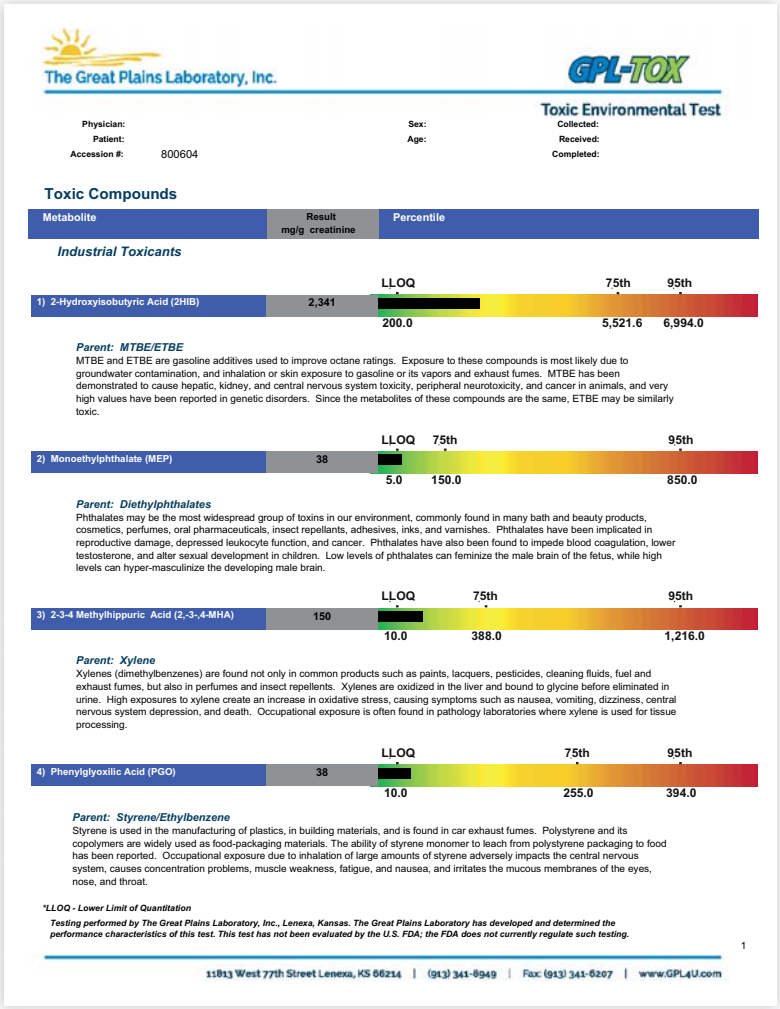
Recommendations for Detoxification of Chemicals

- Exercise frequently to develop sweating. Many chemicals are released in sweat. Use a towel to remove sweat frequently, since chemicals may be reabsorbed back into the body.
- Use infrared (IFR) sauna therapy to sweat out toxins. This has shown to be very effective at removing toxins that have been stored in the body for years, as well as those absorbed via acute exposure.
- Take supplements of folate, B6, B12, and Trimethylglycine (TMG). They help reduce homocysteine that inhibits the ability of paraoxonase to detoxify organophosphate pesticides. Oral or intravenous glutathione helps remove toxins, as do chlorella and activated charcoal.
- Drink purified water – by distillation, deionization, or reverse osmosis. Store in glass containers, preferably, or in plastic containers with 1, 2, or 5 designations on the bottom. Adding lemon to water helps with detoxification. There are also many detox herbal teas available, including ingredients like dandelion root, licorice root, and burdock root.
- Use chelation therapy if there is significant body burden of toxic metals.



The Great Plains Laboratory, Inc.

GPL-TOX

Toxic Environmental Test

Physician:
Patient:
Accession #: 800604
Sex:
Age:
Collected:
Received:
Completed:

Toxic Compounds

Metabolite	Result mg/g creatinine	Percentile
Industrial Toxicants		
1) 2-Hydroxyisobutyric Acid (2HIB)	2,341	LLOQ 200.0 · 75th 5,521.6 · 95th 6,994.0

Parent: MTBE/ETBE
MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, and inhalation or skin exposure to gasoline or its vapors and exhaust fumes. MTBE has been demonstrated to cause hepatic, kidney, and central nervous system toxicity, peripheral neurotoxicity, and cancer in animals, and very high values have been reported in genetic disorders. Since the metabolites of these compounds are the same, ETBE may be similarly toxic.

2) Monoethylphthalate (MEP)	38	LLOQ 5.0 · 75th 150.0 · 95th 850.0

Parent: Diethylphthalates
Phthalates may be the most widespread group of toxins in our environment, commonly found in many bath and beauty products, cosmetics, perfumes, oral pharmaceuticals, insect repellants, adhesives, inks, and varnishes. Phthalates have been implicated in reproductive damage, depressed leukocyte function, and cancer. Phthalates have also been found to impede blood coagulation, lower testosterone, and alter sexual development in children. Low levels of phthalates can feminize the male brain of the fetus, while high levels can hyper-masculinize the developing male brain.

3) 2-3-4 Methylhippuric Acid (2,-3-,4-MHA)	150	LLOQ 10.0 · 75th 388.0 · 95th 1,216.0

Parent: Xylene
Xylenes (dimethylbenzenes) are found not only in common products such as paints, lacquers, pesticides, cleaning fluids, fuel and exhaust fumes, but also in perfumes and insect repellents. Xylenes are oxidized in the liver and bound to glycine before eliminated in urine. High exposures to xylene create an increase in oxidative stress, causing symptoms such as nausea, vomiting, dizziness, central nervous system depression, and death. Occupational exposure is often found in pathology laboratories where xylene is used for tissue processing.

4) Phenylglyoxilic Acid (PGO)	38	LLOQ 10.0 · 75th 255.0 · 95th 394.0

Parent: Styrene/Ethylbenzene
Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food-packaging materials. The ability of styrene monomer to leach from polystyrene packaging to food has been reported. Occupational exposure due to inhalation of large amounts of styrene adversely impacts the central nervous system, causes concentration problems, muscle weakness, fatigue, and nausea, and irritates the mucous membranes of the eyes, nose, and throat.

**LLOQ - Lower Limit of Quantitation*

Testing performed by The Great Plains Laboratory, Inc., Lenexa, Kansas. The Great Plains Laboratory has developed and determined the performance characteristics of this test. This test has not been evaluated by the U.S. FDA; the FDA does not currently regulate such testing.

1

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